Imperial College London

UK Flexible Sigmoidoscopy Screening Trial

Colorectal cancer incidence and mortality reduction 11 years after a single screening examination

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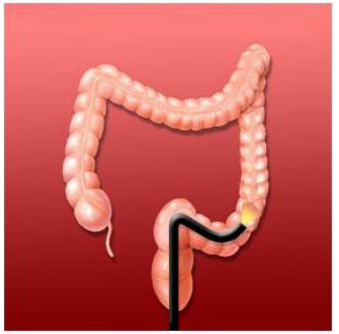
UK Flexible Sigmoidoscopy Screening Trial

Examine efficacy and duration of effect of:

- a once-only flexible sigmoidoscopy screen between ages 55 and 64 years
- removal of small polyps (< 10 mm) during screening
- colonoscopy only for high-risk adenomas:

  ≥3, ≥ 10 mm, ≥ 25% villous, high grade dysplasia



Atkin et al., J Med Screen 2001;8:137-

Outcomes

Primary

- Incidence colorectal cancer, all sites
- Mortality due to colorectal cancer

Sample size: 170,000

- 90% power
- 20% reduction in CRC incidence at 10 years, mortality at 15 years
- 2:1 ratio of controls to intervention (screening) groups
- 55% attendance for screening

Secondary

- Incidence distal cancer (rectum and sigmoid colon)
- Incidence proximal cancer (proximal to the sigmoid colon)
- All-cause mortality

Atkin et al. Lancet. 2010;375: 1624-33

Trial Centres

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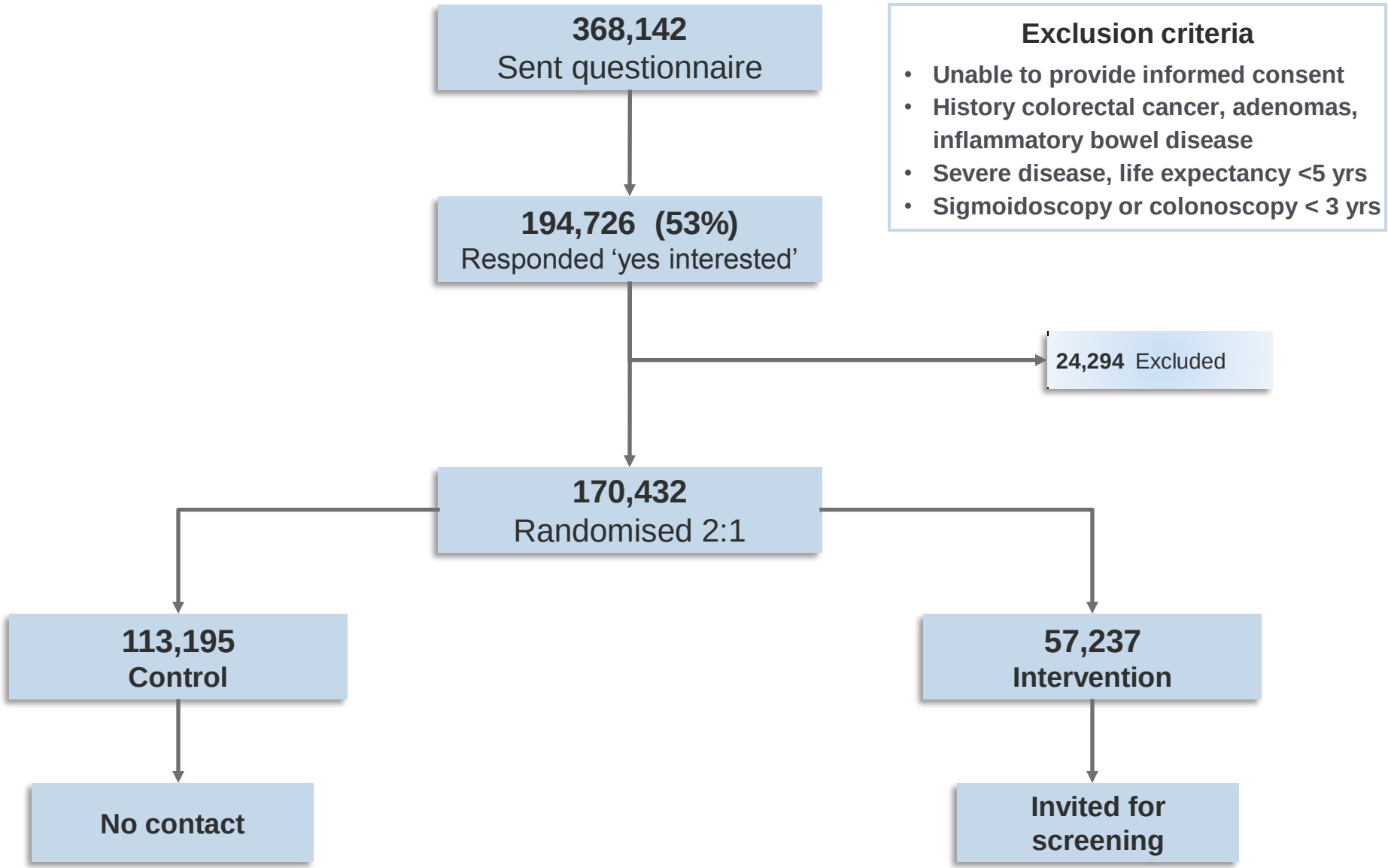
Trial recruitment



