Int. J. Cancer: **122,** 1357–1367 (2008)

Colorectal cancer screening: A comparison of 35 initiatives in 17 countries

Victoria S. Benson[1], Julietta Patnick[1,2], Anna K. Davies[3], Marion R. Nadel[4], Robert A. Smith[5] and Wendy S. Atkin[6*] on behalf of the International Colorectal Cancer Screening Network

[1]*Cancer Epidemiology Unit, University of Oxford, England, United Kingdom*
[2]*NHS Cancer Screening Programmes, Fulwood House, Sheffield, England, United Kingdom*
[3]*Department of Clinical Health Psychology, University College London, England, United Kingdom*
[4]*Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA*
[5]*Cancer Control Department, American Cancer Society, Atlanta, GA*
[6]*Cancer Research UK Colorectal Cancer Unit, St Mark's Hospital, NW London Hospitals Trust, Harrow, Middlesex, England, United Kingdom*

Although in its infancy, organized screening for colorectal cancer (CRC) in the general population is increasing at regional and national levels. Documenting and describing these initiatives is critical to identifying, sharing and promoting best practice in the delivery of CRC screening. Subsequently, the International Colorectal Cancer Screening Network (ICRCSN) was established in 2003 to promote best practice in the delivery of organized screening programs. The initial aim was to identify and document organized screening initiatives that commenced before May 2004. Each identified initiative was sent 1 questionnaire per screening modality: fecal occult blood test, flexible sigmoidoscopy or total colonoscopy. Information was collected on screening methodology, testing details and initiative status. In total, 35 organized initiatives were identified in 17 countries, including 10 routine population-based screening programs, 9 pilots and 16 research projects. Fecal occult blood tests were the most frequently used screening modality, and total colonoscopy was seldom used as a primary screening test. The eligible age for screening ranged from 40 years old to no upper limit; most initiatives included participants aged 50 to 64. Recruitment was usually done by a mailed invitation or during a visit to a family physician. In conclusion, this is the first investigation describing the delivery of CRC screening protocols to various populations. The work of the ICRCSN is enabling valuable information to be shared and a common nomenclature to be established.

Key words: colonoscopy; colorectal cancer screening; fecal occult blood test; flexible sigmoidoscopy; geographic variation

Worldwide each year, more than 940,000 new cases of colorectal cancer (CRC) are diagnosed and nearly 500,000 people die from the disease.[1] CRC is the third most common cancer in both men and women worldwide, and the second most common cancer in the industrialized world.[2]

Early detection of CRC has been shown to improve outcomes through the detection of early-stage cancers and precursor lesions.[3] Because early-stage disease frequently is asymptomatic, screening of the general population could decrease CRC incidence and mortality. There are 3 frequently used screening modalities: fecal occult blood test (FOBt), which reveals traces of blood in

Abbreviations: CoCaP, Colon Cancer Prevention Program; CRC, colorectal cancer; FIT, fecal immunochemical test; FOBt, fecal occult blood test; FS, flexible sigmoidoscopy; gFOBt, guaiac fecal occult blood test; ICRCSN, International Colorectal Cancer Screening Network; PLCO, Prostate, Lung, Colon and Ovarian; TC, total colonoscopy; VA, Veterans Affairs.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Grant sponsors: American Cancer Society, Centers for Disease Control and Prevention.

International Colorectal Cancer Screening Network members: *Principal Investigators*, W.S. Atkin, J. Patnick; *Expert working group*, W.S. Atkin, J. Patnick, A. Miles, S.M. Moss, D. Weller, R. Ancelle-Park, N. Segnan, C. Senore, R.C. Klabunde, R.A. Smith, M. Nadel; *Collaborators* (in alphabetical order of department or institution), Cancer Care Ontario, Toronto, ON, Canada: T. Sullivan; Cancer Control Department, American Cancer Society, Atlanta, GA, USA: R.A. Smith; Cancer Office, General Direction of Health, Ministry of Health, Paris, France: M. Chedru, H. Creusvaux; Cancer Epidemiology Unit, University of Oxford, England, UK: V.S. Benson, J. Green, J. Watson; Cancer Research UK Health Behaviour Unit, Department of Epidemiology and Public Health, University College London, England, UK: A. Miles; Cancer Screening Technology Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, Japan: H. Saito; Carmel Medicine Centre, Haifa, Israel: G. Rennert; Catalan Institute of Oncology, Barcelona, Spain: J. Espinas Pinol; Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA, USA: M.R. Nadel; Centro di Prevenzione Oncologica, Rome, Italy: M. Crespi, D Lisi; Center for the Study of Cancer, Florence, Italy: M. Zappa; CPO Piemonte, Turin, Italy: N. Segnan, C. Senore; Department of Clinical Health Psychology, University College London, England, UK: A.K. Davies; Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York: S.J. Winawer; Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, USA: A.G. Zauber; Department of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong: J Sung, B. Wong; Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD, USA: C. Klabunde; Division of Community Health Sciences, University of Edinburgh, Scotland, UK: D. Weller; Division of Gasteroenterology, Sunnybrook and Womens College Health, Toronto, ON, Canada: L. Rabeneck; Division of Gasteroenterology, Hepatology and Nutrition, University of Pittsburgh, Pittsburgh, PA, USA: R. Schoen; Flinders Medical Centre, Adelaide, Australia: G. Young; Finnish Cancer Registry, Helsinki, Finland: N. Malila; Institut de Veille Sanitaire, Saint Maurice, France: R. Ancelle-Park, H. Goulard; Institut Jules Bordet, Brussels, Belgium: A. Grivegnée; Institute for Studies in Gastroenterology, Prague, Czech Republic: M. Zavoral; Institute of Cancer Research, London, England, UK: S.M. Moss; Institute of Oncology, Warsaw, Poland: E. Butruk, J. Regula; Institute of Preventative Medicine, National Taiwan University, Taipei, Taiwan: T, Hsiu-His Chen; Istito Oncologico Veneto, Padova, Italy: M. Vettorazzi, M. Zorzi; Servizio di Gastroenterologia, Verona, Italy: A. Ederle, A. Fantin; Kaiser Permanente, Oakland, CA, USA: T.R. Levin; Kirurgisk Afdeling A, Odense Universitets Hospital, Odense K, Denmark: O. Kronborg; National Cancer Control Initiative, Carlton, Victoria, Australia: J. St. John; NHS Cancer Screening Programmes, Sheffield, England: J. Patnick; Population Screening Section, Australian Government Department of Health and Aging, Canberra, Australia: A. Koukari, M. Otuszewski; Veteran Affairs Medical Center, Portland, OR, USA: D. Lieberman; Quästor der GMS, Kantonsspitla Uri, Switzerland: U. Marbet; Registre des Cancers, Dijon, France: J. Faivre; Shin Kong Wu Hol Su Memorial Hospital, Taipei, Taiwan: K. Yang; The Cancer Registry of Norway, Montebello, Norway: G. Hoff; The Scarborough Hospital, Scarborough, ON, Canada: T.F. Shapero; UK Colorectal Cancer Unit, St Mark's Hospital, NW London Hospitals Trust, Harrow, Middlesex, England, UK: W.S. Atkin; University of Western Australia, Western Australia, Australia: J. Olynyk.

