Efficacy, effectiveness, quality: sources of data

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screening kolorektálního karcinomu

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Key Questions

- What data have we available for CRC screening efficacy?
- How to monitor CRC screening quality (and why)?
- What data should be publicly reported?
- How should we use information we have?

Efficacy of CRC screening - FOBT

„Evidence exists concerning the efficacy of screening for breast cancer and colorectal cancer, derived from randomised trials, and for cervical cancer, derived from observational studies.“ (Council Recommendation)

Colorectal cancer screening with <u>FOBT</u>

Mandel *et al* (1993) – United States
- decrease in mortality by 33 %

Hardcastle *et al* (1996) – United Kingdom
- decrease in mortality by 15 %

Kronborg *et al* (2004) – Denmark
- decrease in mortality by 11 %,
  by **43% in persons participating in all 9 rounds**

Mandel *et al* (2000) – United States
- decrease in incidence by 20 %

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Hewitson *et al* (2008) – Cochrane systematic review

Review: Screening for colorectal cancer using the faecal occult blood test, Hemoccult (published update)
Comparison: 01 All Hemoccult Screening Groups Versus Control Groups
Outcome: 01 Colorectal cancer mortality (Fixed)

Study or sub-category	Screening n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 Randomised controlled trials					
Minnesota 1999	269/31157	177/15394		14.34	0.75 [0.62, 0.91]
Nottingham 2002	593/76466	684/76384		41.42	0.87 [0.78, 0.97]
Funen 2004	362/30967	431/30966		26.09	0.84 [0.73, 0.96]
Goteborg 2005	252/34144	300/34164		18.15	0.84 [0.71, 0.99]
Subtotal (95% CI)	172734	156908		100.00	0.84 [0.78, 0.90]
Total events: 1476 (Screening), 1592 (Control)					
Test for heterogeneity: Chi² = 1.65, df = 3 (*P* = 0.65), I² = 0%					
Test for overall effect: *Z* = 4.89 (*P* < 0.00001)					
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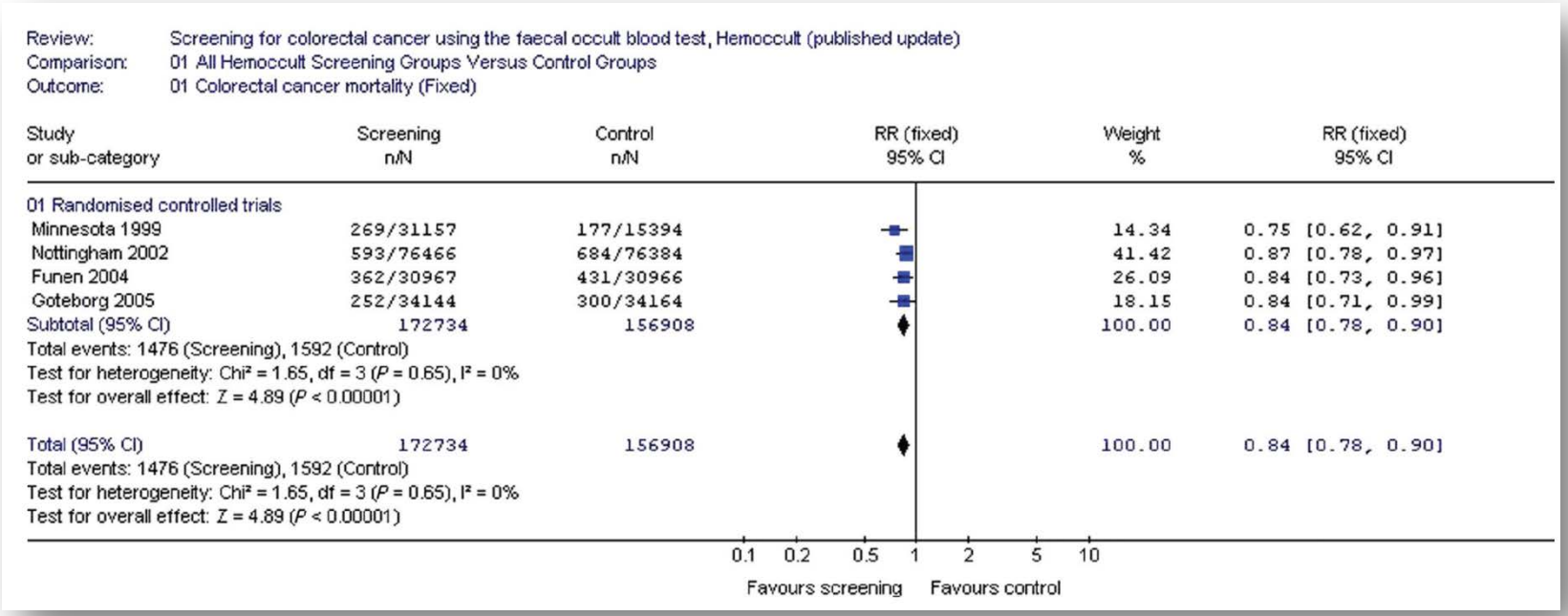

