Evidence on CANCER SCREENING

in the ECAC

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12. Take part in organised cancer screening programmes:

- Bowel cancer (men and women)
- Breast cancer (women)
- Cervical cancer (women)

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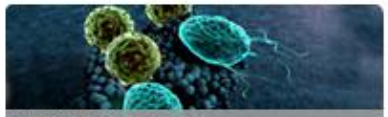
Print the Code



Find out more about the 12 recommendations:

- TOBACCO
- SUN/UV EXPOSURE
- SECOND-HAND SMOKE
- POLLUTANTS
- HEALTHY BODY WEIGHT
- RADIATION
- PHYSICAL ACTIVITY
- BREASTFEEDING
- HORMONAL THERAPY
- DIET
- VACCINATION AND INFECTIONS
- ALCOHOL
- SCREENING

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Screening

Take part in organized cancer screening programmes for:

- **Bowel cancer (men and women)**
- **Breast cancer (women)**
- **Cervical cancer (women).**

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Some types of cancer can be found and treated before they cause symptoms. Checking for cancer, or for conditions that may lead to cancer, in people who have no symptoms is called screening. The main aim of cancer screening is to prevent death from cancer. Screening can also make it possible to use less severe treatment methods if the cancer is detected early enough. For some cancers, such as cervical cancer and bowel cancer, screening can actually prevent the cancer from developing.

In the European Union, screening is recommended for bowel, breast, and cervical cancer when offered as part of an organized programme with adequate resources for high quality. Organized breast cancer screening programmes are currently established in most European Union countries, and organized bowel cancer and cervical cancer screening programmes are available in many (More information about organized programmes).

Comprehensive guidelines covering all aspects of bowel, breast and cervical cancer screening have been developed by experts and published by the European Commission. These European Guidelines provide guiding principles and detailed protocols, standards and recommendation that, if followed, ensure that screening services of high quality are provided to the population (More information about quality in cancer screening).

If you would like to participate in cancer screening but are unsure whether a programme exists in your country, contact the department of health.

Screening definition

Organized screening in the European Union

Link to the European Guidelines

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CANCER SCREENING: KEY POINTS

BOWEL CANCER SCREENING

BREAST CANCER SCREENING

CERVICAL CANCER SCREENING

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Key points about cancer screening

7

- What is an "organized" screening programme?
- Why is quality important in cancer screening?
- Why is screening recommended only for certain types of cancer?
- Why is prostate cancer screening not recommended?
- Should I wait for an invitation to participate in screening?
- I have received an invitation to participate in screening; can I refuse?
- Can screening cause cancer?

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Breast cancer screening

8

- What is breast cancer?
- What is breast cancer screening?
- When should I participate in breast cancer screening?
- My last screening test result was normal; why should I undergo screening again?
- What is the chance of a breast cancer not being found at screening?
- Can I develop breast cancer after a screening examination with a normal result?
- What will happen if I have an abnormal mammography result?
- Is there any harm or other risk from breast cancer screening using mammography?

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Bowel cancer screening

9

- What is bowel cancer?
- What is bowel cancer screening?
- When should I participate in bowel cancer screening?
- Is it better to use the guaiac faecal occult blood test (FOBT) or faecal immunochemical test (FIT)?
- My last screening test result was normal; why should I undergo screening again?
- What is the chance of a bowel cancer not being found at screening?
- Can I develop bowel cancer after a screening examination with a normal result?
- What will happen if I have an abnormal screening result?
- Is there any harm or other risk from bowel cancer screening?

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Cervical cancer screening

9

- What is cervical cancer?
- What is cervical cancer screening?
- When should I participate in cervical cancer screening?
- My last screening test result was normal; why should I undergo screening again?
- What is the chance of a cervical cancer not being found at screening?
- Can I develop cervical cancer after a negative screening examination?
- What will happen if I have an abnormal screening result?
- I have been vaccinated against human papillomavirus (HPV); should I still participate in cervical cancer screening?
- Is there any harm or other risk from cervical cancer screening?

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The evidence was retrieved initially from the IARC Handbooks of Cancer Prevention and the European Guidelines for Quality Assurance in Cancer Screening published between 2003 and January 2013

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A systematic update of the evidence on impact on mortality/incidence, age, interval and optimal test, further benefits and harms was performed using systematic literature searches based on 38 clinical PICOS-based questions

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Scientific Justification

The European Code Against Cancer and the answers to the Questions and Answers were developed based on scientific evidence. You can find below the different manuscripts that explain this evidence.

- 12 ways (PDF)
- Methodology (PDF)
- Tobacco (PDF)
- Obesity and Body Fatness (PDF)
- Physical Activity (PDF)
- Diet (PDF)
- Alcohol (PDF)*
- UV (PDF)
- Environment and Occupation (PDF)
- Radiation (PDF)
- Breastfeeding (PDF)
- Hormonal Therapy (PDF)
- Infections and vaccination (PDF)
- Screening (PDF)

* The article "European Code against Cancer 4th Edition: Alcohol drinking and cancer" was replaced with a new version on 23 November 2016. Reasons specified in the Corrigendum (PDF)

Cancer Epidemiology 39S (2015) S139–S152

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

European Code against Cancer, 4th Edition: Cancer screening☆

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What is an “organized” screening programme?

