

Appendix: Supplementary material

Web-table 1: Procedural characteristics in women in 5-years categories. Numbers are percentages if not stated otherwise.

	NORCCAP			SCORE		PLCO			
	50-54	55-59	60-64	55-59	60-64	55-59	60-64	65-69	70-74
Compliance rate	60.4	65.9	66.1	55.1	52.9	82.4	81.8	79.8	76.4
Mean insertion (cm, sigmo)	44.1	43.4	43.3	NA	NA	NA	NA	NA	NA
Inadequate screen*	14.7	15.2	17.1	16.9	19.0	13.9	14.4	16.3	18.8
Cleansing (flexible sigmoidoscopy: good/adequate)	77.0	78.2	75.9	83.1	81.0	NA	NA	NA	NA
Cleansing (colonoscopy, good/adequate)	78.1	78.8	79.7	NA	NA	NA	NA	NA	NA
Referred colonoscopy	14.2	16.7	19.2	6.7	7.5	16.3	18.7	20.3	19.9
Attended colonoscopy (of those referred)	97.3	97.5	96.6	91.8	91.0	73.9	74.8	79.1	80.3
Coecum intubation rate (of those who had a colonoscopy)	86.3	86.2	84.2	70.9	76.6	NA	NA	NA	NA

*Inadequate screen was defined in NORCCAP and SCORE as less than good/adequate cleansing and failure to insert the colonoscope beyond the sigmoid-descending junction. In PLCO, inadequate screen was defined as visualization of less than 90% of the mucosa and insertion depth < 50cm.

Web-table 2: Procedural characteristics in men in 5-years categories. Numbers are percentages if not stated otherwise.

	NORCCAP			SCORE		PLCO			
	50-54	55-59	60-64	55-59	60-64	55-59	60-64	65-69	70-74
Compliance rate	57.8	62.5	61.7	63.0	59.6	85.9	86.7	86.5	84.9
Mean insertion (cm, sigmo)	49.2	48.7	47.4	NA	NA	NA	NA	NA	NA
Inadequate screen	14.6	16.0	15.5	11.4	13.2	6.2	6.5	7.7	8.7
Cleansing (flexible sigmoidoscopy, good/adequate)	75.1	75.5	74.9	88.6	86.9	NA	NA	NA	NA
Cleansing (colonoscopy, good/adequate)	79.7	76.3	74.1	NA	NA	NA	NA	NA	NA
Referred colonoscopy	19.2	25.3	28.5	11.0	13.4	26.2	29.4	29.9	27.7
Attended colonoscopy	92.9	95.3	94.2	92.9	96.2	72.6	72.4	73.8	72.9
Coecum intubation rate (of those who had a colonoscopy)	94.4	94.1	92.4	76.4	77.0	NA	NA	NA	NA

*Inadequate screen was defined in NORCCAP and SCORE as less than good/adequate cleansing and failure to insert the colonoscope beyond the sigmoid-descending junction. In PLCO, inadequate screen was defined as visualization of less than 90% of the mucosa and insertion depth < 50cm.

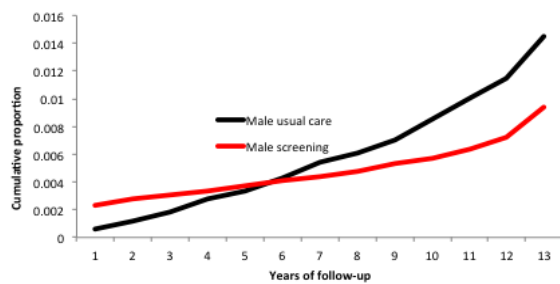
Web-table 3: Comparing CRC incidence overall and by site in screening versus control group in individuals 55-64 years old. Age- and sex-stratified pairwise comparisons using Mantel-Haenszel fixed effect model.