***Correspondence to:** Cancer Research UK Colorectal Cancer Unit, St Mark's Hospital, NW London Hospitals Trust, Harrow, Middlesex, England, UK HA1 3UJ. Fax: +44-20-8235-4277.
E-mail: wendy.atkin@cancer.org.uk

Received 20 August 2007; Accepted after revision 1 October 2007
DOI 10.1002/ijc.23273
Published online 21 November 2007 in Wiley InterScience (www.interscience.wiley.com).

stool samples (an early sign of CRC); flexible sigmoidoscopy (FS), which involves visual inspection of the distal bowel for polyps and cancers; and total colonoscopy (TC), which visualizes the entire bowel and therefore is a more invasive examination.

Biennial screening using a guaiac FOBt (gFOBt) was found to decrease mortality by ~15% after 13 years of follow-up in a large randomized trial in Funen, Denmark,[4,5] and by 13% after an 11-year follow-up in Nottingham, United Kingdom.[6,7] Neither study found a decrease in incidence, although follow-up continues. A more complex trial in Minnesota, USA, compared annual and biennial screening using FOBt.[8] After an 18-year follow-up, mortality decreased by 33% in participants screened annually, and 21% in those screened biennially.[9] Reductions in incidence of 20% and 17% were also observed for annually and biennially screened individuals, respectively.[10]

Four large-scale randomized clinical trials are evaluating FS as a screening tool. Baseline findings have been published showing that FS screening is safe (no major complications and relatively few perforations) and acceptable to the population.[11–15] A randomized clinical trial of FS screening in Telemark, Norway reported an 80% reduction in CRC incidence rates with a 13-year follow-up. The numbers in this study were small, however.[16]

Although TC detects adenomas beyond the reach of FS no randomized clinical trials have been conducted. However, the U.S. National Polyp Study reported a reduction in the incidence of CRC when comparing those who had a complete colonoscopy where all adenomas were removed, to 3 reference groups: patients with polyps $\geq$1 cm who declined to undergo surgery; patients who had all rectal adenomas removed; and the final cohort was a sample of the general population.[17]

A country's screening initiatives need to be adapted to suit its population size, health care system and methods of funding. However, it will be beneficial to collect and share implementation and performance data among countries. Information on the effectiveness of technologies and methodologies can benefit existing programs. It can also provide insights and guidance to those in the planning stages of screening initiatives. Additionally, comparing the effectiveness of different screening modalities within a country could inform decision-making about an appropriate national screening protocol specific to the needs of that country. To facilitate the sharing of such information and comparisons, it is important to have a common nomenclature and for initiatives to be collecting the appropriate data. However, because colorectal screening is in its infancy in most countries, a common language to describe the screening process and common measures by which quality can be examined for all tests and types of programs have yet to be established.

In June 2002, the International Union Against Cancer and the American Cancer Society sponsored an international workshop in Oslo, Norway, on facilitating screening for CRC.[18] From this meeting it was clear that a great deal of CRC screening activity was taking place worldwide, and that it would be beneficial to describe the activity and build a network to share experience and knowledge. Subsequently, the Centers for Disease Control and Prevention and the American Cancer Society supported a collaborative effort with Cancer Research UK to develop the International Colorectal Cancer Screening Network (ICRCSN).

The first aim of the ICRCSN was to identify and document the status of organized screening initiatives, and that information is reported in the present article. As a next step, the ICRCSN is focused on establishing a consensus minimum set of screening program descriptors and quality assurance measures with common definitions and measurement metrics to enable program evaluation and comparisons.

Methods

Known colorectal screening initiatives in progress (either screening or in follow-up after screening) as of May 2004 were contacted to assess their interest and potential for involvement in the ICRCSN. Initial approaches were made through personal knowledge of grant holders, conference contacts and literature and internet searches. Each contact was asked to identify other initiatives. The lead of each initiative was identified and a working group, composed of 11 members from 5 countries, was convened to develop the methodology and principles for the survey.

To be included in the Network, screening initiatives were required to meet a set of criteria. Initiatives were required to be carrying out screening of the general population, targeting asymptomatic people within a defined age range, and in an organized manner, as defined by the International Agency for Research on Cancer (IARC).[19] Characteristics of an organized screening program include an explicit policy with specified age categories, method and interval for screening; a defined target population; a management team responsible for implementation; a health care team for decisions and care; a quality assurance structure; and a method for identifying cancer occurrence in the target population. Initiatives were further classified as (*i*) programs in which screening is offered as part of routine health care; (*ii*) pilot studies carried out in a limited population for a limited time to assess feasibility, with a view to possibly extending to a program, or (*iii*) research projects with a fixed sample size and duration aimed at answering a specific question. If an initiative used more than 1 screening modality, then each modality (or combination of modalities offered to the same participant) was considered a separate activity.

Between November 2003 and March 2004, 2 questionnaires were designed to elicit information about screening initiatives in the countries and regions represented by members of the ICRCSN. The questionnaires were patterned after instrumentation developed by the International Breast Cancer Screening Network to characterize breast cancer screening activities among participating countries (http://appliedresearch.cancer.gov/ICSN/). The first questionnaire, the National Questionnaire, asked about a country's policies and guidelines on CRC screening, as well as for specific information about screening initiatives. The questionnaire included details of modality, target population and some information about protocol.

