

Long term cancer risk in the UK FlexiSig Screening Trial

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UK Flexible Sigmoidoscopy Screening Trial

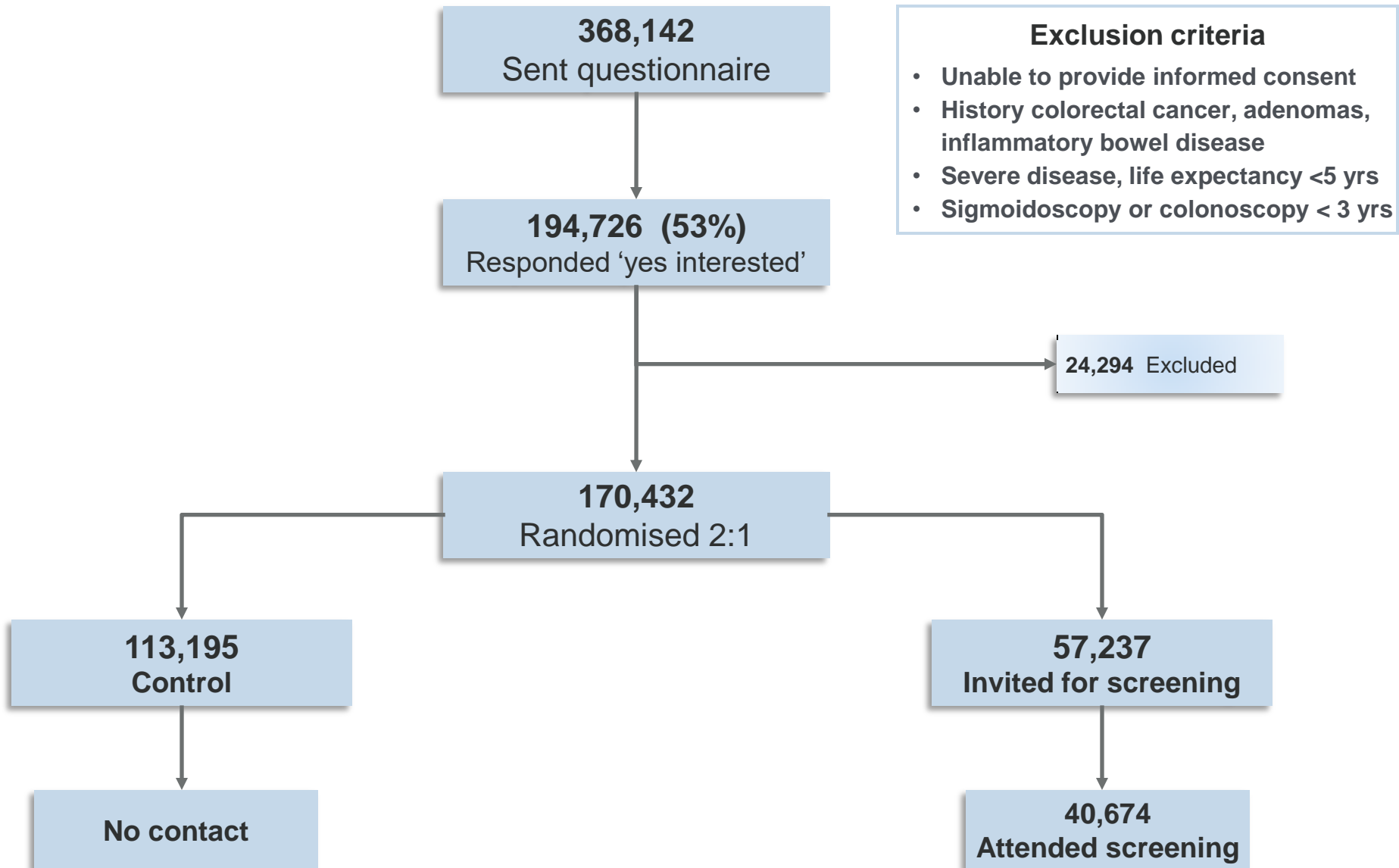


Examine efficacy and duration of effect of:

