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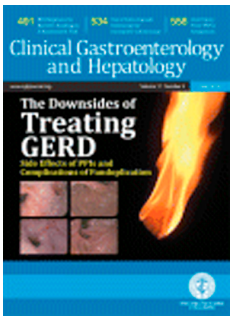
Published in:
Clinical Gastroenterology and Hepatology

DOI:
10.1016/j.cgh.2020.06.019

Publication date:
2021

Document version:
Accepted manuscript

Journal Pre-proof



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PII: S1542-3565(20)30825-9
DOI: https://doi.org/10.1016/j.cgh.2020.06.019
Reference: YJCGH 57293

To appear in: *Clinical Gastroenterology and Hepatology*
Accepted Date: 6 June 2020

Please cite this article as: Shaukat A, Kaalby L, Baatrup G, Kronborg O, Duval S, Shyne M, Mandel JS, Church TR, Effects of Screening Compliance on Long-term Reductions in All-cause and Colorectal Cancer Mortality, *Clinical Gastroenterology and Hepatology* (2020), doi: https://doi.org/10.1016/j.cgh.2020.06.019.

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Aasma Shaukat, Lasse Kaalby, Gunnar Baatrup, Ole Kronborg, Sue Duval, Michael Shyne, Jack S. Mandel, Timothy R. Church

Division of Gastroenterology (A.S.) and Cardiovascular disease (S.D.), Minneapolis Veterans Affairs Health Care system; Department of Medicine (A.S.,S.D.), University of Minnesota School of Medicine; Division of Biostatistics (M.S.) and Environmental Health Sciences (T.R.C., A.S.), University of Minnesota School of Public Health; and Department of Epidemiology, Department of Clinical Research, University of Southern Denmark and Department of Surgery, Odense University Hospital (L.K, G.B, O.K)

Corresponding and reprint author:

Aasma Shaukat MD MPH
One-Veterans drive, 111-D
Minneapolis MN 55417
Ph: 612-467-4100
Email:Shaukat@umn.edu
Fax: 612-725-2248

Funded by Veterans Affairs Merit program CX 008-16F
Word count: 2613
Conflicts on interest: none for any of the authors

Abstract

Background & Aims: Randomized trials have shown that biennial fecal occult blood test (FOBT) screening reduces mortality from colorectal cancer (CRC), but not overall mortality. Differences in benefit for men vs women, and by age, are unknown. We sought to evaluate long-term reduction in all-cause and CRC-specific mortality in men and women who comply with offered screening, and in different age groups, using individual participant data from 2 large randomized trials of biennial FOBT screening, compared with an intention to treat analysis.

Methods: We updated the CRC and all-cause mortality from the Danish CRC screening trial (n=61,933) through 30 years of follow up and pooled individual participant data with individual 30-year follow-up data from the Minnesota Colon Cancer Control trial (n=46,551). We compared the biennial screening groups to usual care (controls) in individuals 50–80 years old using Kaplan Meier estimates of relative risks and risk differences, adjusted for study differences in age, sex, and compliance.

Results: Through 30 years of follow up, there were 33,478 (71.9%) and 33,479 (72.2%) total deaths and 1023 (2.2%) and 1146 (2.5%) CRC deaths in the biennial screening (n=46,553) and control groups (n=46,358), respectively. Among compliers, biennial FOBT screening significantly reduced CRC mortality by 16% (relative risk [RR], 0.84; 95% CI, 0.74–0.96) and all-cause mortality by 2% (RR, 0.98; 95% CI, 0.97–0.99). Among compliers, the reduction in CRC mortality was larger for men (RR, 0.75; 95% CI, 0.62–0.90) than women (RR, 0.91; 95% CI, 0.75–1.09). The largest reduction in CRC mortality was in compliant men 60–69 years old (RR, 0.59; 95% CI, 0.42–0.81) and women 70 years and older (RR, 0.53; 95% CI, 0.30–0.94).

Conclusions: Long-term CRC mortality outcomes of screening among compliers using biennial FOBT are sustained, with a statistically significant reduction in all-cause mortality. The reduction in CRC mortality is greater in men than women—the benefit in women lags that of men by about 10 years.

KEY WORDS: colon cancer, survival, early detection, compliance

Introduction:

Several modalities are available for colorectal cancer (CRC) screening, including fecal occult blood testing (FOBT) at intervals of one or two years. While annual testing is employed in the U.S., biennial screening is practiced in many European countries and Canada.(1, 2) Biennial screening reduced CRC mortality by 13%, 18%, and 21% in three large trials with follow-up of 18 – 19.5 years.(3-5) However none of the trials were sufficiently powered to study all-cause mortality, the effect of compliance adjustment or whether the screening effects vary by age and sex. Given that these trials were initiated in the mid-1970s and early 1980s, long-term follow-up provides additional events and person-years of follow-up for meaningful comparisons. Previously, the Minnesota fecal occult blood trial updated the follow-up of the participants of the Minnesota trial (annual and biennial screening versus controls) through 30 years and reported a sustained reduction in CRC mortality of 18% with biennial screening.(6) They also observed non-significant differences in screening effects for men and women and by age. Since then, others have published updated follow-up and pooled analyses of the flexible sigmoidoscopy trials for CRC screening and reported significant differences in benefits of CRC screening between men and women.(7, 8). None of the trials reported a reduction in all-cause mortality, while one meta-analysis of CRC screening trials reported a significant increase in non-CRC mortality (9). Our aims were to assess the long-term effects of biennial screening on all-cause and CRC mortality using intention to treat and compliance adjustment, and evaluate age- and sex-specific effects by pooling individual participant data from the available randomized controlled trials of biennial FOBT screening, updated through 30 years of follow-up.