- Organized screening programmes are designed and managed by national or regional health services to ensure that everyone has an equal opportunity to participate in screening and to ensure that if a screening test result is abnormal, the patient receives the correct further testing, support, and treatment. Screening is most effective if it is available to all people in the eligible population and if they choose to participate.

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What is an “organized” screening programme?

- Organized screening programmes are recommended in the European Union because they employ a team of people responsible for ensuring the quality of the services provided. That includes checking that guidelines are followed and that the results of the screening programme are regularly reported and evaluated.

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Organized screening programs

are preferable because they provide better conditions to ensure that the Guidelines for Quality Assurance in Screening are followed in order to achieve the greatest benefit with the least harm.

Screening is recommended only for those cancers where a demonstrated life- saving effect substantially outweighs the potential harm

EU citizens are recommended to participate each time an invitation from the national or regional screening program is received and after having read the information provided and carefully considered the potential benefits and harms of screening

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For each screening programme are reported

- screening primary test
- age
- interval between screening tests

Cervical cancer screening

Either cytology (Pap) testing or human papillomavirus (HPV).

If cytology is used for screening, women starting at age 25–30 years and from then on, every 3 or 5 years.

If HPV testing is used for screening, women starting at age 35 years (usually not before age 30 years) and from then on, every 5 years.

Irrespective of the test used, women continue participating in screening until the age of 60 or 65 years, and continue beyond this age unless the most recent test results are normal

Cervical cancer screening EFFECTIVENESS

Is screening for cervical cancer effective in reducing cervical cancer incidence and mortality?

Evidence of effectiveness of **conventional cytology** testing with Papanicolaou staining is derived from **observational studies**

Significant reduction in incidence of invasive cancer from cytology testing observed in **cohort studies** ranged from **80% to 30%**

Pooled analysis from **case–control studies** showed a **significant reduction in incidence** of **66%** (OR, 0.34, 95%CI: 0.31–0.38)

The **impact** of the reduction was **greater** in countries that conducted **organized screening** than in countries that did not

Cervical cancer screening EFFECTIVENESS

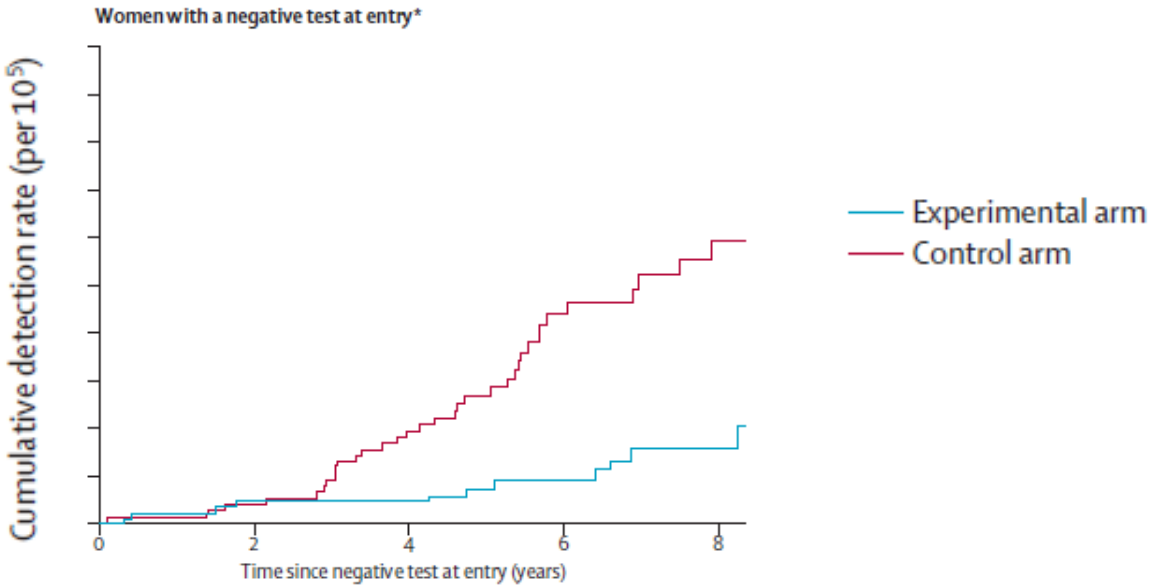
Is screening for cervical cancer effective in reducing cervical cancer incidence and mortality?

A **pooled analysis** of follow-up data from **four RCTs** conducted in Sweden (Swedescreen), the Netherlands (POBAS-CAM), England (ARTISTIC), and Italy (NTCC) has demonstrated that, compared to cytology, **HPV-based screening** provides **60–70% greater protection** against invasive cervical carcinomas

Cervical cancer screening EFFECTIVENESS

Is screening for cervical cancer effective in reducing cervical cancer incidence and mortality?