In addition to the National Questionnaire, modality-specific questionnaires were designed for FOBt, FS and TC. The questionnaires contained 6 sections: contact details for activity leads and other individuals involved in the activity, screening methodology, testing details, status of the initiative/activity, screening performance and outcomes and quality assurance.

Drafts were reviewed by a subgroup of the working group and pilot tested with a sample of initiative representatives of the ICRCSN. The finalized questionnaires were distributed in March 2004 via email to representatives from all known initiatives.

An international workshop for survey respondents was held in London in May 2004. Results of the survey were described and discussed. Areas requiring classification or confirmation were identified and refinements made. Unclear responses to the questionnaire were clarified by subsequent communications with the initiative leads.

Results

A total of 35 organized independent initiatives delivering CRC screening to asymptomatic populations were identified. These were then analyzed by geographic location, screening modality and type of initiative.

Geographical variation

The 35 organized initiatives were identified in 17 countries in 3 geographic regions (as defined by the World Health Organization, or by proximity where necessary): Europe ($n = 23$), the Americas ($n = 6$) and the Western Pacific ($n = 6$) (Table I). Initiatives were funded primarily by public funds, usually from central and local

TABLE I – A DESCRIPTION OF EACH INITIATIVE, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004

Country	Initiative type	Modality	Name of initiative	Region(s)	Target population	Age range	Target population in age range	Funding source	Year activity began	Total screening episodes before May 2004
EUROPE										
Belgium	Research	FS	Screening for CRC Using Sigmoidoscopy	All	HMO members	50–75	10,000	S	1993	1,912
Czech Republic	Program	FOBt	National Program of Screening for CRC	All	Population visiting FP	50+	3,700,000	CG, HI	2001	1,000,000
Denmark	Research	FOBt	Randomized Study of Screening for CRC with FOBt	Funen	Resident population	45–75	140,000	PC, CG	1985	128,703
France	Research	FOBt	Burgundy Study	Burgundy, Saône-et-Loire	Resident population	45–74	155,000	CG, HI	1988	45,642
	Pilot	FOBt	National Program for CRC	22 Départements	Resident population	50–74	4,500,000	CG, HI	2003	716,522[1]
Israel	Program	FOBt	CHS National CRC Screening Program	All	HMO members	50–74	700,000	HMO	1993	60,000
Italy	Research	FS	SCORE	Arezzo, Biella, Genova, Milan, Rimini, Turin	Volunteers	55–64	256,000	PC	1995	9,999
	Pilot	FOBt FS	SCORE 2	Biella, Florence, Milan, Rimini, Turin	Resident population	55–64	122,000	LG, PC	1999	5,120 9,525
	Program	FOBt	NHS Funded Regional Screening Program	Tuscany	Residential population of 7 local health units	50–70	969,000	LG	2000	259,227
	Program	FOBt	NHS Funded Regional Screening Program	Veneto	Resident population of 4 local health units	50–69	173,000	LG	2002	42,800
	Research	FOBt TC	Accademia Multidisciplinare Oncologia Digestiva (AMOD)	65 FP centers within 9 regions	FP patients	55–64	9,899[2]	PC	2002	732 236
	Program	FS	Un'occhiata ti salva la vita	Veneto	Residential population of 1 local health unit	60	5,000	LG	2003	1,600
	Research	FOBt FS TC	SCORE 3	Biella, Florence. Milan, Rimini, Turin, Verona	Resident population	55–64	122,000	LG, PC	2003	1,965 1,944 1,597
	Program	FOBt	NHS Funded Regional Screening Program (Prevenzione Serena)	Turin, Novara	Resident population	58	17,900	LG	2003	5,333
		FS		Turin	Resident population	59–69	125,000		2004	3,284
Norway	Research	FS only FS + FOBt	NORCCAP-1	Oslo, Telemark	Resident population	50–64	100,000	CG, PC	1999	6,695 6,266
Poland	Program	TC	Colonoscopic CRC Screening	All	FP patients	50–65	6,500,000	CG	2000	30,360
Spain	Pilot	FOBt	Catalan CRC Pilot Screening Programme	Catalonia, l'Hospitalet	Resident population	50–69	69,000	LG	2000	10,962
	Research	FOBt	Sigmoidoscopy Screening Research Project	Catalonia, Vilafranca del Penedès	Resident population	50–69	4,726	LG	2004	322
		FS					2,023			1,084
Switzerland	Research	FOBt	–	Glarus, Vallée du Joux, Uri	Resident population	50–80	20,000	O	2000	297
		FS								112
		TC								2,044
		FS + FOBt								278

TABLE I – A DESCRIPTION OF EACH INITIATIVE, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004 (CONTINUED)

Country	Initiative type	Modality	Name of initiative	Region(s)	Target population	Age range	Target population in age range	Funding source	Year activity began	Total screening episodes before May 2004
United Kingdom	Research	FOBt	The Nottingham CRC Screening Trial	Nottingham, England	FP patients	45–74	153,000[2]	CG	1981	134,128
	Research	FS	UK FS Screening Trial	14 areas in England, Scotland and Wales	FP patients	55–64	376,000	CG, PC	1996	40,674
	Pilot	FOBt	The UK Pilot of CRC Screening	England (3 areas) and NE Scotland (2 areas)	Resident population	50–69	476,000	CG	2000	260,000
	Research	FS	Nurses Led FS Screening Study	Harrow, North London	FP patients	60–64	500	PC	2003	150
THE AMERICAS										
Canada	Program	FS	Colon Cancer Detection Clinic	Ontario	FP patients	50+	500,000	HI	1999	1,865
	Pilot	FOBt	Ontario FOBT Pilot Study	Ontario	6 regions of FP patients, public health units	50–75	440,000	LG	2004	Not known
United States of America	Research	FS	PLCO Cancer Screening Trial	10 states	10 Clinical Centers	55–74	154,000	CG	1993	64,700
	Program	FS	CoCaP (Kaiser Permanente)	Northern California	HMO members	50+	500,000	CG, HMO, O	1994	350,000
	Pilot	FOBt	FOBt in Veterans Affairs	All	Veterans Affairs patients	50+	30,000	CG	2000	Not known
	Research	TC	National Colonoscopy Study (Phase I)	3 states	HMO members, wellness clinic, resident population	50–64	975,000	CG	2000	622
WESTERN PACIFIC										
Australia	Pilot	FS	FS for CRC in Average-Risk Subjects	Fremantle, WA	Resident suburban population	55–64	80,000	LG	1995	3,500
	Research	FOBt	Relative performance and acceptability of FOBt types	Adelaide, SA	Southern residential population	50+	100,000	CG, PC, O	1997	4,165
	Pilot	FOBt	The Australian Bowel Cancer Screening Pilot	Melbourne, Vic; Adelaide SA; MacKay, Qld	Resident population	55–74	57,000	LG, CG	2002	25,840
Hong Kong	Research	TC	Screening for CRC in Chinese	All	Resident population	50–70	480,000	PC	2000	510
Japan	Program	FOBt	National CRC Screening Program	All	National health insurance holders	40+	35,000,000	CG, S	1992	~6.4 million
Taiwan[3]	Pilot	FOBt	Keelung Community-based Integrated Screening	Kelung, Northern Taiwan	Resident population	50–79	81,000	LG	1999	22,716