Methods:

We performed a systematic literature search for randomized trials evaluating annual or biennial FOBT screening for reduction in CRC mortality. We identified five trials. We excluded two trials for lack of follow-up colonoscopy in FOBT positive participants (10) and lack of individual randomization design.(11) The investigators of the remaining three trials: the Minnesota trial (US), the Funen trial (Denmark), and the

Nottingham trial (United Kingdom) were asked to contribute data. The UK investigators elected not to participate. A collaborative agreement was reached between the Minnesota and Danish trial investigators. The study was approved by the Institutional Review Board at University of Minnesota and by the Danish Data Protection Agency. The University of Minnesota and the University of Southern Denmark executed data sharing agreements to allow the meta-analysis.

Minnesota Colon Cancer Control Study (MCCCS):

The Minnesota Colon Cancer Control Study (5, 12-14) randomized healthy volunteers aged 50 to 80 years to annual screening, biennial screening, or usual care (control) (n=46,551). The primary endpoint was CRC mortality. Individuals were recruited and randomized from 1975 to 1992 with a four-year hiatus from 1982 to 1986. In total, six rounds of screening were offered to the biennial group. Adherence to one or more rounds of screening was 90%. Those with a positive test were invited to the University of Minnesota for a cost-free diagnostic work-up that included colonoscopy. Polyps found during colonoscopy were removed during the procedure. If the colonoscopy was incomplete, an air-contrast barium enema was performed. Compliance with a follow-up diagnostic examination after a positive screen was 83%. Annual follow-up using written questionnaires and telephone calls took place between 1976 and 1999 with response to these annual follow-ups over 99% in all three groups. The role of CRC in deaths was determined by the deaths review committee for approximately the first 15 years, and thereafter based on coded death certificates through 2001. Death certificates were coded according to ICD-08a, -09, or -10, depending on the date of death. In 2011 the study updated the cause of death through 30 years of follow-up by conducting an NDI-plus search for vital status and cause of death for participants alive at last follow-up, using identifiers including name, sex, date of birth, social security number and state of residence to obtain the best possible match. Updated results of the 30-year follow-up of the MCCCS have been published previously(6) and showed a sustained reduction in CRC

mortality of 33% and 22% in the annual and biennial screening arms, respectively. For the present study we only used the biennial screening and control arms.

Funen Fecal Occult Blood Trial:

The Funen fecal occult blood trial (4, 15-17) randomized individuals aged 45 to 75 years to biennial screening or usual care (control) (n=61,933). The primary endpoint was CRC mortality. In 1985, individuals residing in Funen were randomized and underwent nine rounds of biennial FOBT screening. Individuals with known colorectal cancer, colorectal adenomas or distant spread from any malignant disease were excluded before randomization. Individuals with positive results underwent a colonoscopy. Polyps found during colonoscopy were removed during the procedure. Adherence to the first round of screening was 67%, and only those that adhered to screening in the previous round and without colorectal neoplasia were invited to the next round of screening. Adherence to diagnostic colonoscopy for those with a positive screen was 83%. Information on CRC was obtained through manual review of medical records, the Funen County database, and the Danish National Registration and Danish Cancer Registry through the first thirteen years of follow-up. CRC as a cause of death was based on manual chart review and coded death certificates. Through 13 years of follow-up, biennial screening reduced CRC mortality by 11%. (4) For the current study in 2018, the study updated the cause of death of all trial participants through 30 years of follow-up using the Danish Civil Registration number as the unique identifier via the Danish National Patient Register, the Central Person Register and the Danish Register of Cause of Death. All diagnoses and death certificates were coded using ICD-8 (until 1994) or ICD-10 (after 1994).

Statistical analysis:

Cumulative mortality from CRC or all causes was estimated by Kaplan-Meier survival analysis(18) through 30 years following randomization, and biennial screening and usual care (control) groups were compared at

multiple follow-up times, first by intention-to-treat, and then restricted to compliers. Cuzick's method (19) estimates the effect of screening among compliers in the group assigned to screening by comparing the outcomes to those in a corresponding group among controls. Compliance was defined as undergoing at least one screening round. This method was applied to cumulative Kaplan-Meier estimates of all-cause and CRC mortality to compliance-adjust absolute mortality relative risks (RR) and risk differences (RD). Unadjusted and adjusted RR and RD were computed for each study and by sex, age, and their combination. Standard errors for the RR were derived from Greenwood's variance approximation. Standard errors for RD were based on normal approximations to the binomial distribution.

We used a two-step approach to the individual participant data (IPD) meta-analysis for biennial screening versus controls, in which study-specific effects were first estimated and then combined into a single estimate for each outcome.(20) Pooled RR and RD were calculated with fixed effect meta-analytic models that were adjusted to the combined age-sex distribution. Proportional hazards models were used to conduct overall tests of interaction between demographic subgroups (age, sex, and age by sex) and screening or control groups. Due to small numbers, compliance-adjusted analysis of the men aged 70 years or older in the Funen trial could not be calculated. The I-squared test was used to measure heterogeneity in effect estimates.