FOBT – modern tests are available now

More sensitive, adjustable positivity

Colonoscopy-controlled intra-individual comparisons to screen relevant neoplasia: faecal immunochemical test vs. guaiac-based faecal occult blood test

F. A. OORT*,[1], J. S. TERHAAR SIVE DROSTE*,[1], R. W. M. VAN DER HULST†, H. A. VAN HEUKELEM‡, R. J. L. F. LOFFELD§, I. C. E. WESDORP¶, R. L. J. VAN WANROOIJ*, L. DE BAAIJ*, E. R. MUTSAERS*, S. VAN DER REIJT*, V. M. H. COUPE**, J. BERKHOF**, A. A. BOUMAN††, G. A. MEIJER‡‡ & C. J. J. MULDER*

Cancer Epidemiology, Biomarkers & Prevention

Research Article

Higher Fecal Immunochemical Test Cutoff Levels: Lower Positivity Rates but Still Acceptable Detection Rates for Early-Stage Colorectal Cancers

Jochim S. Terhaar sive Droste[1], Frank A. Oort[1], René W.M. van der Hulst[2], Henk A. van Heukelem[3], Ruud J.L.F. Loffeld[4], Sietze T. van Turenhout[1], Ilhame Ben Larbi[1], Shannon L. Kanis[1], Maarten Neerincx[1], Mirre Räkers[1], Veerle M.H. Coupé[5], Anneke A. Bouman[6], Gerrit A. Meijer[7], and Chris J.J. Mulder[1]