CG, central government; FOBt, fecal occult blood test; FP, family practitioner; FS, flexible sigmoidoscopy; HI, health insurance; HMO, Health Maintenance Organization; LG, local government; O, other; PC, private/charity; S, self-funded; TC, total colonoscopy.

[1]The number of screening episodes at the end of 2004.–[2]Size of trial population.–[3]Not a country defined in the WHO regions, but is located in the Western Pacific.

TABLE IIa – A DESCRIPTION OF EACH ACTIVITY, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004. FOBT PROTOCOL

Country, region (initiative)	Type of initiative	Type of test	Brand name of test	Screening interval	Number of bowel movements sampled	Total samples	Routine dietary restriction
EUROPE							
Czech Republic (National study)	Program	G	Hemoccult	Biennial	3	3	Yes
Denmark, Funen	Research	G	Hemoccult II	Biennial	3	6	Yes
France (National pilot)	Pilot	G	Hemoccult	Biennial	3	6	No
France, Burgundy	Research	G	Hemoccult	Biennial	3	6	No
Israel (National study)	Program	G	Hemoccult SENSA	Annual	3	6	Yes
Italy (SCORE 2)	Pilot	I	RPHA immudia	Biennial	1	1	No
Italy, Tuscany	Program	I	Alpha Wasserman	Biennial	1	1	No
Italy (AMOD)	Research	G	Hemoccult SENSA II	Annual	3	6	Yes
Italy, Veneto	Program	I	Alpha Wasserman, Sentinel	Biennial	1	1	No
Italy (SCORE 3)	Research	I	RPHA immudia	Biennial	1	1	No
Italy (Prevenzione Serena)	Program	I	Alpha Wasserman	Biennial	1	1	No
Norway (NORCCAP-1)[1]	Research	I	FlexSure OBT	Once	3	3	No
Spain, Catalonia	Pilot	G	Hema Screen	Biennial	3	6	No
Spain, Catalonia	Research	G	Hema Screen	Biennial	3	6	No
Switzerland	Research	G	Hemoccult	Annual	3	3	No
Switzerland[1]	Research	G	Hemoccult	Annual	3	3	No
United Kingdom, Nottingham	Research	G	Hemoccult	Biennial	3	6	Yes
United Kingdom, England and Scotland	Pilot	G	Hema Screen	Biennial	3	6	No
THE AMERICAS							
Canada, Ontario	Pilot	G	Hemoccult II	Once	3	6	No
United States of America (Veterans Affairs)	Pilot	G	Hemoccult II	Annual	3	3	No
WESTERN PACIFIC							
Australia, Adelaide	Research	G, I	Hemoccult, InSure	Annual	3	3	Yes
			Inform		2	2	No
Australia (Pilot)	Pilot	I	Magstream HemS, Inform	Biennial	2	2	No
Japan	Program	I	Not specified	Annual	2	2	No
Taiwan[2]	Pilot	I	Eiken	Annual	1	1	No

G, guaiac; I, immunochemical.
[1]In combination with flexible sigmoidoscopy.–[2]Not a country defined in the WHO regions, but is located in the Western Pacific.

governments. Forty-six percent of the initiatives were funded only by government funds, and 31% were funded by the government and at least one other source. Initiatives were funded to a lesser extent by charities, health insurance and self-funding. A very small contribution came from industry or other private sources.

Modality analysis

We gathered information on 3 screening modalities: FOBt (Table IIa), FS (Table IIb) and TC (Table IIc). Seven initiatives used more than 1 modality or combination of modalities. Due to different protocols, each activity was described separately, which resulted in 45 activities overall.

Of the 45 activities, 22 were using FOBt only. In addition, 2 research projects, 1 in Norway and 1 in Switzerland, used FOBt in combination with FS. Fourteen were using a gFOBt only, 9 used a fecal immunochemical test (FIT) only and 1, an Australian research project, used both types. Fourteen of the FOBt activities used biennial screening, 8 screened annually, and 2 screened once only during the study period.

The age groups of the target populations varied widely. Although all FOBt activities included adults aged 59–64 years, some enrolled participants in their 40s. Some activities had no upper age limit, while others ended recruitment between ages 64 and 80. Dietary restriction was common for those using gFOBt, with counseling to remove vitamin C, red meats and nonsteroidal anti-inflammatory drugs from the diet prior to stool samples being taken. Every activity used colonoscopy for investigation after a positive FOBt result. The definition of a positive test varied. For example, some activities recorded a participant as positive if 1 or more test squares were positive on the FOBt card (pilot studies in particular). Other activities deemed a participant as positive if 5 or more squares on multiple cards were positive.

Fourteen of the initiatives were using FS only as their screening modality. In addition, 1 initiative in Norway and 1 in Switzerland used FS in combination with FOBt. Nine of these 16 activities were "once only" screening, although whether this was offered at a particular age (58 or 60 years old) or to an age range (50–64 years old) varied. Six of the activities offered screening every 5 years; one, the Colon Cancer Prevention Program (CoCaP) in Northern California, offered screening every 10 years. Many of the activities used a home-based enema administered by the patient as their bowel preparation, whereas Australia, Norway and Switzerland routinely used enemas in the screening unit. The CoCaP also used laxatives as part of its bowel preparation.