Exclusion criteria

- Unable to provide informed consent
- History colorectal cancer, adenomas, inflammatory bowel disease
- Severe disease, life expectancy <5 yrs
- Sigmoidoscopy or colonoscopy < 3 yrs

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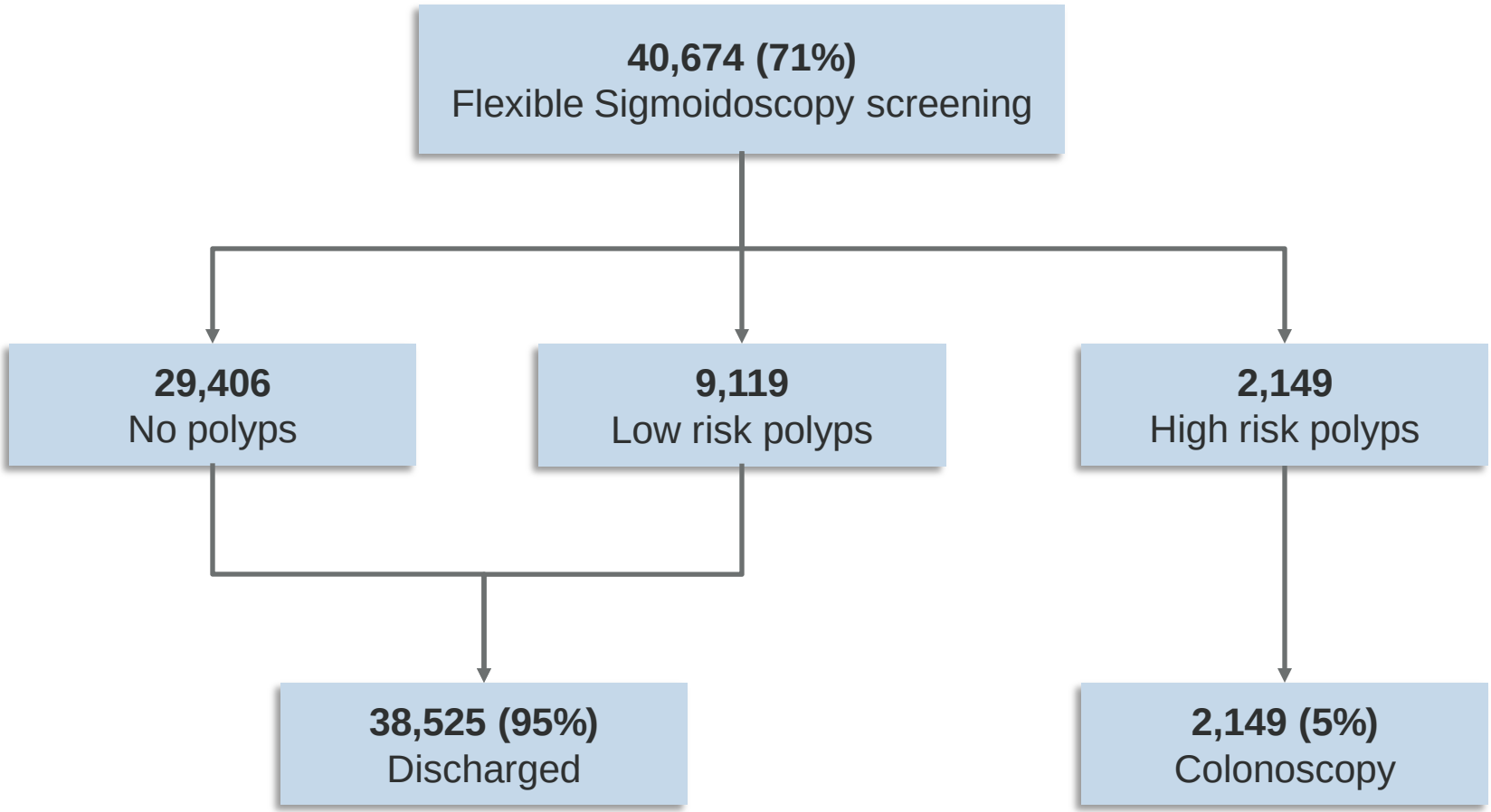
Baseline results of screening