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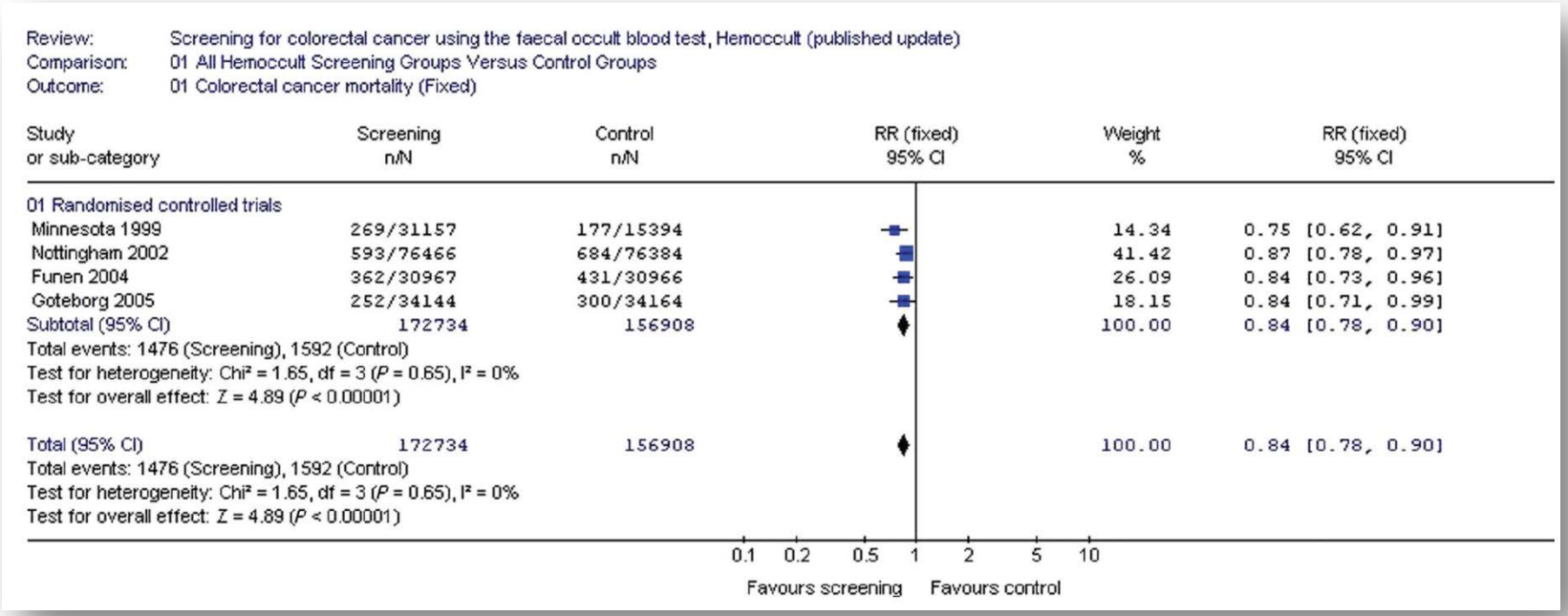


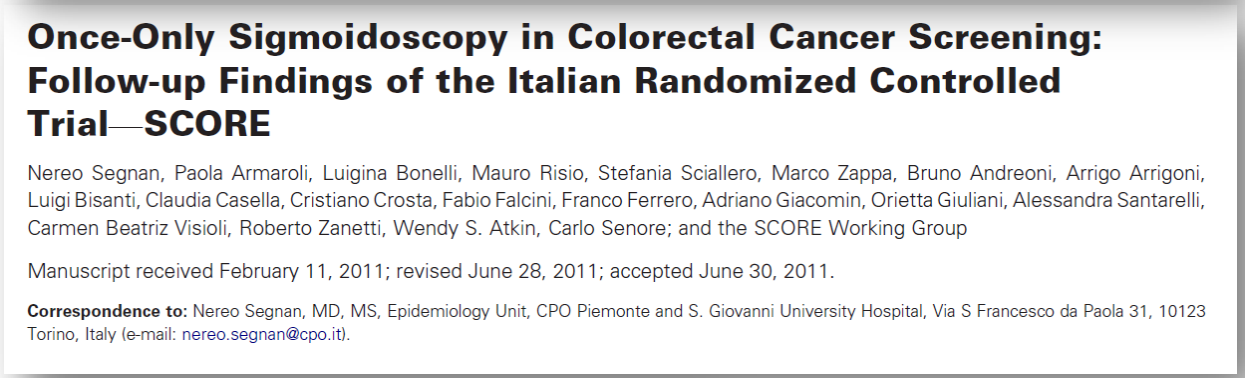
Efficacy of CRC screening – sigmoideoscopy (only once)

Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

Atkin *et al* (2010)

- decrease in mortality by 31%
- decrease in incidence by 33% (per protocol)



Once-Only Sigmoidoscopy in Colorectal Cancer Screening: Follow-up Findings of the Italian Randomized Controlled Trial—SCORE