Nurses performed endoscopy in a program in Ontario, Canada and a research study in the United Kingdom. Nurses, gastroenterologists or primary care practitioners performed endoscopy in the U.S. Prostate, Lung, Colon and Ovarian (PLCO) cancer screening trial and the CoCaP program. Elsewhere, gastroenterologists and (to a lesser extent) surgeons performed the procedure.

Most activities had clear protocols for polyp removal and criteria for referral for a colonoscopy. In Australia (the pilot study), Belgium, Canada, Norway, Switzerland and the U.S. PLCO trial, polyps were not removed during FS and patients were referred for colonoscopy.

Six activities used colonoscopy as a screening technique; 3 on a once-only basis, 1 at 5-year intervals, and 2 at 10-year intervals. All colonoscopy activities offered screening to participants aged 55–64; however, the age at screening ranged from 50 to 80, depending on the activity. Colonoscopies were routinely conducted in the hospital, except in the Swiss research project (in which they also were carried out in a doctor's office) and in the

TABLE IIb – A DESCRIPTION OF EACH ACTIVITY, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004. FLEXIBLE SIGMOIDOSCOPY PROTOCOL

Country, region (initiative)	Type of initiative	Screening interval	Discipline of endoscopist	Where is screening conducted?	Bowel preparation	Bowel preparation location	Criteria for polyp removal at sigmoidoscopy	Criteria for colonoscopy
EUROPE								
Belgium	Research	Every 5 years	G	Hospital	Enema	Home	None removed	5+ adenomas, adenomas ≥ 10 mm, adenomas with >25% villous structure, high-grade dysplasia
Italy (SCORE)	Research	Once	G	Hospital	Enema	Home	Polyps ≤5 mm	Polyps >5 mm , high risk small polyps
Italy (SCORE 2)	Pilot	Once	G, S	Hospital	Enema	Home	Polyps <10 mm	3 adenomas <10 mm, polyps ≥10 mm, CRC, polyps with severe dysplasia or villous component <20%
Italy, Veneto	Program	Once	G	Hospital	Enema	Home	Polyps <6 mm	3 adenomas <10 mm, polyps ≥10 mm, CRC, polyps with severe dysplasia or villous component <20%
Italy (Prevenzione Serena)	Program	Once	G, S	Hospital	Enema	Home	Polyps <10 mm	3 adenomas <10 mm, polyps ≥10 mm, CRC, polyps with severe dysplasia or villous component <20%
Italy (SCORE 3)	Research	Once	G, S	Hospital	Enema	Home	Polyps <10 mm	3 adenomas <10 mm, polyps ≥10 mm, CRC, polyps with severe dysplasia or villous component <20%
Norway[1]	Research	Once	M	Hospital	Enema	Unit	None removed	Polyp >10 mm and any adenoma
Spain	Research	Once	G	Hospital	Enema	Home	Polyps <10 mm	3+ adenomas, polyps 10 mm, tubulovillous or villous histology, or severe dysplastic or neoplastic polyp
Switzerland	Research	Every 5 years	G	Hospital, office	Enema	Unit	None removed	Any polyp
Switzerland[1]	Research	Every 5 years	G	Hospital, office	Enema	Unit	None removed	Any polyp
United Kingdom (Nurse-led Study)	Research	Once	N	Hospital	Enema	Home	Polyps <10 mm	3+ adenomas, polyps >10 mm
United Kingdom (Flexisig trial)	Research	Once	G, S	Hospital	Enema	Home	Polyps <10 mm	3+ adenomas, 20+ hyperplastic polyps above the distal rectum, polyps ≥10 mm, tubulovillous or villous histology, severe dysplasia
THE AMERICAS								
Canada, Ontario	Program	Every 5 years	N	Hospital	Enema	Home	None removed	Any polyp
United States of America (PLCO)	Research	Every 5 years	G, N	Hospital, office	Enema	Home	None removed	As per FP
United States of America (CoCaP)	Program	Every 10 years	G, PCP, N	Hospital	Enema, laxative	Home	Polyps <5 mm	2+ tubulovillous adenomas (1 if family history), polyps >10 mm, with villous histology or high grade dysplasia
WESTERN PACIFIC								
Australia, Fremantle	Pilot	Every 5 years	G, S	Hospital	Enema	Unit	None removed	Adenomas, multiple hyperplastic polyps

G, gastroenterologist; M, medics: consultants and specially trained junior doctors; N, nurse; P, program; PCP, primary care practitioner; PS, pilot study; RP, research project; S, surgeon.
[1]In combination with fecal occult blood tests.

TABLE IIc – A DESCRIPTION OF EACH ACTIVITY, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004. TOTAL COLONOSCOPY PROTOCOL

Country, region (initiative)	Type of initiative	Screening interval	Discipline of endoscopist	Where is screening conducted?
EUROPE				
Italy (AMOD)	Research	Once	G	Hospital
Italy (SCORE 3)	Research	Once	G	Hospital
Poland	Program	Every 10 years	G, S	Hospital
Switzerland	Research	Every 10 years	G	Hospital, office[1]
THE AMERICAS				
United States of America (National Study)	Research	Once	G	Outpatient endoscopy unit
WESTERN PACIFIC				
Hong Kong	Research	Every 5 years	G	Hospital

G, gastroenterologist; S, surgeon.
[1]Office of the endoscopist.

U.S. National Colonoscopy Study (in which colonoscopies were performed in an outpatient endoscopy unit). In all studies, gastroenterologists performed the screening colonoscopy. In Poland, surgeons were also able to perform colonoscopy.

Initiative designs

Ten routine population screening programs were identified in 7 countries. Eight countries (9 initiatives) were running pilot studies, and research projects continued in 11 countries (16 initiatives). Italy was running a number of different local programs, rather than a single national program. Research projects coexisted in countries that were operating pilot projects or full programs.

Programs

Five of the identified programs offered FOBt only, 3 offered FS only, 1 offered TC only and 1 program in Italy (Prevenzione Serena) offered both FOBt and FS (Table IIIa). The most established programs were in Japan and Israel, as well as CoCaP in the United States. These programs began recruitment in 1992, 1993 and 1994, respectively. A variety of recruitment methods were used; a mailed invitation, usually personalized, was the most popular method where population registers were available. Other methods included referral by a family practitioner and the use of media. Practice varied as to whether the written results were sent to the patient, the patient's usual family physician, or both. All programs had mechanisms to follow up all positive FOBt or FS results, except for the Czech Republic and the CoCaP program. All programs had evaluation systems in place.