The respective **pooled cumulative detection rate ratio** for invasive cervical carcinoma among women **with a negative screening test** at entry was **0.30** (95%CI 0.15–0.60)



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Cervical cancer screening EFFECTIVENESS

Is screening for cervical cancer effective in reducing cervical cancer incidence and mortality?

RCTs used ***different strategies*** for **managing HPV-positive women** (by cytology triage or direct referral to colposcopy), and **for primary screening** using primary HPV testing alone, or in combination with cytology.

The biopsy rate was **doubled** (rate ratio 2.24; 95%CI: 2.09– 2.39) in the NTCC trial, where all HPV-positive women were **directly referred for colposcopy**, while it was **not increased** in studies using cytological **triage** (POBASCAM, Swedescreen, ARTISTIC)

Co-testing of all women with both HPV and cytology compared with primary HPV testing alone led to increased unnecessary colposcopy

As the efficacy results were similar, the data support **primary HPV screening with triaging by cytology before referral**

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Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Age to begin

Evidence based on cohort and case–control studies shows that **HPV infections** and cytological abnormalities among women **younger than 25 years** are **common and transient**, whereas cervical intraepithelial neoplasia of grade 3 or worse **(CIN3+)** is much **less common** in this group than in women aged 25 years and older.

Cytology screening in women **younger than 25 years** has lower detection rates, higher false-positive rates, and **lower effectiveness** than in older women

Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Age to begin

HPV testing is **more sensitive** in detecting CIN2+ than cytology (96.1% versus 53.0%) but **less specific** (90.7% versus 96.3%).

The specificity of both tests increased with age, but **loss in specificity** with HPV testing versus cytology is very **large at young ages**

Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Age to begin

In pooled data from four RCTs considering age at enrolment, the **greatest protective effect** (rate ratio 0.36, 95%CI: 0.14–0.94) was noted in women aged **30–34 years**.

However, the efficacy of HPV testing did not differ significantly between women aged 30–34 years and those 35 years and older (P = 0.13).

These results suggest **a gain in efficacy** with **HPV testing, starting at age 30 years**

Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Age to stop

In an **HPV-negative woman**, the **risk of acquiring a new infection** and the **long time needed for progression** from infection to invasive cancer should be taken into account.

In Europe the **prevalence of infection** by oncogenic HPV types strongly **decreases with age up to about age 45**; it remains fairly **constant after that age**, and little is known about the age-specific occurrence of new infections.

Also, **no CIN3** was detected during the second round of screening among women aged **50–60 years** in the **HPV group**, and five cases of CIN3 were detected in the cytology group

These issues suggest a **longer protection** of HPV screening at **older ages** and an **earlier age at which to stop screening** than with cytology screening

Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Interval

Evidence of reduced risk of cervical cancer after a negative Pap smear result was reported in several studies

In the IARC multicentre study, the **reduction in cumulative incidence** of invasive squamous-cell carcinomas of the cervix uteri was reported at

93% when screening every year,

91% when screening every 3 years,

84% when screening every 5 years

Estimation of the relative risk of carcinoma of the cervix uteri in the Netherlands following a negative screening result, compared with the risk in the absence of screening indicates that almost **as much benefit** is expected **from 3-yearly screening as from annual rescreening among women aged 35–64 years.**

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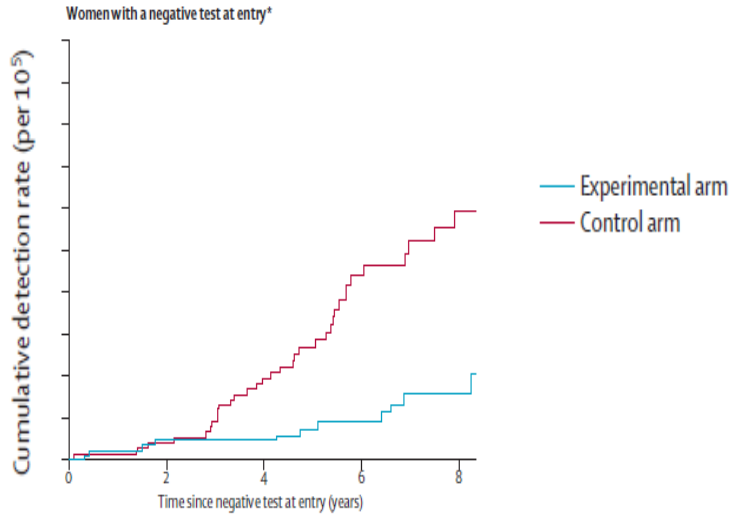
Cervical cancer screening Age range and interval

What is the optimal age range in which to perform cervical cancer screening, and what is the best time interval?

Interval

According to pooled data from the 4 RCTs, comparing HPV-based screening with cytology-based cervical screening, the **cumulative incidence** of invasive carcinoma in women with negative entry tests was **lower 5.5 years after a negative HPV test than 3.5 years after a negative cytology** result, indicating that **5-year intervals for HPV screening are safer than 3-year intervals for cytology**



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Cervical cancer screening HARMS

What is the risk of overdiagnosis in the cervical cancer screening process?