	Screening group vs control group
	RR (95% CI)
Colorectum overall	
Both sexes	0.80 (0.74-0.87)
Men	0.76 (0.69-0.85)
60-64	0.76 (0.66-0.88)
55-59	0.77 (0.65-0.90)
Women	0.85 (0.75-0.96)
60-64	0.97 (0.83-1.14)
55-59	0.72 (0.59-0.87)
Distal colon	
Both sexes	0.76 (0.68-0.85)
Men	0.73 (0.64-0.85)
60-64	0.75 (0.62-0.90)
55-59	0.72 (0.58-0.89)
Women	0.80 (0.67-0.96)
60-64	0.81 (0.63-1.04)
55-59	0.80 (0.61-1.04)
Proximal colon	
Both sexes	0.86 (0.77-0.97)
Men	0.82 (0.69-0.97)
60-64	0.81 (0.65-1.01)
55-59	0.83 (0.64-1.07)
Women	0.91 (0.77-1.07)
60-64	1.12 (0.91-1.39)
55-59	0.65 (0.49-0.86)

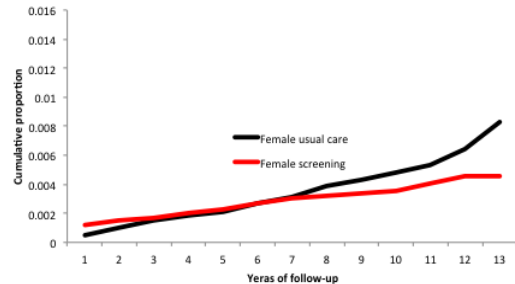
Abbreviations RR: Risk ratio, CI: Confidence interval

Web-figure 1: Cumulative proportion of individuals diagnosed with rectosigmoid colorectal cancer in PLCO, SCORE and NORCCAP. Panel A: Male 55-59 years. Panel B: Female 55-59 years. Panel C: Male 60-64 years. Panel D: Female 60-64 years.

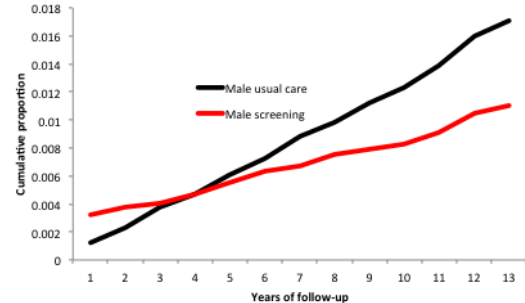
A: Male 55-59 years



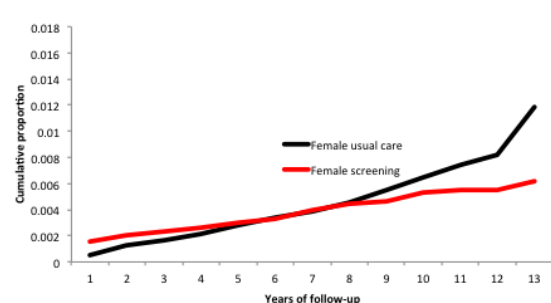
B: Female 55-59 years



A: Male 60-64 years

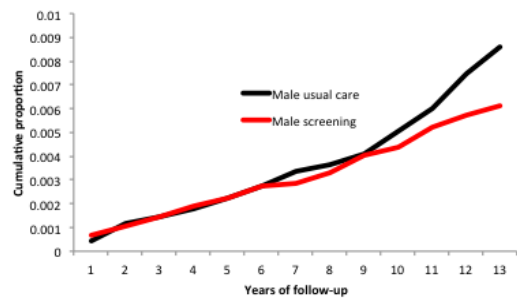


B: Female 60-64 years

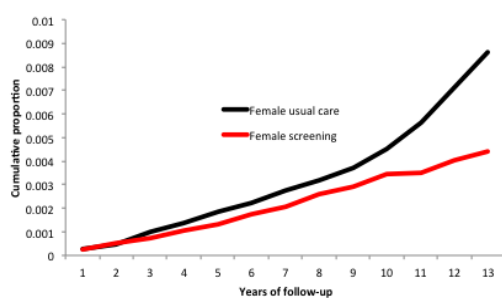


Web-figure 2: Cumulative proportion of individuals diagnosed with proximal colorectal cancer (proximal to the sigmoid colon) in PLCO, SCORE and NORCCAP. Panel A: Male 55-59 years. Panel B: Female 55-59 years. Panel C: Male 60-64 years. Panel D: Female 60-64 years.