Results:

The demographic characteristics of participants, person-years and events from the two trials are presented in Table 1. In the Funen trial, there were 45,009 (72.7%) deaths in the biennial screening and control groups combined through 30 years of follow-up. There were 1637 (2.6%) deaths from CRC: 786 (2.5%) in the screening group and 851 (2.7%) in the control group. In the Minnesota trial, there were 21,948 (70.8%) deaths through 30 years of follow-up, with 532 deaths from CRC: 237 (1.5%) in the screening group and 295 (1.9%) in the control group. Combined, there were 33,478 (71.9%) and 33,479 (72.2%) total deaths and 1023 (2.2%) and 1146 (2.5%) CRC deaths in the biennial screening (n=46,553) and control groups (n=46,358), respectively.

CRC mortality:

In the Funen trial, there was a small but not statistically significant difference in 30-year CRC mortality between the screening and control groups (RR 0.94; 95% CI 0.85, 1.04 and RD −0.27%; 95% CI −0.72%, 0.19%). In the Minnesota trial there was a significant reduction in 30-year CRC mortality between the screening and control groups (RR 0.78; 95% CI 0.65, 0.93 and RD −0.66%; 95% CI −1.13%, −0.18%). Combined, biennial fecal occult blood screening reduced deaths from CRC by 10% (RR 0.90, 95% CI: 0.82, 0.98 and RD -0.45%; 95% CI −0.78%, −0.13%) (I^2 63.5% (0%-91.6%). However, among compliers, the relative risk for CRC mortality was 0.84 (95% CI 0.74, 0.96) and RD was -0.55% (95% CI -0.96%, -0.15%). (Figures 1 and 2 and supplementary figure 1)

All-cause mortality:

In neither the Funen nor the Minnesota trial was either RR or RD statistically significant in 30-year all-cause mortality using intention to treat. When the datasets were combined, the relative and absolute reduction in all-cause mortality were not statistically significant (RR 1.00; 95% CI 0.99, 1.00 and RD −0.28%; 95% CI −0.86%, 0.29%), but among compliers, all-cause mortality was statistically significantly reduced (RR 0.98; 98% CI 0.97, 0.99 and RD −0.55%; 95% CI −0.96%, −0.15%; I^2 0%) (Figures 2 and 3 and supplementary figure 2).

Sub-group analyses:

Figure 4 shows a forest plot with the numbers of participants who were randomized, CRC deaths, and compliance-adjusted RRs for age and sex subgroups, for the screening, control and the combined groups.

The RR (95% CI) for CRC mortality in the screening versus the control group varied noticeably by age, with the largest benefit in those 60-69 years old. The compliance-adjusted RR for 50-59, 60–69 and ≥70 years of age were 0.89 (0.72, 1.09), 0.71 (0.58, 0.88) and 0.60 (0.37, 0.99), respectively (p for trend = 0.46).

The risk difference among compliers increased with age and was -0.15% (-0.61%, 0.31%), -1.45% (-2.38%, -0.52%) and -2.48% (-5.85%, 0.89%), for 50-59, 60-69 and ≥70 year old individuals respectively. (Figure 5)

The reduction in CRC mortality, among compliers was larger for men, but not statistically significant compared to women [RR (95% CI): 0.75 (0.62, 0.90) and 0.91 (0.75, 1.09), respectively; p for trend = 0.25]. The RD was larger for men compared to women (-1.06%; 95% CI-1.71%, -0.41%) and -0.20%; 95% CI-0.71%, 0.31% respectively). Screening men 60–69 years showed a strong effect on CRC mortality [RR 0.59; 95% CI 0.42, 0.81); p trend = 0.19].

Among women, the largest benefit of screening was seen in the 70 and older age group for reduction in CRC mortality [RR 0.53 (0.30, 0.94)]. No statistical nor numerical benefit was seen in the 50-59-year-old women [RR 1.08 (0.80, 1.46); p trend 0.21]

Discussion:

In the 30-year follow-up of all participants randomized to biennial FOBT screening versus controls, we found a statistically significant 10% relative reduction in CRC mortality and no difference in all-cause mortality in intention-to-treat analysis with long-term follow-up, similar to prior studies. There are several potential explanations for the inability to demonstrate a decrease in all cause mortality. First, it is possible that the benefits gained in reduced deaths from CRC in the screened group is balanced by an increased death rate from non-CRC related deaths. The second possibility is that there is simply too much noise in the various published studies due to non-compliance and cross-over to allow for the demonstration of a small expected difference in all-cause mortality. These two explanations have major differing clinical implications. If the former were correct, there truly is no benefit to all cause mortality from screening, which causes as many deaths as it prevents. One could make the case that such information should be included as part of the informed consent. The latter explanation assumes that there truly is a difference in all cause mortality that has yet to be demonstrated because of the low fraction of all deaths accounted for by CRC. Differentiating

between these two possible explanation clearly would be of interest to both health professionals as well as subjects undergoing screening.