- once-only flexible sigmoidoscopy screen between 55 and 64 years
- removal of small polyps (< 10 mm) during screening
- colonoscopy only for high-risk adenomas:
 ≥ 3 , ≥ 10 mm, $\geq 25\%$ villous, high grade dysplasia



Trial recruitment



Participant characteristics by randomisation and compliance with screening

	Control group (n=112 936)	Intervention group (n=57 098)		
		Total (n=57 098)	Not screened (n=16 477)	Screened (n=40 621)
Age at randomization (years)	60.0 (2.9)	60.0 (2.9)	60.1 (2.9)	60.0 (2.9)
Sex				
Men	55 339 (49%)	49%	46%	50%
Women	57 597 (51%)	51%	54%	50%
Household size				
Single person	71 556 (63%)	63%	66%	62%
Two person	41 248 (37%)	36%	34%	37%
Other	132 (<1%)	<1%	<1%	<1%
Length of follow-up (years) *	17.1 (16.4-17.8)	17.1 (16.4-17.8)	17.0 (15.4-17.6)	17.1 (16.6-17.9)

Data are mean (SD), n (%) or median (IQR).

*Years from date of randomisation to date of death, emigration, loss to follow-up, or Dec 31, 2014.

Hazard ratios for CRC incidence and mortality in control and intervention groups after 17 years

	Control (n=112 936)		Intervention (n=57 098)		HR (95% CI); intervention vs control	p value
	Cases	Rate*	Cases	Rate*		
Incidence						
All-site	3253	184	1230	137	0.74 (0.70-0.80)	<0.0001
Distal	1987	112	592	66	0.59 (0.54-0.64)	<0.0001
Proximal	1255	71	612	68	0.96 (0.87-1.06)	0.436
Mortality						
Colorectal cancer	996	56	353	39	0.70 (0.62-0.79)	<0.0001
Distal colorectal cancer	544	31	149	17	0.54 (0.45-0.65)	<0.0001
Proximal colon cancer	403	23	185	21	0.91 (0.76-1.08)	0.262

* Rates are per 100 000 person-years

Hazard ratios for CRC incidence and mortality by randomisation and screening compliance after 17 years

	Control (n=112 936)		Intervention (n=57 098)				HR (95% CI); screened vs control group
			Not screened (n=16 477)		Screened (n=40 621)		
	Cases	Rate*	Cases	Rate*	Cases	Rate*	
Incidence							
All-site	3253	184	454	184	776	120	0.65 (0.59-0.71)
Distal	1987	112	267	108	325	50	0.44 (0.38-0.50)
Proximal	1255	71	182	73	430	66	0.95 (0.83-1.09)
Mortality							
Colorectal cancer (CRC)	996	56	138	55	215	33	0.59 (0.49-0.70)
Distal CRC	544	31	83	33	66	10	0.34 (0.26-0.46)
Proximal colon cancer	403	23	50	20	135	21	0.88 (0.70-1.10)
Non-CRC causes	25 413	1427	4716	1893	8210	1257	1.01 (0.97-1.04)
All cause	26 409	1483	4854	1948	8425	1290	0.99 (0.96-1.02)

* Rates are per 100 000 person-years

Colorectal cancer incidence and mortality by randomisation and compliance with screening after 10 years and 17 years

	Screened vs. control Hazard ratio adjusted* (95% CI)	Screened vs control Hazard ratio adjusted* (95% CI)
	10 years	17 years
Incidence		
All-site colorectal cancer	0.67 (0.60 - 0.76)	0.65 (0.59 - 0.71)
Distal	0.50 (0.42 - 0.59)	0.44 (0.38 - 0.50)
Proximal	0.97 (0.80 - 1.17)	0.95 (0.83 - 1.09)
Mortality		
Colorectal cancer	0.57 (0.45 - 0.72)	0.59 (0.49 - 0.70)

Cuzick et al. Stat Med. 1997; 16:1017-1029.