CIN is a pre-invasive lesion, and **1 out of every 4-7 progress** to an invasive lesion if not treated. It could be concluded that diagnoses of non-progressive lesions are cases of overdiagnosis, but **progressive lesions cannot be distinguished from regressive ones**.

Overdiagnosis of **regressive lesions** has been evaluated in RCTs by comparing the overall detection of regressive lesions in the HPV arm and in the cytology arm up to the second screening round and beyond.

Results suggest overdiagnosis of regressive CIN2 ***in younger*** women for HPV-based screening compared with cytology-based screening

Cervical cancer screening HARMS

Potential harms related to diagnosis and treatment of CIN

Risks of **colposcopy and cervical biopsy** include pain, bleeding, infection, failure to diagnose (inadequate sampling), and cost to the patient (e.g. time off work and psychological impact).

An observational study within the TOMBOLA cohort reported ***pain, bleeding, or discharge at 6 weeks among 14–18% of women aged 20–59 years with colposcopy and no biopsy***.

Of those who had **colposcopic biopsy**, **53% reported pain, 79% reported bleeding, and 46% reported discharge**. For women who had the loop electrosurgical excision procedure (LEEP), these proportions were 67%, 87%, and 63%, respectively. The duration of bleeding and discharge was longer for women treated by LEEP than women in the other groups reporting these symptoms

Cervical cancer screening HARMS

Potential harms related to diagnosis and treatment of CIN

A 2008 review of **excisional or ablative therapies** found that:

Cold- knife conization was associated with an *increased risk of* ***preterm birth*** (<30 weeks: four studies; RR, 5.33; 95%CI: 1.63–17.40; <34 weeks: five studies; RR, 2.78; 95%CI: 1.72–4.51), ***low birth weight*** (<2000 g: one study; RR, 2.86; 95%CI: 1.37–5.97), and **perinatal mortality** (seven studies; RR, 2.87; 95%CI: 1.42–5.81)

LEEP was not associated with an increased risk of perinatal mortality, preterm birth (<32–34 weeks), or preterm labor (<28–30 weeks), low birth weight (<2000 or 1500 g).

Breast cancer screening

Most programmes in Europe invite women

starting at age 50 years and not before age of 40 years,

and from then on, every 2 years until age 70–75 years

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Mammographic screening- EFFECTIVENESS

Is mammography screening effective in reducing breast cancer mortality in the general female population at average risk of breast cancer?

Three meta-analyses of ***RCTs***: a statistically **significant reduction** in breast cancer **mortality** when women of all age ranges between 40 and 74 were considered together

RR, 0.81; 95%CI: 0.74–0.87
RR, 0.82; 95%CI: 0.74– 0.91
RR, 0.80; 95%CI: 0.73–0.89

an approximate ***20% reduction in relative risk of breast cancer mortality from invitation to screening***

Mammographic screening- EFFECTIVENESS

Is mammography screening effective in reducing breast cancer mortality in the general female population at average risk of breast cancer?

Results from ***observational studies***: pooled breast cancer mortality reduction

-among ***invited*** *(intention-to-treat analysis)* women:

7 incidence-based mortality studies: ***25%*** (RR, 0.75, 95%CI: 0.69–0.81),

7 case–control studies: ***31%*** (OR, 0.69; 95%CI: 0.57–0.83).

-among actually ***screened*** *(per-protocol analysis)* women:

-in incidence-based mortality studies: ***38%*** (RR, 0.62; 95%CI: 0.56–0.69)

-in the case– control studies: ***48%*** (OR, 0.52, 95%CI: 0.42–0.65),

when adjusted for self-selection.

Mammographic screening Age and interval

What is the optimal age range in which to perform mammography screening for breast cancer, and what is the optimal time interval for such screening?

All **meta-analyses** of both RCTs and observational studies of invitation to breast cancer screening:

-All age ranges between **40 and 74** considered together: statistically significant breast cancer mortality reduction.

Narrower age **ranges** considered separately: results from **RCTs**

-**greatest reduction** for 60–69 years (RR, 0.69, 95%CI: 0.57–0.83, 5 trials included, RR, 0.68, 95%CI: 0.54–0.87, 2 trials included)

-40–49 and 50–59 years: statistically **significant reduction even less** than age ranges 40–74

-40–49 years: RR, 0.85; 95% CI: 0.75–0.96, 8 trials included

-50–59 years: RR, 0.82; 95%CI: 0.68–0.98, 7 trials included, RR, 0.86; 95%CI: 0.75–0.99, 6 trials included)

-70–74 years: **nearly statistically significant** reduction (RR, 0.68; 95%CI: 0.45–1.01, 2 trials included; RR, 1.12; 95%CI: 0.73–1.72, 1 trial included)

Breast-Cancer Screening — Viewpoint of the IARC Working Group

Objective: to assess the cancer-preventive and adverse effects of different methods of screening for breast cancer, to update of the 2002 IARC handbook on breast-cancer screening

Table 1. Evaluation of Evidence Regarding the Beneficial and Adverse Effects of Different Methods of Screening for Breast Cancer in the General Population and in High-Risk Women.*

Method	Strength of Evidence†
Mammography	
Reduces breast-cancer mortality in women 50–69 yr of age	Sufficient
Reduces breast-cancer mortality in women 70–74 yr of age‡	Sufficient
Reduces breast-cancer mortality in women 40–44 yr of age§	Limited
Reduces breast-cancer mortality in women 45–49 yr of age§	Limited¶

‡ The evidence for a reduction in breast-cancer mortality from mammography screening in women in this age group was considered to be sufficient. However, published data for this age category did not allow for the evaluation of the net benefit.