One source of “noise” in randomized CRC screening studies is non-compliance in the screened group, which we have defined as failure to undergo a single screening procedure. While no possible benefit from screening can be expected for such individuals, they are included in the intention to treat analysis as screened, to keep randomization intact. To this end, we applied Cuzick’s method (19) which takes focuses on the differences between compliant and non-compliant subjects and makes possible an accurate estimate of the effect of screening on just the compliers in the group randomized to screening. Among compliers there was a 16% reduction in CRC mortality rate in the screened group versus the 10% reduction observed in the non-adjusted (intent to treat) analysis. More important, a statistically significant 2% relative reduction in all-cause mortality was observed, the first such reduction reported in occult blood screening studies. The benefit in those that comply may be due to benefit of undergoing the screening, as well as other healthy behaviors that may contribute to lower risk of dying, such as non-smoking, healthy eating and lifestyle choices. The benefit could also be explained by indirect effects of accessing the healthcare system as a consequence of screening. While we do not have information on what may have led to the compliant group having lower all cause mortality, the results reinforce that trying to achieve 100% compliance to screening is an important public health goal. If confirmed by other studies, the reduction in all-cause mortality in addition to reduction in CRC mortality is an important finding, laying to rest the concern that reductions in CRC mortality due to screening are being offset by increases in other causes.

Analysis by sex showed that reduction in CRC mortality was statistically significant only for men, despite comparable number of deaths from CRC in men (585) and women (561) in the control groups. The observed effect of screening on reducing deaths from CRC was greatest in men ages 60-69, and in women over the age of 70. The sample size of individuals 70 and over was too small to draw meaningful conclusions. For 50-59-year-old women, screening was associated with a small but not statistically significant increase in CRC mortality.

Lack of a significant reduction in CRC mortality for women has also been evaluated in the pooled flexible sigmoidoscopy trials (21) with no reduction in CRC mortality. The explanation for the lack of a significant benefit of biennial fecal occult blood testing in women is not clear. One possibility is that women may have proportionally more right-sided adenomas and CRC. (22-24) There may be important differences in the underlying biological pathways for women, including tumors that are less sensitive to detection with FOBT, or tumors that rapidly grow, such that biennial interval is not effective in detecting these at early stages. Independent of the explanation of the gender difference, it could be argued that biennial FOBT screening is not an effective screening modality in females.

Our findings are also consistent with the updated 15-year follow-up of the Norwegian flexible sigmoidoscopy screening trial, which reported no significant reduction in CRC mortality from screening in women 50-64, but a 37% reduction in CRC mortality in men 50-64, despite similar or higher compliance with screening among women.(8) These findings are consistent with differences in incidence and mortality rates of CRC between men and women. Women's age-specific cumulative incidence rates lag behind that of men , as illustrated by Brenner et al.(25) At ages 50, 55, and 60, women achieved comparable 10-year cumulative incidence rates four to six years later than men.

This finding also needs to be factored into recent recommendations for reducing the age at which CRC screening should commence. Our data suggest that greater screening efficiency could be achieved by starting women at a later age then men and perhaps going longer compared to men.

While reduction in CRC mortality is a laudatory goal, the overall 10% reduction in CRC deaths observed with biennial screening in the present study is at the lower end of the effectiveness claims for various other screening modalities and well below the 33% reduction seen in annual screening with rehydrated FOBT.(13). The newer generation of more accurate and user friendly occult blood tests methods such as fecal immunochemical testing or endoscopic methods like colonoscopy may be more effective, and their impact on CRC mortality and all-cause mortality remains an area of active research.

Our study has several limitations. First, the compliance was different in the two trials. To avoid this bias, we used the extent possible, we accounted and adjusted for this through Cuzick's method, which focusses on compliers and their control group counterparts, similar to other long-term clinical trials for CRC screening (26-28). Second, we were unable to pool or compare our findings with the individual data from the Nottingham trial, which has double the number of participants of our combined trials. Third, we do not have information on screening history of trial participants after the two original trials ended. CRC screening started to become widespread in the late 1990s in the US and after 2000 in Denmark. It is possible that since then many participants in the control group may have undergone screening and many individuals that were screened may not have undergone subsequent screening. Thus our results show the combined 30-year effect of nine and six rounds of biennial screening for the Funen and Minnesota FOBT trials respectively, plus whatever screening and surveillance behaviors persisted after the trials ended.

In conclusion, our study shows that screening using biennial FOBT results in sustained reductions in CRC mortality and a statistically significant reduction in compliance-adjusted all-cause mortality. The reduction in CRC mortality is greater in men compared to women, and the benefit in women lags that for men by about 10 years. We did not observe a benefit due to screening in women age 50-59.

Acknowledgements: We would like to thank Robert Smith from American Cancer Society for his input and support on the project.

What you need to know:
-Screening for CRC using fecal occult blood testing results in a long-term sustained reduction in CRC mortality
-Adjusting for compliance shows a reducing in all cause mortality with screening for CRC

Tables and figures legend:

Table 1. Characteristics of the included trials

Figure 1. Compliance adjusted plot of combined cumulative CRC mortality Figure 2. Forest plot of relative risks and absolute risk differences for CRC and all-cause mortality

Figure 3. Compliance adjusted plot of cumulative combined all-cause

Figure 4. Forest plot of relative risks of CRC mortality for age and sex subgroups (Minnesota, Funen, and combined trials)

Figure 5. Risk difference for CRC mortality by age and sex subgroups (Minnesota, Funen, and combined trials)

Supplementary figure 1: Kaplan Meier plot of combined cumulative CRC mortality (unadjusted) (p=0.03)

Supplementary figure 2: Kaplan Meier plot of cumulative combined all-cause (unadjusted) (p=0.1)