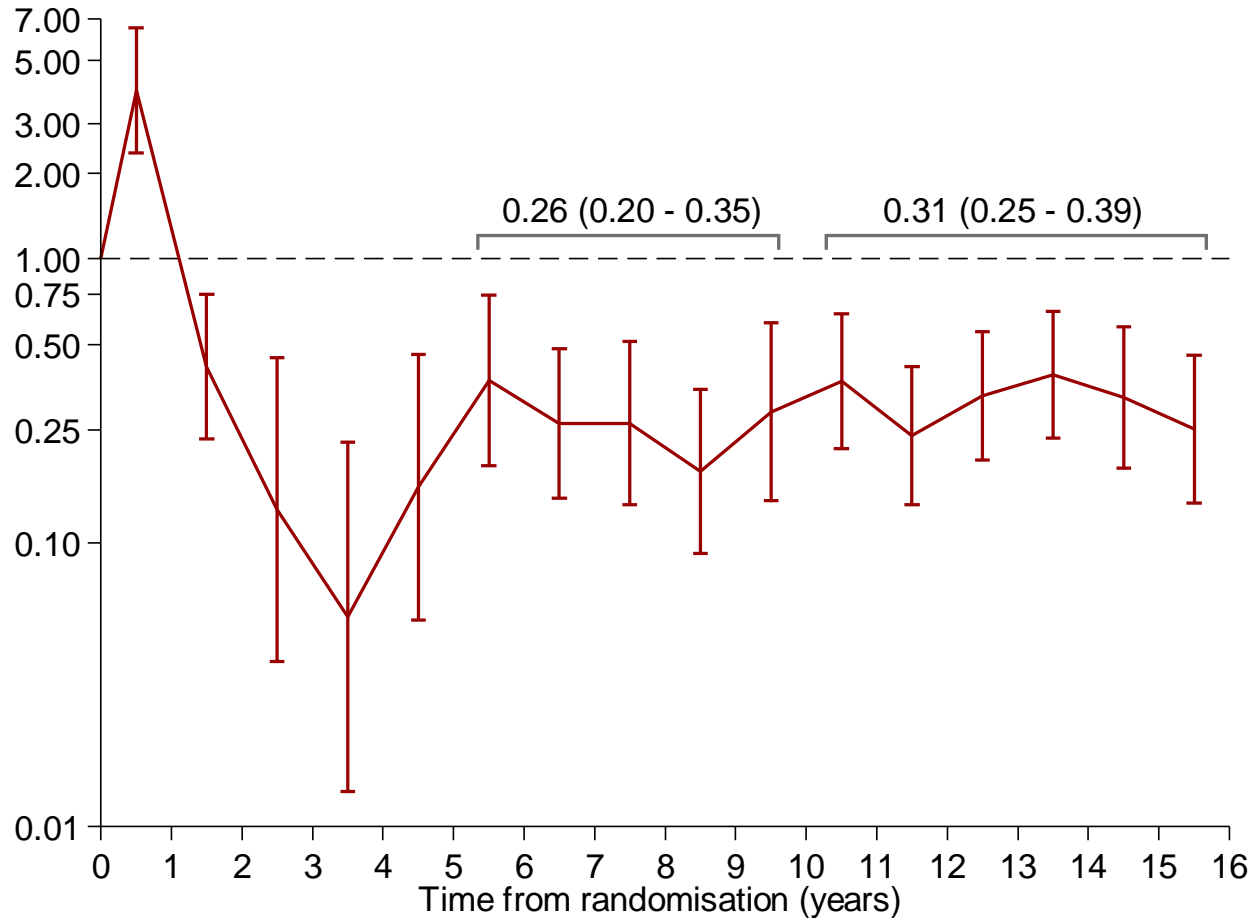
• Rates are per 100 000 person-years

** Adjusted for non-compliance

Atkin et al., Lancet 2017; 389: 1299–311

Annual rate ratios for distal CRC incidence

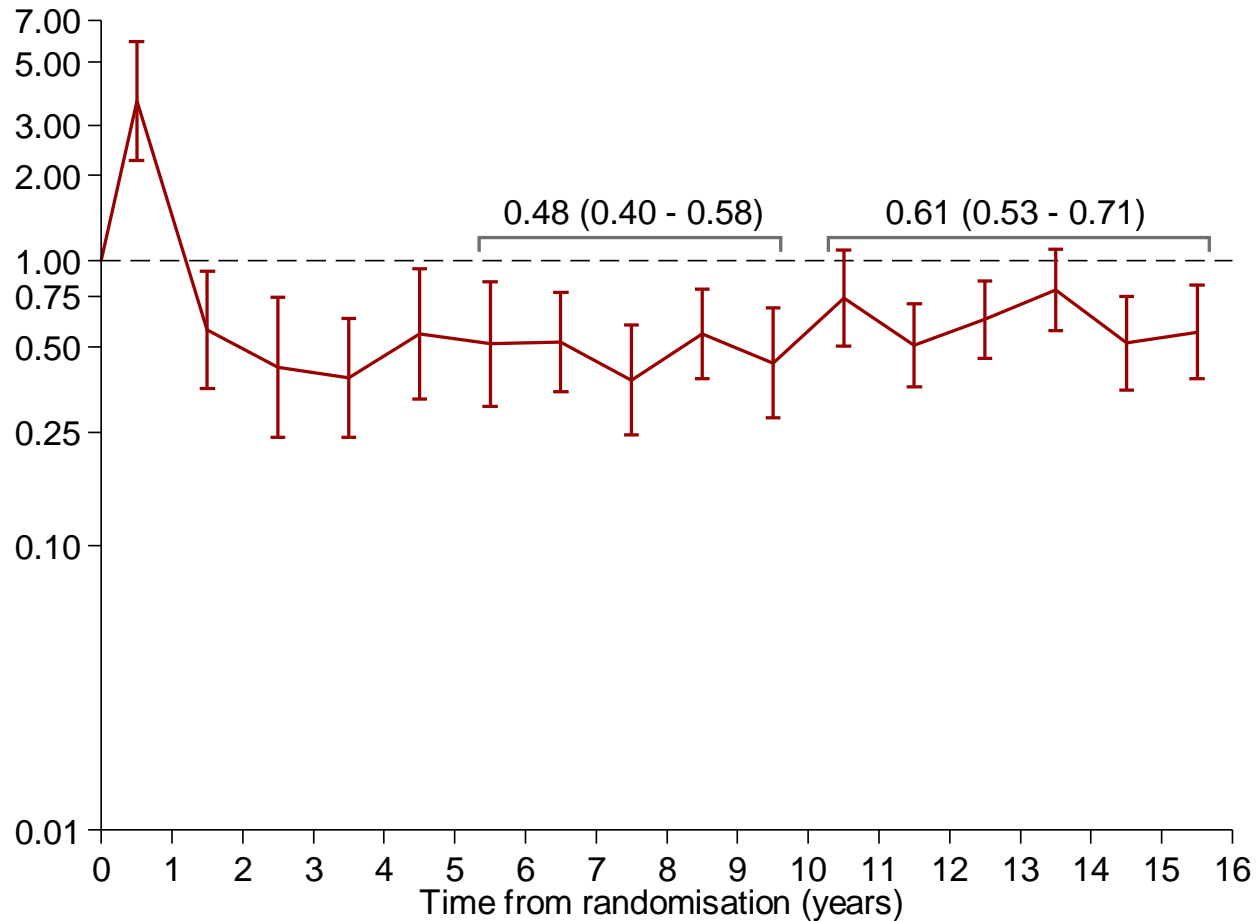
Screened versus control group*



*Adjusted for non-compliance with screening.

Annual rate ratios for all-site CRC incidence

Screened versus control group*



*Adjusted for non-compliance with screening.