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Follow-up

Median follow-up time

- 11.2 years
- 1.8 million person-years

Sources of data for whole UK

- NHS Central Register

Cancer registrations, dates of death, emigrations, name changes

- Office for National Statistics

Causes of death, underlying cause of death

- UK cancer registries, Hospital Episodes Statistics (HES)

Reduce time to ascertainment of cancer registrations

Follow-up censored

- Emigration, death or 31st December 2008

Atkin et al. Lancet. 2010;375: 1624-33

RESULTS

1. **Intent-to-treat analysis**
   - Compared intervention and control groups, irrespective of attendance
   - Effectiveness in those invited for screening

2. **Per-protocol analysis**
   - Compared screened and control groups
   - Adjusted for non-compliance with screening to avoid bias
   - *Cuzick, J, Edwards R Segnan N. Stat Med. 1997; 16:1017-1029.*
   - Effectiveness in those undergoing the screening

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Intent-to-treat analysis

	Control group 112,939		Intervention group 57,099		Intervention vs. Control	
	Cases N	Rate /100,000 py	Cases N	Rate /100,000 py	**Hazard ratio** *(95% CI)*	**p-value**
Incidence						
Distal	1,192	98	386	62	**0.64** *(0.57 - 0.72)*	<0.01
Proximal	628	51	311	50	**0.98** *(0.85 - 1.12)*	ns
Colorectal cancer all sites	1,818	149	706	114	**0.77** *(0.70 - 0.84)*	<0.01
Mortality						
Colorectal cancer	538	44	189	30	**0.69** *(0.59 - 0.82)*	<0.01

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Screened vs control groups (adjusted*)

	Control group (n=112,939)		Screened (n=40,621)		Screened vs. Control
	Cases N	Rate /100,000 py	Cases N	Rate /100,000 py	Hazard ratio adjusted* (95% CI)
Incidence					
Distal	1,192	98	215	48	**0.50** *(0.42 - 0.59)*
Proximal	628	51	224	50	**0.97** *(0.80 - 1.17)*
Colorectal cancer all sites	1,818	149	445	100	**0.67** *(0.60 - 0.76)*
Mortality					
Colorectal cancer	538	44	111	25	**0.57** *(0.45 - 0.72)*