Characteristic	Trial	Screening	Control
Number of participants	Funen	30,966	30,964
	MN	15,587	15,394
	Pooled	46,553	46,358
Female, n (%)			
	Funen	16,103 (52.0%)	16,111 (52.0%)
	MN	8,143 (52.2%)	7,960 (51.7%)
	Pooled	24,246 (52.1%)	24,071 (51.9%)
Age (mean±SD), years			
	Funen	59.4 (±8.50)	59.4 (±8.50)
	MN	62.3 (±7.80)	62.3 (±7.70)
	Pooled	60.4 (±8.40)	60.3 (±8.40)
Follow-up:			
person-years	Funen	605,023	603,953
	MN	328,287	323,993
	Pooled	933,310	927,946
Deaths at 30 years:			
all cause	Funen	22,474 (72.6%)	22,535 (72.8%)
	MN	11,004 (70.6%)	10,944 (71.1%)
	Pooled	33,478 (71.9%)	33,479 (72.2%)
colorectal cancer	Funen	786 (2.5%)	851 (2.7%)
	MN	237 (1.5%)	295 (1.9%)
	Pooled	1,023 (2.2%)	1,146 (2.5%)
Compliers:			
	Funen	20,694 (66.8%)	
	MN	13,806 (88.6%)	
	Pooled	34,500 (74.1%)	

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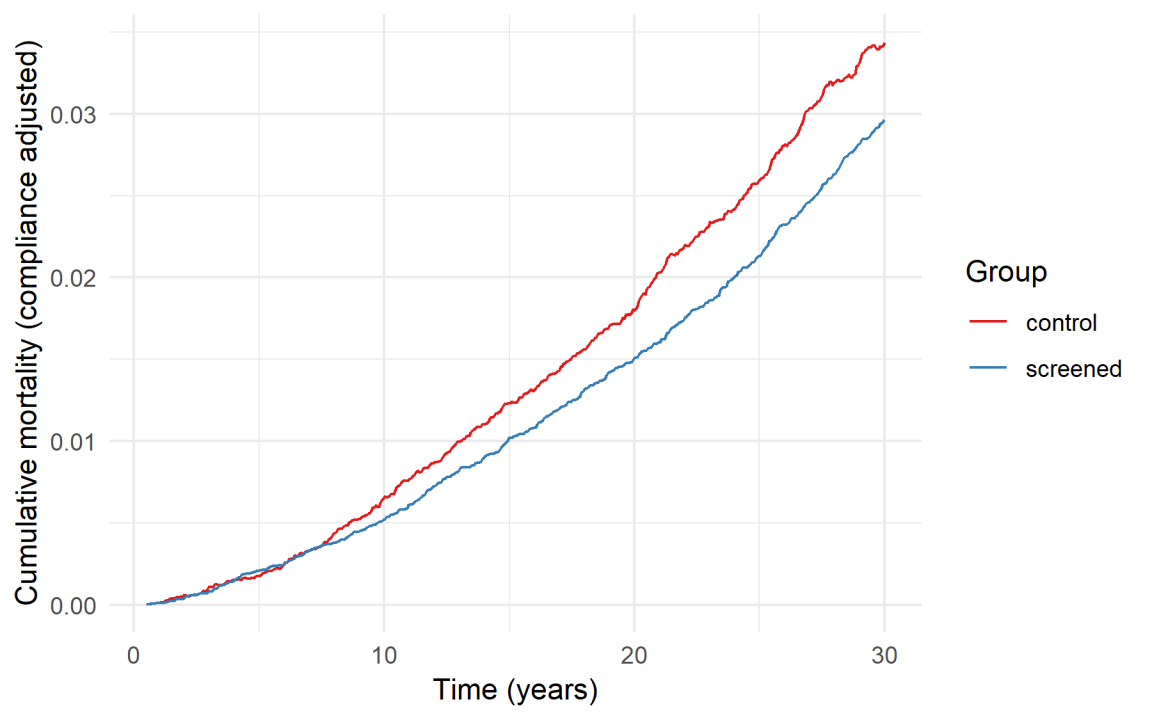
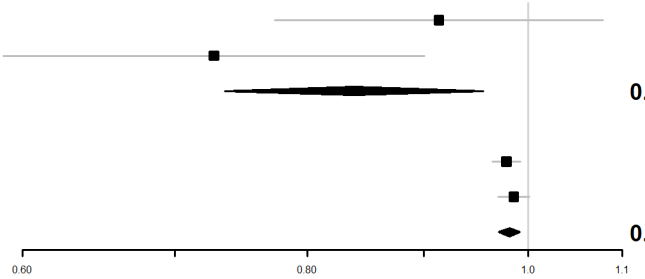

Cumulative mortality (compliance adjusted)
0.00
0.01
0.02
0.03
0
10
20
30
Time (years)
Group
control
screened