Hazard ratios for CRC incidence by sex

	Hazard ratio (95% CI); Intervention vs control	Hazard ratio (95% CI); screened vs control
All sites		
Men	0.70 (0.65-0.77)	0.60 (0.53-0.68)
Women	0.81 (0.73-0.89)	0.73 (0.63-0.84)
Distal		
Men	0.58 (0.52-0.65)	0.44 (0.37-0.51)
Women	0.60 (0.51-0.70)	0.44 (0.35-0.55)
Proximal		
Men	0.89 (0.78-1.02)	0.86 (0.71-1.03)
Women	1.05 (0.91-1.20)	1.07 (0.87-1.31)

Hazard ratios for CRC mortality by sex

	Hazard ratio (95% CI); Intervention vs control	Hazard ratio (95% CI); screened vs control
CRC		
Men	0.67 (0.57-0.79)	0.55 (0.44-0.69)
Women	0.74 (0.61-0.90)	0.65 (0.49-0.84)
Distal CRC		
Men	0.51 (0.41-0.64)	0.32 (0.23-0.45)
Women	0.61 (0.45-0.83)	0.39 (0.23-0.66)
Proximal CC		
Men	0.95 (0.75-1.21)	0.94 (0.67-1.30)
Women	0.86 (0.67-1.10)	0.82 (0.59-1.13)
Non-CRC		
Men	1.02 (0.99-1.04)	1.03 (0.98-1.07)
Women	0.99 (0.95-1.02)	0.98 (0.93-1.03)
All cause		
Men	1.00 (0.98-1.03)	1.00 (0.96-1.05)
Women	0.98 (0.95-1.01)	0.96 (0.91-1.02)

Number needed to screen to prevent one CRC by sex

	Number needed to screen to prevent one event (95% CI)
All participants	
Diagnosis of CRC	98 (81-125)
CRC death	270 (204-397)
CRC death (verified)	220 (171-307)
Men	
Diagnosis of colorectal cancer	70 (57-91)
Colorectal cancer death	204 (149-323)
Colorectal cancer death (verified)	162 (123-239)
Women	
Diagnosis of colorectal cancer	165 (113-308)
Colorectal cancer death	402 (249-1039)
Colorectal cancer death (verified)	345 (220-798)

Hazard ratios for CRC incidence by age group

Age group (years) & sub-site	Hazard ratio (95% CI); Intervention vs control	Hazard ratio (95% CI); screened vs control
All sites		
55-59	0.74 (0.67-0.82)	0.64 (0.56-0.74)
60-64	0.75 (0.69-0.82)	0.65 (0.58-0.74)
Distal		
55-59	0.56 (0.48-0.64)	0.41 (0.34-0.50)
60-64	0.61 (0.54-0.69)	0.46 (0.38-0.55)
Proximal		
55-59	0.99 (0.85-1.15)	0.99 (0.80-1.22)
60-64	0.94 (0.83-1.07)	0.92 (0.77-1.09)

Hazard ratios for CRC mortality by age group

Age group (years) & sub-site	Hazard ratio (95% CI); Intervention vs control	Hazard ratio (95% CI); screened vs control
CRC		
55-59	0.67 (0.55-0.81)	0.52 (0.39-0.69)
60-64	0.72 (0.62-0.84)	0.63 (0.51-0.78)
Distal CRC		
55-59	0.51 (0.39-0.67)	0.30 (0.17-0.44)
60-64	0.56 (0.44-0.71)	0.40 (0.28-0.56)
Proximal CC		
55-59	0.87 (0.66-1.15)	0.82 (0.55-1.21)
60-64	0.93 (0.74-1.15)	0.91 (0.68-1.20)
Non-CRC		
55-59	1.01 (0.98-1.05)	1.02 (0.97-1.08)
60-64	0.99 (0.97-1.02)	0.99 (0.95-1.03)
All cause		
55-59	1.00 (0.97-1.03)	1.00 (0.95-1.05)
60-64	0.98 (0.96-1.01)	0.98 (0.94-1.02)

Number needed to screen to prevent one CRC death by age group

	Number needed to screen to prevent one event (95% CI)
All participants	
Diagnosis of colorectal cancer	98 (81-125)
Colorectal cancer death	270 (204-397)
Colorectal cancer death (verified)	220 (171-307)
Age 55-59 years	
Diagnosis of colorectal cancer	111 (85-161)
Colorectal cancer death	288 (201-507)
Colorectal cancer death (verified)	244 (174-407)
Age 60-64 years	
Diagnosis of colorectal cancer	87 (68-122)
Colorectal cancer death	252 (172-470)
Colorectal cancer death (verified)	200 (142-330)

Conclusions

Thank you.

Any questions?