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

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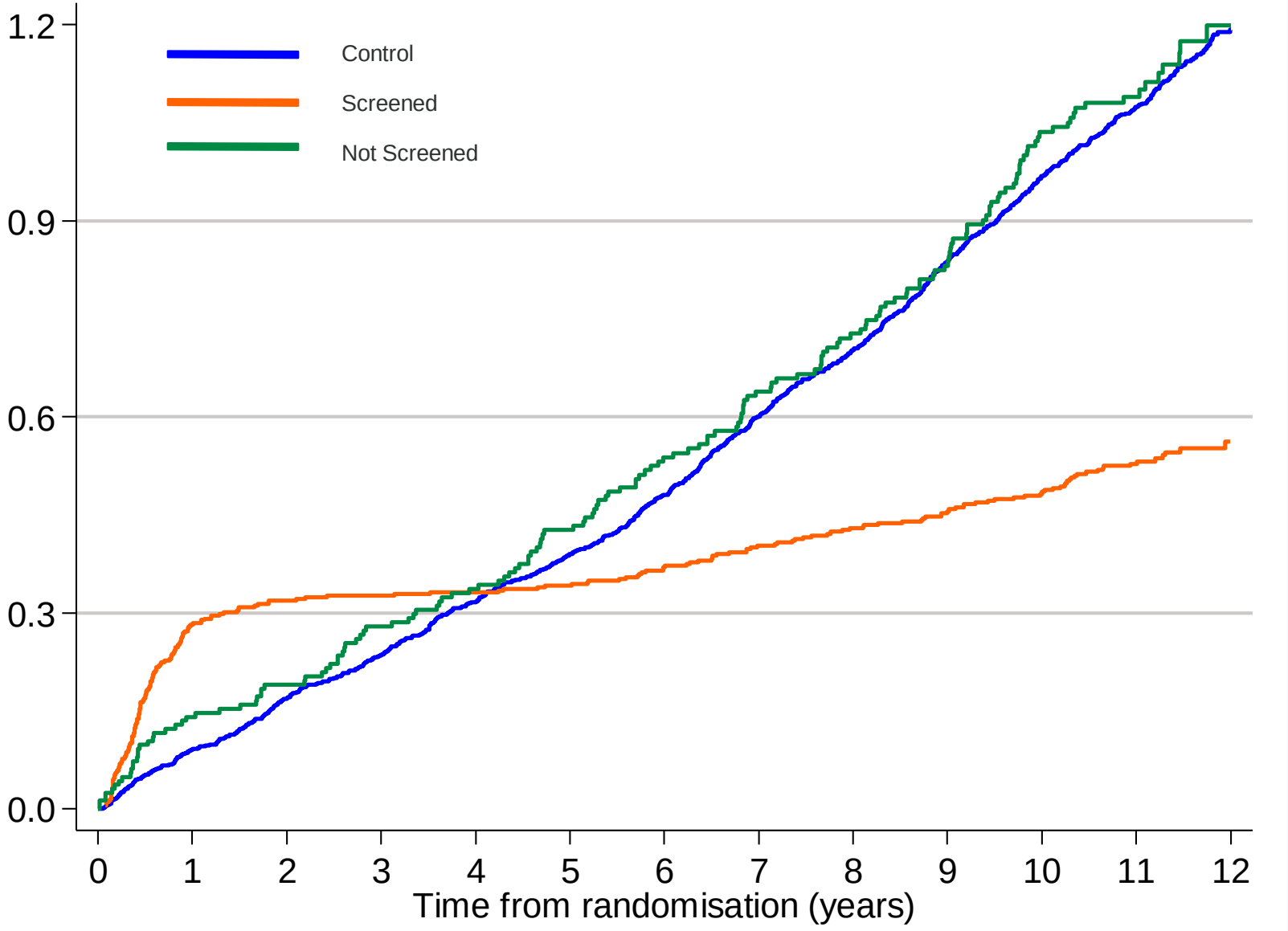
Cumulative incidence distal cancer (%)