§ The evidence for a reduction of breast-cancer mortality from mammography screening in women in this age group was considered to be limited. Consequently, the net benefit for women in this age group was not assessed.

¶ The majority of the voting members of the IARC Working Group considered the evidence as limited; however, the vote was almost evenly divided between limited and sufficient evidence.

Mammographic screening Age and interval

What is the optimal age range in which to perform mammography screening for breast cancer, and what is the optimal time interval for such screening?

From available evidence from ***RCTs*** on breast cancer mortality,

-*40–49 years*, 1 RCT estimated a significant reduction in mortality for an **interval <24** *months*.

-*50–69 years*, a significant reduction in mortality was observed for an interval of *24–33 months,* and for the age ranges from 39–69 when the interval was <24 months

Mammographic screening HARMS

-What is the (cumulative) False Positive rate in the screening age period?

-What is the risk of overdiagnosis in the screening process?

- Pain, Psychological effects

- Radiation exposure

Mammographic screening HARMS

What is the (cumulative) False Positive rate in the screening age period?

According to a review of studies performed after 2000 in the context of European mammography screening programs (for a total of 390,000 screened women aged 50–69 years undergoing ten biennial screening tests):

- ***cumulative risk of a false-positive screening result: 8%-21%,***
- cumulative risk of an invasive procedure with a benign outcome: 1.8%-6.3%;
-cumulative risk of a false-positive screening result without an invasive procedure: 16.8%,
-risk of undergoing surgical intervention with benign outcome was 0.9%.

Mammographic screening HARMS

What is the risk of overdiagnosis in the screening process?

Overdiagnosis is the diagnosis of breast cancer which would never have surfaced as clinically diagnosed cancer during the women's lives, without screening, leading to unnecessary treatment.

Overdiagnosis has been assessed and evaluated in several ways among the systematic reviews and meta-analyses considered, suggesting that the existing phenomenon is difficult to define and determine.

Mammographic screening HARMS

What is the risk of overdiagnosis in the screening process?

Estimates from ***RCTs:***

-30%;

-19% (95%CI 15–23) (when overdiagnosis is defined as excess cancers as a proportion of cancers diagnosed during the active screening period in women invited for screening);

- 11% (95%CI 9–12) (when overdiagnosis is defined as excess cancers as a proportion of cancers diagnosed in the long term in women invited for screening)

Mammographic screening HARMS

What is the risk of overdiagnosis in the screening process?

Estimates of overdiagnosis, expressed as a percentage of the expected incidence in the absence of screening from ***population-based mammography screening in seven Western European countries***:

-adjusted for breast cancer risk and lead-time bias: Netherlands, 2.8%; Italy, 4.6% and 1.0%; Denmark, 7.0%; England and Wales, 10% and 3.3%.

-unadjusted or incompletely adjusted for breast cancer risk and lead-time bias: 0%-54%.

According to the previous considerations, the most plausible estimates of risk of overdiagnosis range from 1% to 10%

Mammographic screening HARMS

Pain

Mammography is considered an acceptable test.

Few women 40–49 years of age agreed that the pain caused by mammography would prevent them from attending future screening. The degree of pain was associated with the stage of menstrual cycle, anxiety, and pre-mammography anticipation of pain.

Psychological effects

Overall, the psychological impact of mammography screening is minimal in women who received a negative result after mammography, while it appears to be negative in women who received a false-positive result.

Mammographic screening HARMS

Radiation exposure

The excess risk of breast cancer induced by radiation ***depends on the X-ray dose*** of mammography and the ***age when starting*** screening.

The risk of ***breast cancer induced*** between the ages of ***40 and 80*** years with ***annual mammography*** is ***1 per 1000 women***. The risk–benefit ratio between 40 and 49 years is one death induced by cancers due to radiation exposure versus three saved lives.

For mammography, it is predicted that the excess relative risk (ERR), defined as proportion of RR due solely to radiation exposure (ERR = RR –1), doubles when screening starts at age 40 instead of 50.

Colorectal cancer screening

Most programmes in Europe invite men and women starting at age 50–60 years,

and from then on, every 2 years if the screening test is the guaiac-based faecal occult blood test (gFOBT) or the fecal immunochemical test (FIT),
or every 10 years or more if the screening test is flexible sigmoidoscopy (FS) or colonoscopy (TC)

Most programs continue sending invitations to screening up to age 70–75 years.