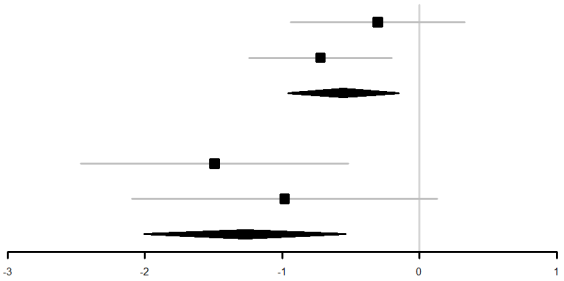
Relative risk

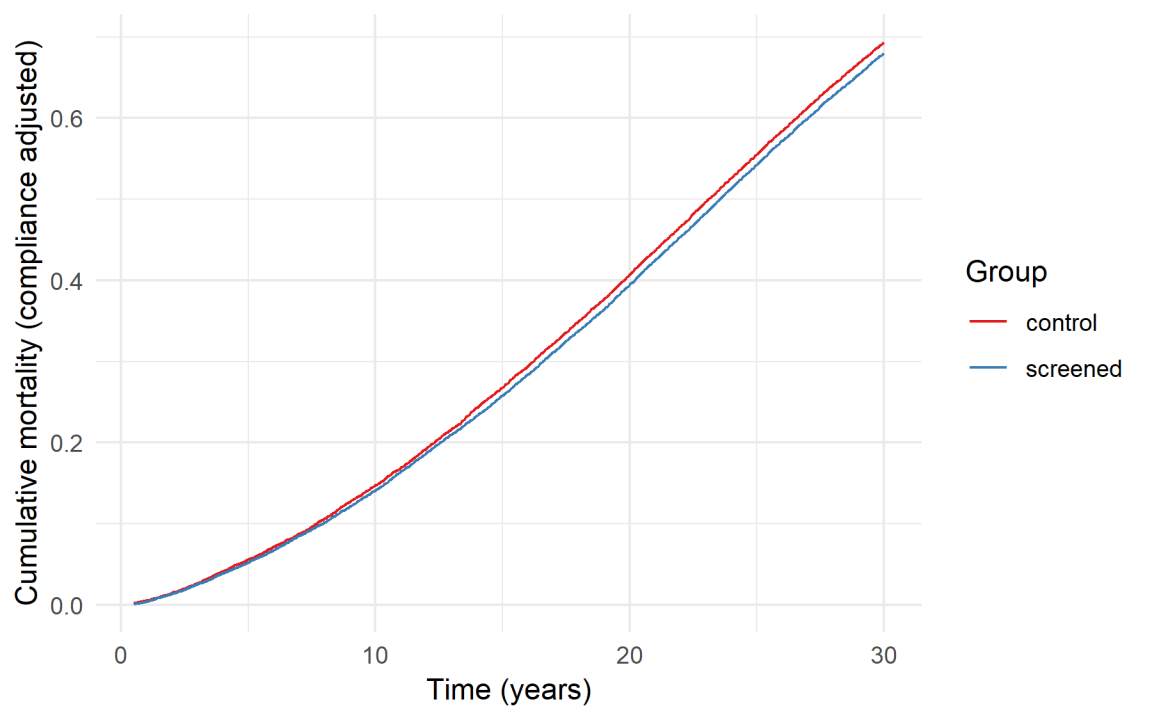
Src	Scrn n	Scrn dths	Ctrl n	Ctrl dths	RR (comp adj) (95% CI)	RR (95% CI)
CRC						
Funen	30966	786	30964	851	0.91 (0.77, 1.08)	0.94 (0.85, 1.04)
MN	15587	237	15394	295	0.73 (0.59, 0.90)	0.78 (0.65, 0.93)
	46553	**1023**	**46358**	**1146**	**0.84 (0.74, 0.96)**	**0.90 (0.82, 0.98)**
All cause						
Funen	30966	22474	30964	22535	0.98 (0.96, 0.99)	1.00 (0.99, 1.01)
MN	15587	11004	15394	10944	0.99 (0.97, 1.00)	0.99 (0.98, 1.01)
	46553	**33478**	**46358**	**22830**	**0.98 (0.97, 0.99)**	**1.00 (0.99, 1.00)**