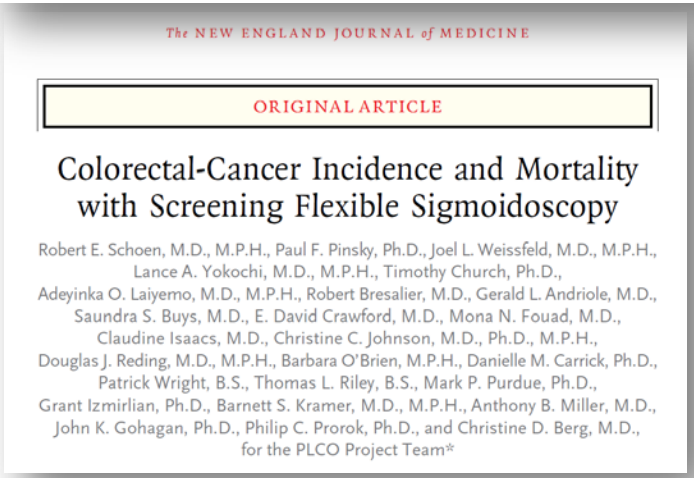
Nereo Segnan, Paola Armaroli, Luigina Bonelli, Mauro Risio, Stefania Sciallero, Marco Zappa, Bruno Andreoni, Arrigo Arrigoni, Luigi Bisanti, Claudia Casella, Cristiano Crosta, Fabio Falcini, Franco Ferrero, Adriano Giacomin, Orietta Giuliani, Alessandra Santarelli, Carmen Beatriz Visioli, Roberto Zanetti, Wendy S. Atkin, Carlo Senore; and the SCORE Working Group

Manuscript received February 11, 2011; revised June 28, 2011; accepted June 30, 2011.

Correspondence to: Nereo Segnan, MD, MS, Epidemiology Unit, CPO Piemonte and S. Giovanni University Hospital, Via S Francesco da Paola 31, 10123 Torino, Italy (e-mail: nereo.segnan@cpo.it).

Segnan *et al* (2011)

- decrease in mortality by 22% (nonsignificant)
- decrease in incidence by 18%



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Colorectal-Cancer Incidence and Mortality with Screening Flexible Sigmoidoscopy

Robert E. Schoen, M.D., M.P.H., Paul F. Pinsky, Ph.D., Joel L. Weissfeld, M.D., M.P.H., Lance A. Yokochi, M.D., M.P.H., Timothy Church, Ph.D., Adeyinka O. Laiyemo, M.D., M.P.H., Robert Bresalier, M.D., Gerald L. Andriole, M.D., Saundra S. Buys, M.D., E. David Crawford, M.D., Mona N. Fouad, M.D., Claudine Isaacs, M.D., Christine C. Johnson, M.D., Ph.D., M.P.H., Douglas J. Reding, M.D., M.P.H., Barbara O'Brien, M.P.H., Danielle M. Carrick, Ph.D., Patrick Wright, B.S., Thomas L. Riley, B.S., Mark P. Purdue, Ph.D., Grant Izmirlian, Ph.D., Barnett S. Kramer, M.D., M.P.H., Anthony B. Miller, M.D., John K. Gohagan, Ph.D., Philip C. Prorok, Ph.D., and Christine D. Berg, M.D., for the PLCO Project Team*

Schoen *et al* (2012) (repeated)

- decrease in mortality by 26%
- decrease in incidence by 21%

Efficacy of CRC screening - colonoscopy

Limited (observational studies) but promising evidence

Winawer *et al* (1993) – United States
- decrease in incidence by 76-90 %

Kahi *et al* (2009) – United States
- decrease in incidence by 67 %, decrease in mortality by 65 %

Brenner *et al* (2010) – Germany
- decrease in advanced neoplasia rate by 48 %

and more...

EDITORIAL | Annals of Internal Medicine

How Much Does Colonoscopy Reduce Colon Cancer Mortality?