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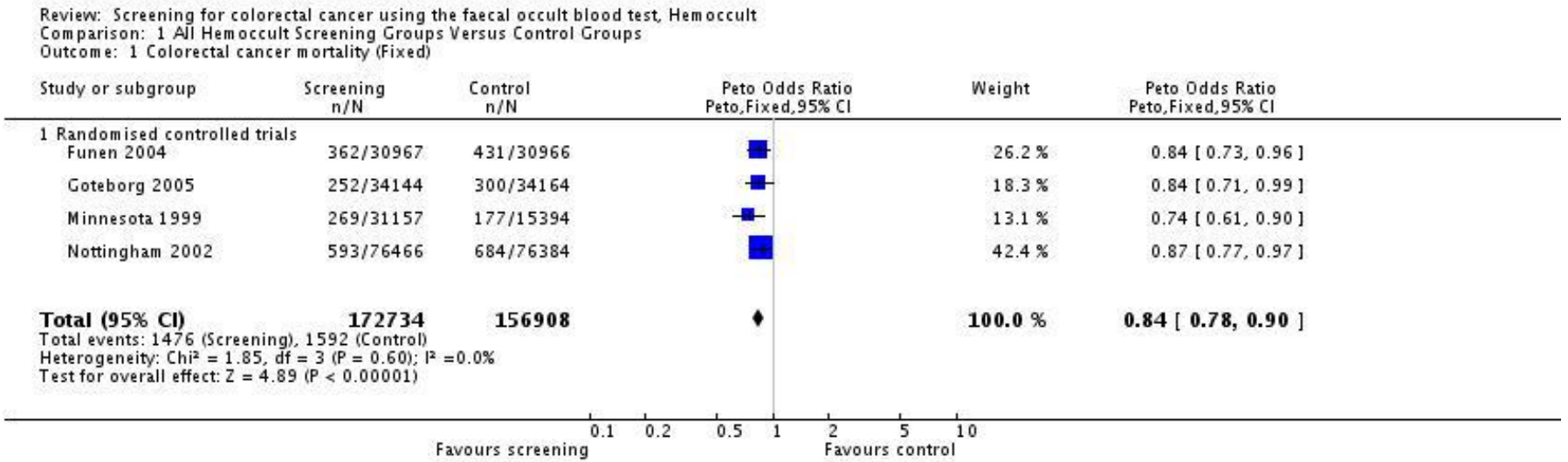
Colorectal cancer screening EFFECTIVENESS

Is FOBT screening offered to the general population effective in reducing colorectal cancer mortality, colorectal cancer incidence, and overall mortality?

Meta-analysis of published **RCTs**, **gFOBT**

CRC mortality:

- statistically significant ***16% reduction***
- when adjusted for mean screening attendance in the individual studies: **25% reduction** (RR, 0.75; 95% CI: 0.66–0.84) for those **attending at least one** round of screening



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Colorectal cancer screening EFFECTIVENESS

Is FOBT screening offered to the general population effective in reducing colorectal cancer mortality, colorectal cancer incidence, and overall mortality?

FIT

-2 case–control studies: significant **reduction** in **CRC mortality**, ranging from ***52% to 83%,*** depending on years since last FIT

-1 case–control study when FIT performed within 3 years before the diagnosis: significant reduction in **advanced CRC incidence** OR, 0.54, 95%CI: 0.30–0.99

-**Recent** publications of **observational studies**, subsequent to the systematic reviews carried out for the Code **consistent** in the reduction of mortality and incidence

Is FS screening offered to the general population effective in reducing CRC mortality, CRC incidence, and overall mortality?

Meta-analysis of published **RCTs** results:

CRC **mortality**

-in the *invited population* (intention-to- treat analysis): a statistically significant ***28% reduction*** (RR, 0.72; 95%CI: 0.65–0.80)

-in *people participating* (per-protocol analysis): a statistically significant ***50% reduction*** (RR, 0.50; 95%CI: 0.35–0.64)

CRC **incidence**

-in the *invited population* (intention-to- treat analysis): a statistically significant ***18% reduction*** (RR, 0.82; 95%CI: 0.73–0.91) was observed in the intention-to-treat analysis.

-in *people participating* (per-protocol analysis): a statistically significant ***32% reduction*** (RR, 0.68; 95%CI: 0.47–0.89)

Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials

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the bmj | *BMJ* 2017;356:i6673 | doi: 10.1136/bmj.i6673

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Table 2 | Colorectal cancer incidence and mortality in pooled analysis. Results correspond to overall analysis (50-74 years), and age (≥60 years *v* <60 years) and sex stratified pairwise comparisons (screening group *v* control group) using Mantel-Haenszel fixed effect model. P values refer to the interaction terms between age and sex from a metaregression model including age, sex, interaction term, and indicator variables for each trial (see methods section)

	Screening group *v* control group			
	Colorectal cancer incidence (relative risk (95% CI))	P for interaction	Colorectal cancer mortality (relative risk (95% CI))	P for interaction
Colon and rectum				
Both sexes*	0.79 (0.74 to 0.84)		0.73 (0.64 to 0.83)	
Men†	0.76 (0.70 to 0.83)		0.67 (0.57 to 0.80)	
≥60 years‡	0.76 (0.68 to 0.84)		0.67 (0.55 to 0.82)	
<60 years§	0.76 (0.65 to 0.88)	0.12	0.67 (0.49 to 0.91)	0.55
Women¶	0.83 (0.75 to 0.92)		0.82 (0.67 to 1.00)	
≥60 years‡	0.90 (0.80 to 1.02)		0.88 (0.69 to 1.12)	
<60 years§	0.71 (0.59 to 0.84)		0.73 (0.53 to 1.02)	