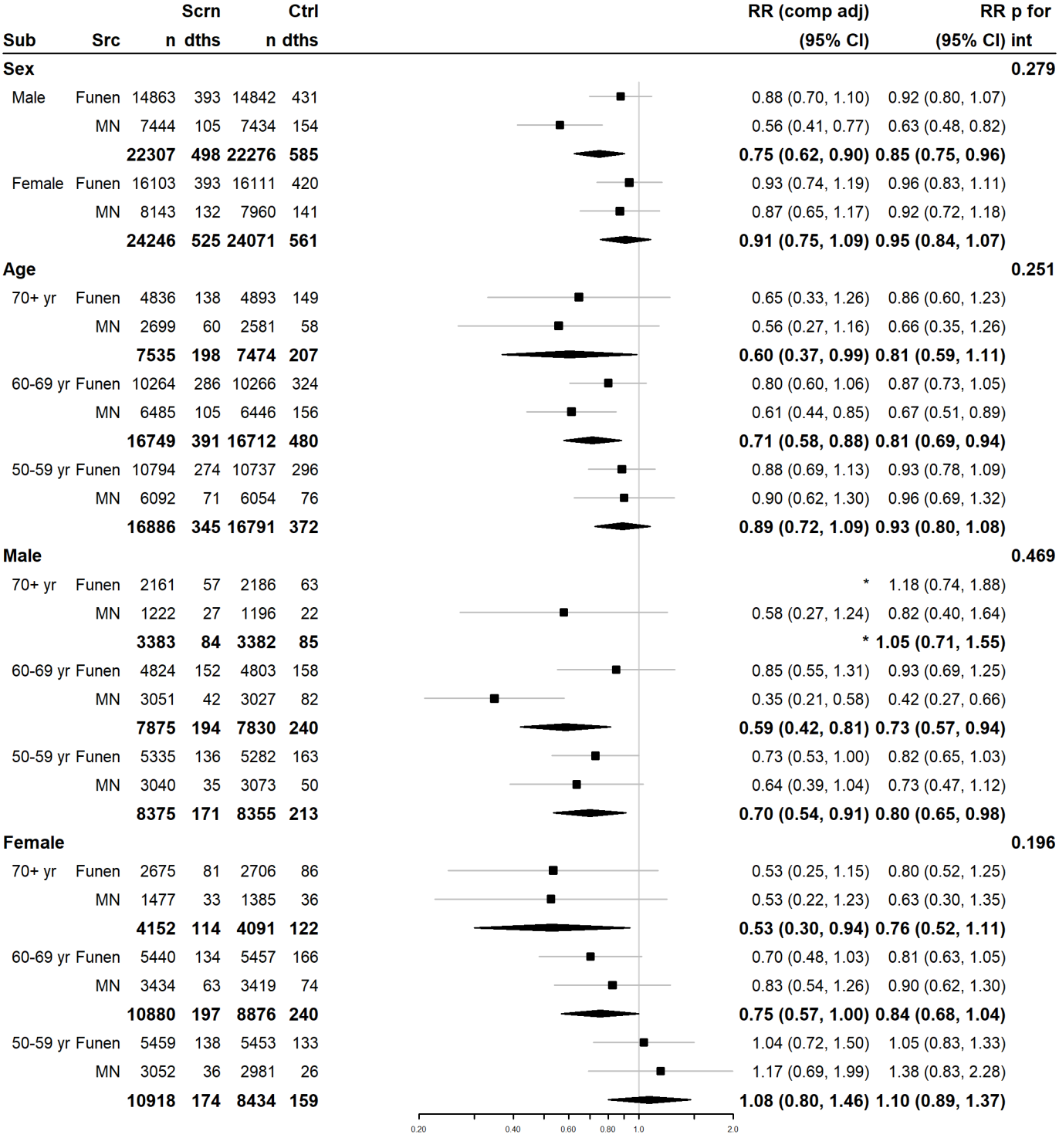


Risk difference

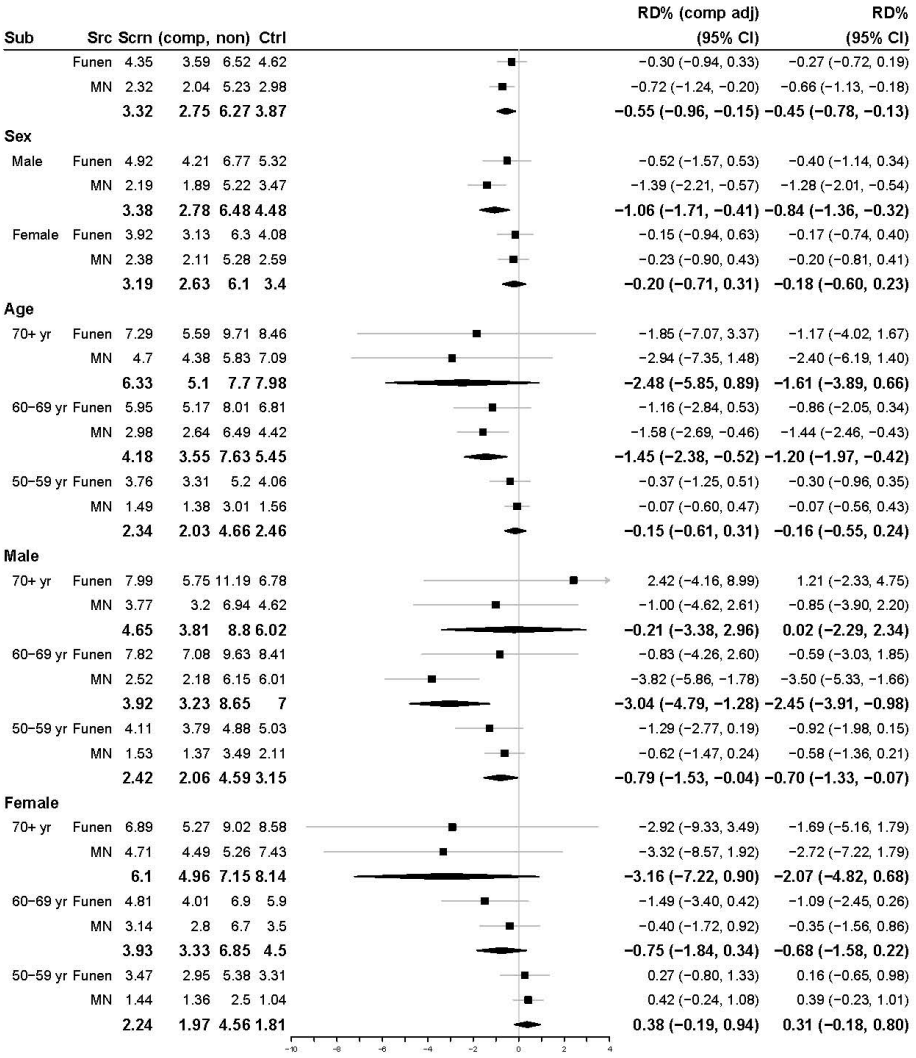
Src	Scrn (comp, non)	Ctrl	RD (comp adj) (95% CI)	RD (95% CI)
CRC				
Funen	4.35	3.59	6.52	4.62	-0.30% (-0.94, 0.33)	-0.27% (-0.72, 0.19)
MN	2.32	2.04	5.23	2.98	-0.72% (-1.24, -0.20)	-0.66% (-1.13, -0.18)
	3.32	**2.75**	**6.27**	**3.87**	**-0.55% (-0.96, -0.15)**	**-0.45% (-0.78, -0.13)**
All cause						
Funen	72.84	67.4	83.89	73.02	-1.49% (-2.47, -0.52)	-0.18% (-0.88, 0.52)
MN	70.6	68.87	84	71.09	-0.98% (-2.10, 0.13)	-0.50% (-1.51, 0.52)
	72.11	**67.99**	**83.9**	**72.4**	**-1.27% (-2.00, -0.54)**	**-0.28% (-0.86, 0.29)**