Ransohoff (2009): We need direct evidence from randomised clinical trials

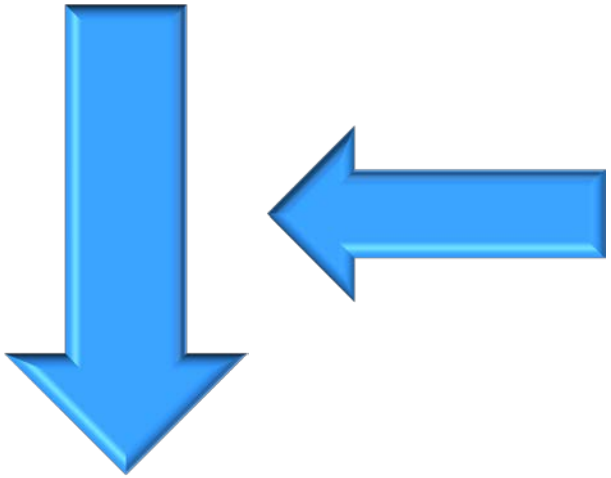
Efficacy of CRC screening - colonoscopy

Bretthauer (2011): it will take some more time

Two large-scale randomized trials investigating colonoscopy for screening are currently in progress. In the Spanish trial, 55 000 individuals between 50 and 69 years of age are being randomly assigned to either iFOBT or colonoscopy screening [44]. The trial started to recruit in 2008, screening is currently in progress at eight centres in Spain, and the final results are expected in 2021 after 10 years of follow-up. The Nordic–European Initiative on Colorectal Cancer (NordICC) is a multicentre, multinational randomisied trial, in which 66 000 individuals are randomly assigned to either colonoscopy or no screening. Screening started in 2009, and a 15-year follow-up period after screening is planned, with an interim analysis after 10 years due around 2022 [45]. Further, a randomized trial in the USA comparing FOBT and colonoscopy screening is currently in the planning stage (personal communication, Jason Dominitz and Doug Robertson, October 2010).

Why to monitor screening?

Efficacy
(in trials)



QUALITY

Effectiveness
(in real life)

How to ensure quality – organised screening

- **Screening for cancer of breast, colorectum and uterine cervix is effective in decreasing mortality of the disease**
- **These programmes are recommended to all member states by the Council of the European Union (2003/878/EC)**
- **To guarantee their effectiveness, safety and cost-effectiveness, it is highly recommended to implement the prevention as organized programmes comprising:**
  - **an explicit policy, with specified age categories, method and interval of screening**
  - **defined target population**
  - **a management team responsible for the implementation**
  - **a health care team for decisions and care**
  - **a quality assurance structure (performance monitoring including collection of all relevant data)**
  - **a method for identifying cancer occurrence in the target population**

IARC Handbooks of Cancer Prevention

Sources of data for colorectal cancer screening information support

Monitoring of Cancer Burden

- epidemiology of cancer in target population
- evaluation of screening programmes impact

Source of data: CZECH NATIONAL CANCER REGISTRY
13 regional data collection points / 57 district points
annual no. of records: 8,236 colorectal cancer cases in 2008

Performance Monitoring of Health Care Facilites

- performance indicators at screening centres
- detection of cancer and precancerous lesions

Source of data: RECOMMENDED HEALTH CARE FACILITIES
160 centres (summer 2011)
annual no. of records: 22,227 preventive colonoscopies in 2010

Monitoring using Administrative Data

- population-based performance indicators
- monitoring of programmes accessibility by target population
- assessment of programmes cost-effectiveness

Source of data: HEALTH INSURANCE COMPANIES – NATIONAL REFERENCE CENTRE
8 health insurance companies / 4,400 general practitioner offices, 1,200 gynaecologist offices
annual no. of records: 521,000 FOBTs performed in 2010