LETTERS

OBSERVATION: BRIEF RESEARCH REPORT

Annals of Internal Medicine
Vol. 167 No. 8 • 17 October 2017 **603**

Reanalysis of All-Cause Mortality in the U.S. Preventive Services Task Force 2016 Evidence Report on Colorectal Cancer Screening

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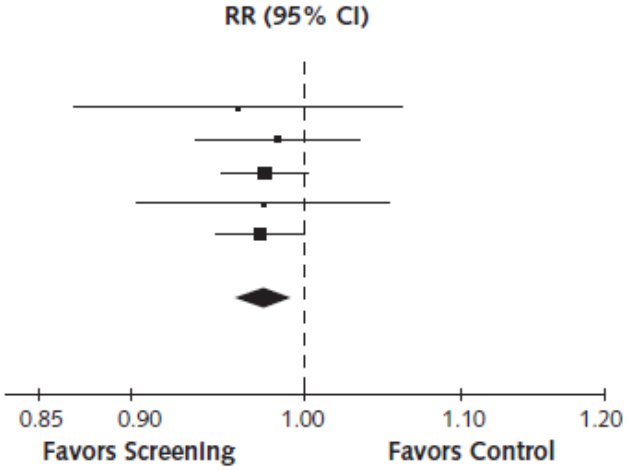
Figure 2. RR for death with screening with flexible sigmoidoscopy in randomized controlled trials.

Trial	Screening			Control			RR (95% CI)
	Deaths, *n*	Persons, *n*	Risk, %	Deaths, *n*	Persons, *n*	Risk, %	
NORCCAP							
Age 50–54 y	427	6920	6.17	2387	37 131	6.43	0.96 (0.87–1.06)
Age 55–64 y	1756	13 652	12.86	5375	41 089	13.08	0.98 (0.94–1.03)
PLCO*	9390	77 445	12.12	9627	77 455	12.43	0.98 (0.95–1.002)
SCORE	1202	17 136	7.01	1233	17 136	7.20	0.97 (0.90–1.05)
UKFSST	6775	57 099	11.87	13 768	112 939	12.19	0.97 (0.95–1.0002)
Subtotal		172 252			285 750		0.975 (0.959–0.992)
Total events	19 550			32 390			

Heterogeneity: chi-square = 0.22 ($P = 0.99$); $I^2 = 0\%$

Test for overall effect: $Z = 2.90$ ($P = 0.004$)



NORCCAP = Norwegian Colorectal Cancer Prevention; PLCO = Prostate, Lung, Colorectal, and Ovarian; RR = relative risk; SCORE = Screening for Colon Rectum; UKFSST = U.K. Flexible Sigmoidoscopy Screening Trial.

* This trial reports a modified all-cause mortality that excludes deaths from prostate, lung, and ovarian cancer because the intervention group was also screened for those types of cancer.

Colorectal cancer screening EFFECTIVENESS

Is TC screening offered to the general population effective in reducing CRC mortality, CRC incidence, and overall mortality?

Observational evidence exists on the efficacy of TC screening in reducing CRC mortality and incidence.

Results from RCTs evaluating CRC mortality and incidence as primary endpoints in screening colonoscopy are ***not available***.

Results of studies including subjects undergoing at least one colonoscopy:

CRC mortality reduction: range 29%-65%,

CRC incidence reduction: range 48%-67%

Reduction in the overall CRC mortality and incidence is always significant; however, stratification by site suggests that colonoscopy *might* ***not be as effective*** in the ***proximal*** colon as in other segments of the colon/rectum

Colorectal cancer screening — Age and interval

What is the optimal age range in which to perform screening with FOBT as the primary screening test?

Study	Age range	RRR CRC mortality	Years follow up
Nottingham	45-75	13% (CI 0.78-0.97)	11 years
Funen	45-74	11% (CI 0.78-1.01)	17 years
Minnesota	50-80	21% (CI 0.62-0.97)	18 years
Goteborg	60-64	16% (CI 0.78-0.90)	15.5 years

RCT gFOBT : *age range of included is **45–80 years***. The observed mortality reduction is significant, and they include analyses of the whole age ranges, with follow-up times varying from 11.7 to 18 years between the trials.

Update from the Nottingham trial after a median of 19.5 years, showed a significant reduction in CRC mortality for the age group **older than 60 years** but not for the age group younger than 60 years.

No evidence is available on the best age range for **FIT** screening. Given the **similarities** between the tests, the age range can be based on the evidence for the optimal age range from gFOBT trials.

What is the best time interval for offering screening by FOBT?