Cumulative mortality (compliance adjusted)
0.0
0.2
0.4
0.6
0
10
20
30
Time (years)
Group
control
screened


Sub
Src
Scrn n
Scrn dths
Ctrl n
Ctrl dths
RR (comp adj) (95% CI)
RR p for (95% CI) int
Sex 0.279
Male Funen 14863 393 14842 431 0.88 (0.70, 1.10) 0.92 (0.80, 1.07)
MN 7444 105 7434 154 0.56 (0.41, 0.77) 0.63 (0.48, 0.82)
22307 498 22276 585 0.75 (0.62, 0.90) 0.85 (0.75, 0.96)
Female Funen 16103 393 16111 420 0.93 (0.74, 1.19) 0.96 (0.83, 1.11)
MN 8143 132 7960 141 0.87 (0.65, 1.17) 0.92 (0.72, 1.18)
24246 525 24071 561 0.91 (0.75, 1.09) 0.95 (0.84, 1.07)
Age 0.251
70+ yr Funen 4836 138 4893 149 0.65 (0.33, 1.26) 0.86 (0.60, 1.23)
MN 2699 60 2581 58 0.56 (0.27, 1.16) 0.66 (0.35, 1.26)
7535 198 7474 207 0.60 (0.37, 0.99) 0.81 (0.59, 1.11)
60-69 yr Funen 10264 286 10266 324 0.80 (0.60, 1.06) 0.87 (0.73, 1.05)
MN 6485 105 6446 156 0.61 (0.44, 0.85) 0.67 (0.51, 0.89)
16749 391 16712 480 0.71 (0.58, 0.88) 0.81 (0.69, 0.94)
50-59 yr Funen 10794 274 10737 296 0.88 (0.69, 1.13) 0.93 (0.78, 1.09)
MN 6092 71 6054 76 0.90 (0.62, 1.30) 0.96 (0.69, 1.32)
16886 345 16791 372 0.89 (0.72, 1.09) 0.93 (0.80, 1.08)
Male 0.469
70+ yr Funen 2161 57 2186 63 * 1.18 (0.74, 1.88)
MN 1222 27 1196 22 0.58 (0.27, 1.24) 0.82 (0.40, 1.64)
3383 84 3382 85 * 1.05 (0.71, 1.55)
60-69 yr Funen 4824 152 4803 158 0.85 (0.55, 1.31) 0.93 (0.69, 1.25)
MN 3051 42 3027 82 0.35 (0.21, 0.58) 0.42 (0.27, 0.66)
7875 194 7830 240 0.59 (0.42, 0.81) 0.73 (0.57, 0.94)
50-59 yr Funen 5335 136 5282 163 0.73 (0.53, 1.00) 0.82 (0.65, 1.03)
MN 3040 35 3073 50 0.64 (0.39, 1.04) 0.73 (0.47, 1.12)
8375 171 8355 213 0.70 (0.54, 0.91) 0.80 (0.65, 0.98)
Female 0.196
70+ yr Funen 2675 81 2706 86 0.53 (0.25, 1.15) 0.80 (0.52, 1.25)
MN 1477 33 1385 36 0.53 (0.22, 1.23) 0.63 (0.30, 1.35)
4152 114 4091 122 0.53 (0.30, 0.94) 0.76 (0.52, 1.11)
60-69 yr Funen 5440 134 5457 166 0.70 (0.48, 1.03) 0.81 (0.63, 1.05)
MN 3434 63 3419 74 0.83 (0.54, 1.26) 0.90 (0.62, 1.30)
10880 197 8876 240 0.75 (0.57, 1.00) 0.84 (0.68, 1.04)
50-59 yr Funen 5459 138 5453 133 1.04 (0.72, 1.50) 1.05 (0.83, 1.33)
MN 3052 36 2981 26 1.17 (0.69, 1.99) 1.38 (0.83, 2.28)
10918 174 8434 159 1.08 (0.80, 1.46) 1.10 (0.89, 1.37)
0.20
0.40
0.60
0.80
1.0
2.0

Risk difference (CRC)



Need to Know

Background: Studies have shown that biennial fecal occult blood test (FOBT) screening reduces mortality from colorectal cancer (CRC), but not overall mortality. Differences in benefit for men vs women, and by age, are unknown.

Findings: Compliance biennial FOBT screening reduces CRC mortality over 30 years, with a statistically significant reduction in all-cause mortality. The reduction in CRC mortality is greater in men than women—the benefit in women lags that of men by about 10 years.

Implications for patient care: Screening programs for CRC should ensure compliance with biennial FOBT to reduce CRC and overall mortality over the long term.