Information Support Provider
MASARYK UNIVERSITY, INSTITUTE OF BIOSTATISTICS AND ANALYSES

Peformance indicators in screening programmes

- EARLY PERFORMANCE INDICATORS
  - relating to target population
    - coverage by examination, positivity → PAYERS – NATIONAL REFERENCE CENTRE
  - relating to screening centres
    - detection rates, complication rates, stage of cancers, PPVs, time intervals → SCREENING REGISTRY
- LONG-TERM IMPACT INDICATORS
  - relating to screening outcomes → CZECH NATIONAL CANCER REGISTRY
    - mortality, incidence rates

→ definite indicator of success

- decrease in mortality is inevitably long-term and difficult to measure

→ MONITORING OF SCREENING PROGRAMMES REQUIRE EARLY PERFORMANCE INDICATORS

Should these things be 100% publicly available?

Table 3: Surgeon Observed, Expected, and Risk-Adjusted Mortality Rates (RAMR) for Coronary Artery Bypass Grafts in New York State, 1996-1998 Discharges

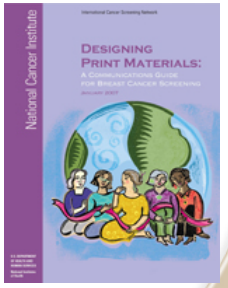
	Cases	No. of Deaths	OMR	EMR	RAMR	95% CI for RAMR
Albany Medical Center Hospital						
##Banker M	7	1	14.29	2.07	15.69	(0.21, 87.29)
Britton L	413	4	0.97	1.52	1.45	(0.39, 3.72)
Canavan T	519	2	0.39	1.50	0.58 **	(0.07, 2.11)
Foster E	239	3	1.26	1.86	1.53	(0.31, 4.48)
#Joyce F	122	2	1.64	1.24	2.99	(0.34, 10.81)
Kelley J	593	18	3.04	1.71	4.04 *	(2.39, 6.38)
Luber J	329	8	2.43	1.91	2.89	(1.24, 5.69)
Miller S	460	3	0.65	2.03	0.73 **	(0.15, 2.14)
#Sardella G	158	0	0.00	1.25	0.00	(0.00, 4.21)
All Others	105	2	1.90	1.72	2.52	(0.28, 9.08)
TOTAL	2945	43	1.46	1.69	1.97	(1.42, 2.65)
Arnot Ogden Memorial Hospital						
Quintos E	266	13	4.89	1.98	5.61 *	(2.98, 9.59)
Vaughan J	89	2	2.25	2.05	2.49	(0.28, 9.01)
All Others	14	0	0.00	1.36	0.00	(0.00, 43.66)
TOTAL	369	15	4.07	1.97	4.68 *	(2.62, 7.72)

By hospital/physician?

How to communicate benefits and risks?

Using an informed decision making approach in developing communication materials for screening promotes:

- **An understanding of the disease and one's risk of getting the disease;**
- **An understanding of information about the screening test, including risks and benefits of the test, uncertainties and limitations, alternatives to the test, and follow-up clinical services;**
- **An understanding of one's personal preferences and values and how to apply them to the screening decision; and**
- **Participation in decision making at the level desired by the person making the decision.**

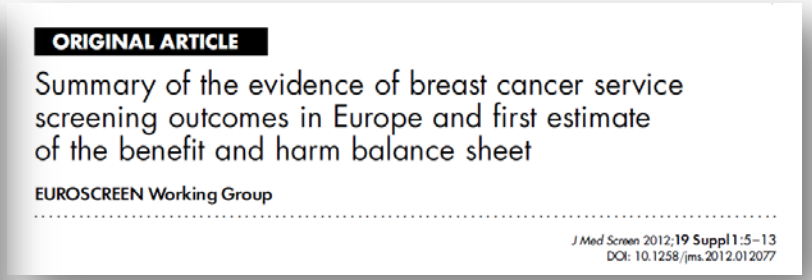


Could it be scarry messages?
example of breast screening

Table 4 Balance sheet for 1000 women aged 50–51 years, screened biennially until 69 years (according to the EU policy on cancer screening[3]) and followed until 79 years