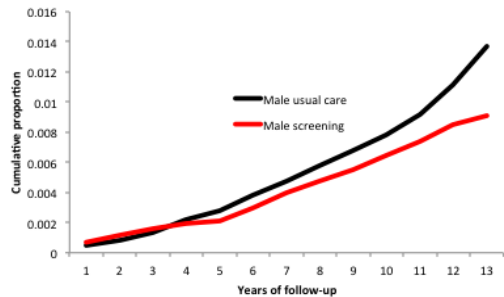
A: Male 55-59 years



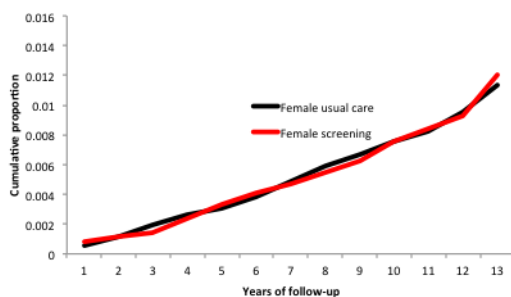
B: Female 55-59 years



A: Male 60-64 years



B: Female 60-64 years



Web-table 4: Comparing CRC incidence overall and by site in screening versus control group in the SCORE and NORCCAP trials (PLCO excluded). Overall, age- and sex-stratified pairwise comparisons using Mantel-Haenszel fixed effect model .

	Screening group vs control group
	RR (95% CI)
Colorectum overall	
Both sexes	0.81 (0.73-0.90)
Men	0.80 (0.69-0.92)
<60 years	0.81 (0.67-0.98)
≥60 years	0.78 (0.64-0.96)
Women	0.82 (0.80-0.96)
<60 years	0.74 (0.59-0.92)
≥60 years	0.92 (0.74-1.15)
Distal colon	
Both sexes	0.76 (0.66-0.88)
Men	0.76 (0.63-0.92)
<60 years	0.72 (0.56-0.93)
≥60 years	0.81 (0.62-1.05)
Women	0.77 (0.61-0.96)
<60 years	0.81 (0.60-1.09)
≥60 years	0.72 (0.51-1.01)
Proximal colon	
Both sexes	0.90 (0.76-1.06)
Men	0.88 (0.70-1.11)
<60 years	0.94 (0.69-1.29)
≥60 years	0.82 (0.58-1.14)
Women	0.92 (0.73-1.16)
<60 years	0.70 (0.49-0.99)
≥60 years	1.18 (0.73-1.61)

Abbreviations RR: Risk ratio, CI: Confidence interval

Web-table 5: Comparing colorectal cancer mortality in screening versus control group in individuals aged 55-64 years old. Overall, age- and sex-stratified pairwise comparisons using Mantel-Haenszel fixed effect model. The meta regression model includes indicator variables for the different trials (see methods section).

	Screening group vs control group
	RR (95% CI)
Colorectum overall	
Both sexes	0.77 (0.65-0.90)
Men	0.70 (0.57-0.86)
60-64	0.70 (0.53-0.93)
55-59	0.69 (0.50-0.96)
Women	0.87 (0.68-1.11)
60-64	1.07 (0.77-1.48)
55-59	0.68 (0.47-0.98)
Distal colon	
Both sexes	0.70 (0.55-0.87)
Men	0.60 (0.45-0.80)
60-64	0.57 (0.39-0.84)
55-59	0.64 (0.41-1.00)
Women	0.90 (0.63-1.30)
60-64	1.12 (0.68-1.83)
55-59	0.69 (0.39-1.21)
Proximal colon	
Both sexes	0.85 (0.67-1.06)
Men	0.84 (0.61-1.15)
60-64	0.97 (0.65-1.45)
55-59	0.67 (0.40-1.12)
Women	0.85 (0.61-1.19)
60-64	1.01 (0.65-1.58)
55-59	0.70 (0.43-1.14)

Abbreviations RR: Risk ratio, CI: Confidence interval