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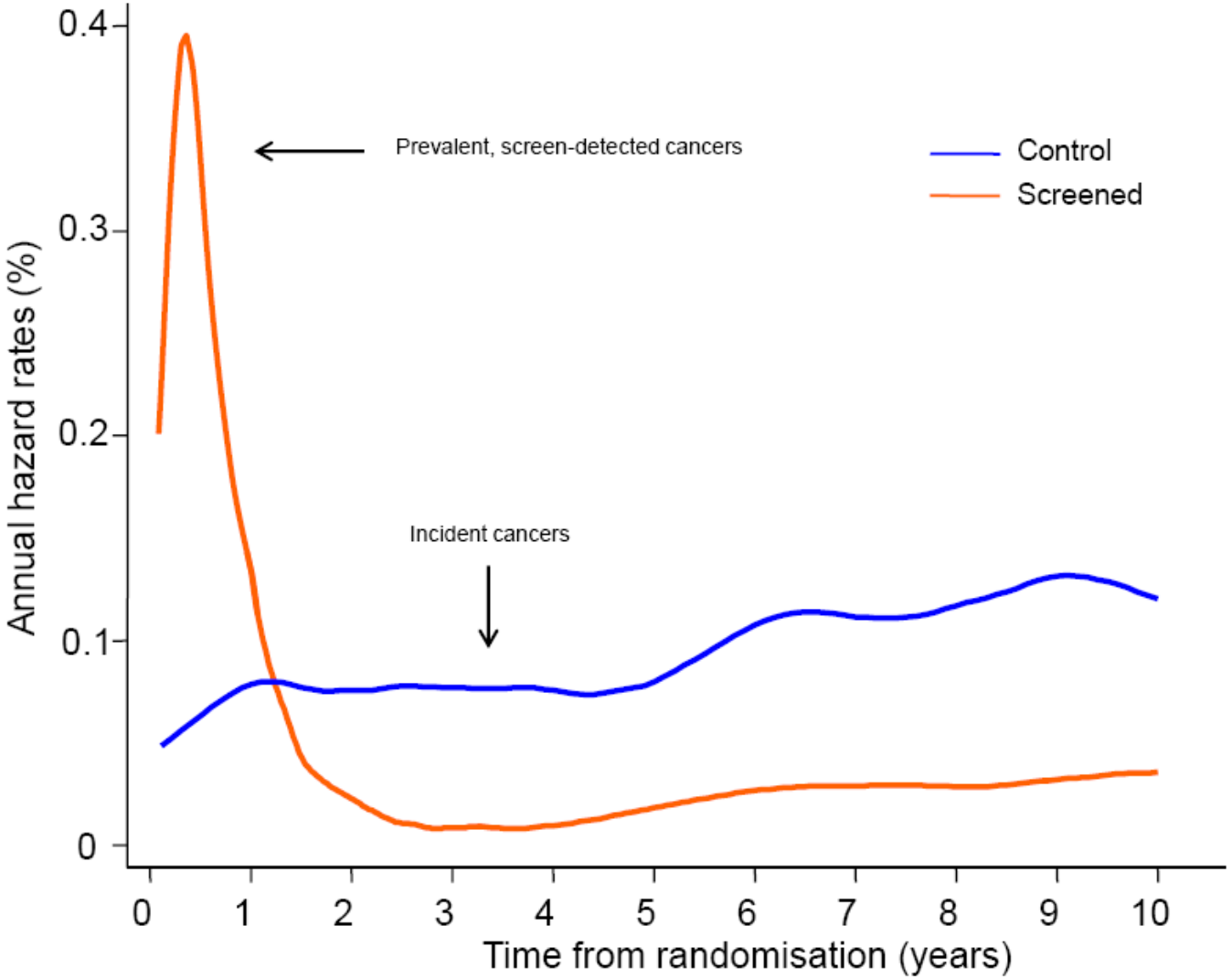
Annual incidence rates for distal cancer (%)



Curves are truncated at 10 years of follow-up because of incomplete ascertainment of cancers in the final calendar year of the study.