The Minnesota trial is the **only trial** to directly compare **annual and biennial** screening. **Both** intervals were found to be **effective** in reducing CRC mortality, with the benefit from annual screening appearing to be greater than that for biennial screening, although not significantly different

Case–control studies suggest that the effect of **FIT** on colorectal cancer mortality was significant only in those subjects screened **within 3 years** before the diagnosis, although power may have been an issue for longer intervals

A population screening study has shown that repeated FIT screening with a 1, 2, or 3-year interval led to a similar diagnostic yield of advanced neoplasia

What is the optimal age range in which to perform screening with FS as the primary screening test, and what is the best time interval for offering screening by FS?

No significant differences for any outcome have been observed **between ages** 55–59, 60–64, and 65–74 years according to the results of the trials in the UK, Italy, and the United States

According to the results from published RCTs, the reduction in incidence/ mortality still remains after 10–11 years of follow-up, and therefore **the interval for offering screening could be longer than 10 years**

In a study in which **FS** was offered **within 5 years** of the previous one, **no increase in the effect** was observed compared to the results of the RCTs offering FS once in a lifetime and with a similar duration of follow-up.

What is the optimal age range in which to perform screening with TC as the primary screening test? What is the best time interval for offering screening by TC?

Available evidence on the age range for TC as the primary screening test includes subjects 50 years and suggests that the **impact is lower among elderly people** (>75 years).

Available evidence on colonoscopy intervals suggests that **interval of at least 10 years is sufficient**

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Colorectal cancer screening HARMS

What is the rate of negative side effects of FOBT screening?

Minor and severe complications

The results of RCTs demonstrate that the FOBT strategy is ***safe***, with **no direct adverse effects**. Complications in an FOBT program occur **from colonoscopies** after positive test results.

False-positive results

False-positive results lead to anxiety and **unnecessary follow-up colonoscopies**.

gFOBT Positive predictive value: CRC: 10%,11%; advanced adenoma: 40%, 45%

FIT Positive predictive value: CRC: 9%, 10%; advanced adenoma: 38%, 53%

False-negative results

Sensitivity for CRC: 25%-79% in cohort diagnostic accuracy studies with follow-up

Acceptability, psychological effects

Highest anxiety levels occurred after notification of a false-positive result and before colonoscopy

What is the rate of negative side effects of FS screening?

Minor and severe complications

Rates of peritonitis-like reaction, glutaraldehyde colitis, allergic reaction to latex gloves, self-limited bleeding, and mild vagal reactions (nausea, feeling faint or feeling dizzy, abdominal pain): ***0.2%-0.6%.***

Rates of hospitalization within 30 days due to ***serious hemorrhage*** involving transfusion, or due to ***perforation***: ***0%-0.03%.***

Rates of severe complications with follow-up colonoscopy: about 10 times higher.

What is the rate of negative side effects of FS screening?

False-negative results

Prospective follow-ups (3 years) of negative screening FS in average-risk populations: 0.8% of subjects had distal advanced neoplasia, no adenocarcinomas.

FS and interval cancers:

- risk of interval distal cancer after a negative FS of 0.07% (33/44,988) after a mean of 11.5 years.

- rate of CRC incidence (interval cancers) after a negative FS lower than in the control group over the entire follow-up period (Nelson–Aalen cumulative hazard ratio 0.41; 95%CI: 0.32–0.54).

Colorectal cancer screening- HARMS

What is the rate of negative side effects of FS screening?

Acceptability, psychological effects

Results from RCTs and studies on patient-reported experiences after FS in a community-based FS screening program show that FS should be considered an **acceptable test**

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Colorectal cancer screening- HARMS

What is the rate of negative side effects of TC screening?

Minor and severe complications

Rates of ***severe*** complications (death, cardiopulmonary events, bleeding, perforation, other clinically relevant complications) from TC (including complications from polypectomy) reported in three European national screening programs and in an ongoing RCT in eight Spanish regions: range ***0.06%-0.5%.***

Pox 2012 reported:

-Complication rate in colonoscopies with polypectomy separately from that in colonoscopies without polypectomy: OR 4.9; 95%CI: 4.6–5.2;

-Rate of minor complications: 1.9 per 1000

Colorectal cancer screening- HARMS

What is the rate of negative side effects of TC screening?

False-negative results

Miss rate for adenoma 10 mm: range from 0-12%

From published data from a colonoscopy-based screening program in Poland, it has been observed that after a mean follow-up of about 4,5 years, the risk of ***interval CRCs*** between screening colonoscopy and scheduled surveillance examination: ***0.09%*** (42/45026)

Colorectal cancer screening- HARMS

What is the rate of negative side effects of TC screening?

Acceptability, psychological effects

Patient-reported experiences: at least ***moderate discomfort*** associated with the ***laxative bowel preparation,*** perceived be the worst part of the colonoscopy. Other reported difficulties were the pre-test fasting and liquid diet, pre-procedural anxiety, worry and anticipation of pain, the instrument insertion, as well as embarrassment with the process, and the length of the procedure that required time away from other duties.

12. Take part in organised cancer screening programmes:

- Bowel cancer (men and women)
- Breast cancer (women)
- Cervical cancer (women)

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Thank you for your attention!

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