Outcome	For every 1000 women screened for 20 years:	The number of women that need to be screened:
Number of breast cancer cases diagnosed	71	14 women: to diagnose 1 case
BC mortality reduction	7–9 women's lives are saved (out of 30 BC deaths expected)*	111–143 women: to save 1 life
Over-diagnosis	4 cases are over-diagnosed (in addition to 67 BC expected)	250 women: to over-diagnose 1 case
False-positive test results among women without breast cancer	200 women recalled for further assessment procedures: 170 women with non-invasive assessment only 30 women with invasive assessment	6 women: to have 1 with at least one who has non-invasive assessment only 33 women: to have 1 with at least one invasive assessment

BC, breast cancer; EU, European Union
*19 out of the 30 expected BC death were diagnosed in ages 50–69



ORIGINAL ARTICLE

Summary of the evidence of breast cancer service screening outcomes in Europe and first estimate of the benefit and harm balance sheet

EUROSCREEN Working Group

J Med Screen 2012;19 Suppl 1:5–13
DOI: 10.1258/jms.2012.012077

Can it negatively affect participation?

Or even more scarry messages?

Benefits

A colonoscopy is the most accurate way to find and remove small polyps and get a biopsy. If you do not have a colonoscopy, polyps or cancer may not be identified until a more advanced stage.[4,5]

Risks

Your doctor will do everything possible to decrease risks, but colonoscopy and sigmoidoscopy, like all procedures, have risks.

The Risk	What Happens	Keeping You Informed
Perforation	Perforation (hole that passes through the entire wall of the colon) is reported in 0 to 2 per 1,000 procedures. The risk can increase for therapeutic procedures. Pressure from the scope, a tear when air is inserted, and polyp removal can cause perforation.[6-12]	Management of perforation depends on the size, whether it's noticed immediately or later, and how you are feeling overall. A large perforation noticed immediately requires surgery. A perforation noticed several days later is treated by rest, intravenous fluids, antibiotics, and close observation. It may also require an operation. Call your doctor if you have fever, abdominal tenderness, or shortness of breath.[3]
Bleeding	Bleeding is reported in 0 to 4 per 1,000 procedures. The risk is greater with large polyp removal.[6-9]	A trace of blood is normal. If there is over 4 tablespoons of bleeding, call your doctor immediately. You will be watched carefully and may be given blood. Surgery is rarely necessary.
Cardiorespiratory	Complications during the procedure can include irregular heart beat (1 per 1,000), low heart rate (8 per 1,000), low blood pressure (12 per 1,000), low oxygen levels (56 per 1,000), and heart attacks and stroke (fewer than 1 per 1,000).[6-9]	Cardiorespiratory complications are usually related to medicine given to keep you comfortable during the procedure. Your doctor will monitor your heart rate, breathing, and oxygen levels. Oxygen and intravenous fluids will be given if needed.
Death	No deaths are reported for screening or therapeutic colonoscopy since 2000.[6-11]	There is a small risk of death (1 per 10,000) with a therapeutic colonoscopy (a colonoscopy for treatment of disease or bleeding).[6-12]

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Colonoscopy

Colonoscopy is a procedure to look at the inner lining of your large intestine (colon).

Can it negatively affect participation?

Summary

Notes:

- **There is convincing evidence that colorectal cancer screening with different screening tests can decrease mortality or incidence from colorectal cancer. It is possible to provide screening with favourable balance of benefits and risks.**
- **Quality should be thoroughly monitored to ensure that this balance really holds in real practice.**

More questions

- **Should information be acquired during monitoring made publicly available (what)?**
- **How should be information about benefits and risks delivered to support informed decision making (but also to improve participation – is that what we want?)**