Pilot studies

Seven of the identified pilot projects offered FOBt, 1 offered FS and 1 in Italy (SCORE 2) offered both (Table IIIa). All 9 projects had some form of population register available, and systems in place for invitations and reminders (except for Canada, the U.S. Veterans Affairs (VA) pilot study and Taiwan). All studies had structured systems in place for evaluations, and 7 sent the results to both the patient and their usual doctor. The exceptions were Canada (only the patient's doctor received the results) and Taiwan (only the patient received the results). Canada, the U.S. VA pilot study and Taiwan had no mechanisms to follow up a positive test.

Research projects

Four of the identified research projects offered FOBt only, 5 offered FS only, 2 offered TC only and 5 offered a combination of 2 or 3 modalities (Table IIIa). Half of the population in the Norwegian study received FOBt screening in combination with FS. All except Hong Kong used some form of population register for recruitment. In addition, the majority of the initiatives had systems in place for evaluation, as well as routinely sending reminders to nonresponders. All projects reported normal and abnormal results to the patients. Eleven also reported normal results to physicians; 13 reported abnormal results to physicians.

Most of the projects were randomized controlled trials. Switzerland and Hong Kong described their studies as cohort studies; Belgium and the nurse-led study in the United Kingdom were described as feasibility studies (Table IIIb). It was in these initiatives that the greatest mix of protocols was found, with various combinations of modalities being used.

Discussion

The publication during the early and mid 1990s of trial and study results demonstrating the efficacy of screening for CRC had led, by the early years of the 21st century, to the implementation of a number of diverse screening initiatives in several countries of the world, in particular those with a high incidence of CRC. This is the first investigation describing the delivery of screening protocols to various populations.

Of the 17 countries identified by the ICRCSN that had begun organized CRC screening prior to May 2004, only 4 provided national programs. Three of these programs offered FOBt (Czech Republic, Israel and Japan) as their screening modality; one, Poland, offered TC. Six other programs (4 in Italy) were offered only at a regional level. In addition, there were 4 central government-funded pilot studies reported (France, United Kingdom, United States and Australia), most of which have subsequently progressed into national programs [France, United Kingdom (http://www.cancerscreening.nhs.uk/bowel/index.html) and the U.S. VA program]. Several of the other pilot studies had local government funding and may advance to regional programs in the future.

Fecal occult blood testing was the most frequently used screening modality, possibly because of the encouraging results in terms of acceptability, feasibility and efficacy from previous randomized clinical trials.[4,6,8] In 1999, FOBt was accepted by the European Union as the standard for CRC screening.[20] Several initiatives have used protocols based on those from the randomized clinical trials (for example, timing of screening, use of gFOBt, taking 2 samples from 3 consecutive bowel movements and dietary restriction). Some more recent FOBt initiatives have used FIT rather than gFOBt.

FS also was frequently used. Although large clinical trials of FS screening do exist (none are completed), they are more recent than those using FOBt, and there are fewer, if any, initiatives following trial protocols.[11,12,14,15] Bowel preparation for FS screening was fairly uniform, in that every participant had an enema that was typically self-administered at home. Screening typically occurred only once, but 5-year and 10-year intervals also were used. Referral for colonoscopy varied from any polyp being identified to criteria based on the number, size and histopathology of polyps found through FS.

TC was used in only 6 initiatives (1 program and 5 research projects), even though it is considered the "gold standard" for CRC identification. Gastroenterologists always performed TC, except in Poland where surgeons also performed the procedure. Colonoscopies were conducted in a hospital for all initiatives, as well as in the

TABLE IIIa – INITIATIVE DESIGNS, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004

Country, region (initiative)	Modality	Invitations and reminders				Structured system for evaluation	Written confirmation of normal and abnormal results	Mechanism to follow up positive test
		System[1]	Population register[2]	Method	Are reminders sent?			
PROGRAMS								
EUROPE								
Czech Republic	FOBt	No	None	Opportunistic: When visit FP, public campaign	No	Yes	Doctor	No
Israel	FOBt	Yes	HMO	Mailed invite and post card to order test kit	No	Yes	Doctor	Yes
Italy, Tuscany	FOBt	Yes	FPR, PR	Mailed personal invite and leaflet from FP, media	Yes	Yes	Patient	Yes
Italy, Veneto	FOBt	Yes	FPR, PR	Mailed personal invite and leaflet from FP, media	Yes	Yes	Doctor, Patient	Yes
Italy, Veneto	FS	Yes	FPR, PR	Mailed personal invite, leaflet and appointment date from FP, age dependent self-referral, media	Yes	Yes	Doctor, Patient	Yes
Italy (Prevenzione Serena)	FS	Yes	FPR, PR	Mailed personal invite, leaflet and prefixed appointment from FP, age dependent self-referral, media	Yes	Yes	Doctor, Patient	Yes
	FOBt			Mailed personal invite and leaflet from FP, media				
Poland	TC	No	None	Opportunistic: When visit FP, media	No	Yes	Patient	N/A
THE AMERICAS								
Canada	FS	No	None	Opportunistic: when visit FP	No	Yes	Doctor	Yes
United States of America (CoCaP)	FS	No	None	Opportunistic: when visit FP	No	Yes	Doctor, Patient	No
WESTERN PACIFIC								
Japan	FOBt	Yes	PR, IR	Opportunistic: news letter issued by local government	No	Yes	Patient	Yes
PILOT STUDIES								
EUROPE								
France	FOBt	Yes	IR	FP if visit FP, mailed invite otherwise	Yes	Yes	Doctor, Patient	Yes
Italy (SCORE 2)	FOBt	Yes	FPR, PR	Mailed personal invite from FP, leaflet and test kit mailed to 1st arm in 1st round	Yes	Yes	Doctor, Patient	Yes
	FS			Mailed personal invite from FP, leaflet, and prefixed appointment				
Spain	FOBt	Yes	FPR	Mailed invite and leaflet	Yes	Yes	Doctor, Patient	Yes
United Kingdom, England and Scotland	FOBt	Yes	LHA	Mailed invite, then test kit, media	Yes	Yes	Doctor, Patient	Yes
THE AMERICAS								
Canada	FOBt	Yes	FPR	Opportunistic: face-to-face, media	No	Yes	Doctor	No
United States of America (VA)	FOBt	Yes	VAR	FP receive annual computer prompt when patient is visiting	No	Yes	Doctor, Patient	No
WESTERN PACIFIC								
Australia, Fremantle	FS	Yes	ER	Mailed invite	Yes	Yes	Doctor, Patient	Yes
Australia (Pilot)	FOBt	Yes	IR	Mailed invite, booklet, questionnaire, consent form and test kit	Yes	Yes	Doctor, Patient	Yes
Taiwan[3]	FOBt	Yes	PR, PSR	Telephone invite	No	Yes	Patient	No

TABLE IIIa – INITIATIVE DESIGNS, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004 (CONTINUED)

Country, region (initiative)	Modality	Invitations and reminders				Structured system for evaluation	Written confirmation of normal and abnormal results	Mechanism to follow up positive test
		System[1]	Population register[2]	Method	Are reminders sent?			
RESEARCH PROJECTS								
EUROPE								
Belgium	FS	Yes	SCR	Opportunistic: when visit FP	Yes	Yes	Doctor, Patient	Yes
Denmark, Funen	FOBt	Yes	PR	Mailed invite and test kit	Yes	Yes	Doctor, Patient[4]	Yes
France, Burgundy	FOBt	Yes	IR	Mailed invite and leaflet	Yes	Yes	Doctor, Patient	Yes
Italy (SCORE)	FS	Yes	FPR	Mailed personal invite and prefixed appointment from FP	Yes	Yes	Doctor, Patient	Yes
Italy (AMOD)	FOBt	Yes	FPR	Personal mailed invite from FP	Yes	Yes	Doctor, Patient	No
	TC				(telephone)			N/A
Italy (SCORE 3)	FOBt	Yes	FPR, PR	Personal mailed invite from FP, media in 1 region	Yes	Yes	Doctor, Patient	Yes
	FS			Personal mailed invite and prefixed appointment from FP, media in 1 region				Yes
	TC			Personal mailed invite and prefixed appointment from FP, media in 1 region				N/A
Norway	FS only	Yes	PR	Mailed invite and appointment date	Yes	Yes	Patient	Yes
	FS + FOBt			Mailed invite, test, and appointment date				
Spain	FS, FOBt	Yes	FPR	Mailed invite and leaflet	Yes	Yes	Doctor, Patient	Yes
Switzerland	FOBt	Yes	PR	Mailed invite, public lectures, media	Yes	Yes	Patient	Yes
	FS				Yes			Yes
	TC				No			N/A
	FS + FOBt				Yes			Yes
Nottingham, United Kingdom	FOBt	Yes	FPR	Personal mailed test kit and invite from FP	No	Yes	Doctor, Patient	Yes
United Kingdom (Flexisig)	FS	Yes	FPR	Mailed invite with prefixed appointment	Yes	Yes	Doctor, Patient	Yes
United Kingdom (Nurse-led study)	FS	Yes	FPR	Mailed leaflet, followed by mailed invite, appointment given, enema posted	Yes	Yes	Doctor, Patient	Yes
THE AMERICAS								
United States of America (PLCO)	FS	Yes	ER	Mailed invite and leaflet, media	Yes	Yes	Doctor, Patient	Yes
United States of America (National TC Study)	TC	Yes	HMO, PR, SCR	Mailed invite, telephone, face-to-face	Yes	Yes	Doctor, Patient	N/A
WESTERN PACIFIC								
Australia, Adelaide	FOBt	Yes	ER	Mailed invite and test kit	Yes	Yes	Doctor, Patient[5]	Yes
Hong Kong	TC	No	None	Health Exhibition, volunteer	No	No	Doctor, Patient	N/A

ER, electoral roll; FOBt, fecal occult blood test; FP, family physician; FPR, family physician registry; FS, flexible sigmoidoscopy; HMO, Health Maintenance Organization; IR, insurance registry; LHA, local health authority; N/A, not applicable; PR, population registry (*e.g.* national registry); PSR, pap smear registry; SCR, screening clinic registry; TC, total colonoscopy; VAR, veteran affairs register.

[1]Is a structured information system used to manage invitations and reminders?–[2]A register that contains a list of possible participants, such as a population census.–[3]Not a country defined in the WHO regions, but is located in the Western Pacific.–[4]Doctor received only normal results.–[5]Doctor received only abnormal results.

TABLE IIIb – RESEARCH PROJECT STATUS, PRESENTED ALPHABETICALLY BY COUNTRY WITHIN REGIONS DEFINED BY THE WORLD HEALTH ORGANIZATION WHERE POSSIBLE, 2004

Country, region (initiative)	Modality	Nature of initiative	Recruitment complete prior to May 2004	Evaluation complete prior to May 2004	Research question
EUROPE					
Belgium	FS	F	No	No	Is left colonoscopy a good screening tool in a population attending general cancer screening visits?
Denmark, Funen	FOBt	RCT	Yes	Yes	Does Biennial screening by FOBt reduce mortality from CRC?
Burgundy, France	FOBt	RCT	Yes	Yes	To assess acceptability and efficiency of FOBt screening in reduction of mortality from CRC
Italy (SCORE)	FS	RCT	Yes	No	To assess the FS screened individuals to controls of usual care
Italy (AMOD)	FOBt, TC	RCT	No	No	To assess the rate of compliance to and relative efficacy of FOBt and TC in screening for CRC
Italy (SCORE 3)	FOBt, FS, TC	RCT	No	No	Comparisons of attendance, detection rates and acceptability of TC, FS and FOBt as primary screening tests for CRC
Norway	FOBt + FS	RCT	Yes	No	Comparison of effectiveness of once-only FS or FOBt and FS combined in detection of CR Neoplasm
Spain	FOBt, FS	RCT	Yes	Yes	Comparisons of acceptability of FS and FOBt
Switzerland	FOBt, FS, TC, FS + FOBt	C	Yes	No	Investigating preference, acceptance, compliance and quality of screening in a population based set-up
United Kingdom, Nottingham	FOBt	RCT	Yes	No	Does Biennial FOB screening reduce mortality from CRC?
United Kingdom (Flexisig)	FS	RCT	Yes	Yes	Is FS screening effective in reducing CRC incidence and mortality?
United Kingdom (Nurse-led study)	FS	F	No	No	To examine the feasibility and acceptability of a nurse-led screening FS service
THE AMERICAS					
United States of America (PLCO)	FS	RCT	Yes	Ongoing	Is FS screening effective in reducing CRC mortality?
United States of America (National TC Study)	TC	RCT	Yes	No	What is the feasibility of screening TC in a mixed gender, geographically representative population as measured by resource utilization, acceptance, outcome and facilitation of access to screening?
WESTERN PACIFIC					
Australia, Adelaide	FOBt	RCT	No	No	Comparison of Guaiac and FIT for screening for CRC, looking mainly at relative performance of different FOBt and behavioural issues
Hong Kong	TC	C	Yes	Yes	Assess the accuracy and safety of FOBt and FS, and compared against TC for screening of CR neoplasms in average-risk Chinese subjects older than 50 years

C, cohort; F, feasibility study; FOBt, fecal occult blood test; FS, flexible sigmoidoscopy; RCT, randomized clinical trial; TC, total colonoscopy.

office of the gastroenterologist in Switzerland and in an outpatient endoscopy unit in the United States. Once-only screening was most common, however, 5-year screening was conducted in Hong Kong, and 10-year screening in Poland and Switzerland.

At this stage there appears to be no preferred method of conducting CRC screening, defining a positive screening test for purposes of initiating follow-up, and for follow-up itself. Information was collected in the survey on screening performance and outcomes and quality assurance measures; however, because of the lack of standardized definitions, more information is required on these topics before conclusions can be drawn. Consequently, continued activity for the ICRCSN will concentrate on the development of quality assurance protocols and indicators to allow commonly understandable results to be reported across all participants in the Network.

Unfortunately, not all organized CRC screening initiatives in existence in 2003/2004 were included in this report. Some initiatives were not brought to the attention of the ICRCSN until after data collection. We will continue to include initiatives as they are identified.

In conclusion, the knowledge gained from programs, research projects and pilot studies can be shared and used in the advancement of CRC screening. The establishment of the ICRCSN has made the sharing of valuable information possible and has created a connection among initiatives across the world. It is the intention that preferred protocols will be established in the future, establishing uniform screening methodologies and guidelines that can be followed by future initiatives. The continued support of the Network's members will help both new and existing initiatives reach their full potentials.

References

1. World Health Organization. Global cancer rates could increase by 50% to 15 million by 2020. 2006. Available at: http://www.who.int/mediacentre/news/releases/2003/pr27/en/ (accessed 26th September 2007).
2. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74–108.
3. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence

for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:132–41.
4. Kronborg O, Fenger C, Olsen J, Jørgensen OD, Søndergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet 1996;348:1467–71.
5. Jorgensen OD, Kronborg O, Fenger C. A randomised study of screening for colorectal cancer using faecal occult blood testing: results after 13 years and seven biennial screening rounds. Gut 2002;50:29–32.
6. Hardcastle JD, Chamberlain JO, Robinson MHE, Moss SM, Amar SS, Balfour TW, James PD, Mangham CM. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet 1996;348:1472–7.
7. Scholefield JH, Moss S, Sufi F, Mangham CM, Hardcastle JD. Effect of faecal occult blood screening on mortality from colorectal cancer: results from a randomised controlled trial. Gut 2002;50:840–4.
8. Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, Ederer F. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med 1993;328:1365–71.
9. Mandel JS, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. J Natl Cancer Inst 1999;91:434–7.
10. Mandel JS, Church TR, Bond JH, Ederer F, Geisser MS, Mongin SJ, Snover DC, Schuman LM. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 2000;343:1603–7.
11. Atkin WS, Cook CF, Cuzick J, Edwards R, Northover JMA, Wardle J. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial. Lancet 2002;359:1291–300.
12. Weissfeld JL, Schoen RE, Pinsky PF, Bresalier RS, Church T, Yurgalevitch S, Austin JH, Prorok PC, Gohagan JK. Flexible sigmoidoscopy in the PLCO cancer screening trial: results from the baseline screening examination of a randomized trial. J Natl Cancer Inst 2005;97:989–97.
13. Prorok PC, Andriole GL, Bresalier RS, Buys SS, Chia D, Crawford ED, Fogel R, Gelmann EP, Gilbert F, Hasson MA, Hayes RB, Johnson CC, et al. Design of the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial. Controlled clinical trials 2000;21:273S–309S.
14. Gondal G, Grotmol T, Hofstad B, Bretthauer M, Eide TJ, Hoff G. The Norwegian Colorectal Cancer Prevention (NORCCAP) screening study: baseline findings and implementations for clinical work-up in age groups 50–64 years. Scand J Gastroenterol 2003;38:635–42.
15. Segnan N, Senore C, Andreoni B, Aste H, Bonelli L, Crosta C, Ferraris R, Gasperoni S, Penna A, Risio M, Rossini FP, Sciallero S, et al. Baseline findings of the Italian multicenter randomized controlled trial of "Once-Only Sigmoidoscopy"—SCORE. J Natl Cancer Inst 2002;94:1763–72.
16. Thiis-Evensen E, Hoff GS, Sauar J, Langman F, Majak BM, Vatn MH. Population-based surveillance by colonoscopy: effect of the incidence of colorectal cancer. Telemark Polyp Study 1. Scand J Gastroenterol 1999;34:414–20.
17. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, Waye JD, Shapiro M, Bond JH, Panish JF, Ackroyd F, Shike M, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993;329:1977–81.
18. Levin B, Smith RA. The global challenge of colorectal cancer. Reports from the UICC International Workshop on Facilitating Screening for Colorectal Cancer: An international agenda. Ann Oncol 2005;16:23.
19. International Agency for Research on Cancer. Use of breast cancer screening. In: International Agency for Research on Cancer, ed. IARC handbooks of cancer prevention: Breast cancer screening. Lyon, France: IARC Press, 2002. 47–86.
20. Advisory Committee on Cancer Prevention. Recommendations on cancer screening in the European Union. Eur J Cancer 1999;36:1473–8.