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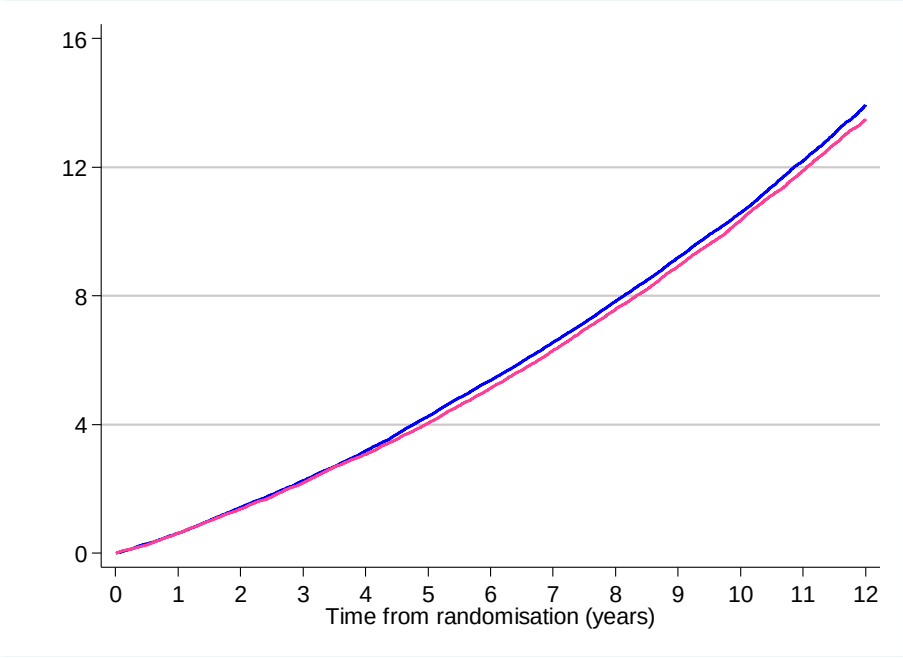
All-cause mortality

	Control group (n=112,939)		Screened (n=40,621)		Screened vs. Control
	Cases N	Rate /100,000 py	Cases N	Rate /100,000 py	Hazard ratio adjusted *(95% CI)*
Mortality					
All-cause	13,768	1,124	4,062	909	**0.95** *(0.91 - 1.00)*



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Efficacy of a once-only flexible sigmoidoscopy

After 11 years of follow-up, in people who had the screening:

- Cumulative incidence, including prevalent cancers detected at screening, reduced by
  - 50% for distal cancers (rectum and sigmoid colon)
  - 33% for colorectal cancer overall
- Colorectal cancer mortality was reduced by 43%
- No sign of a waning of effect at longer follow-up times

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Conclusion

Flexible sigmoidoscopy screening - with removal of small polyps during the exam- is safe, and when offered only once between ages 55 and 64 years, confers a substantial and long lasting benefit.

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Trial endoscopists

Number of examinations performed:

Andy Hart	4042
Andrew Pascoe	3723
John Painter	3354
Steve McKain	3305
Sheikh Ahmad	3301
John Martin	3237
Clare Adams	3140
Mark Watson	3139
Chris Macklin	3057
Nagi Iskander	2986
Tom Cecil	2949
Jon Hanson	2924
Richard Evans	2754
Roger Aubrey	309
Peter McIntyre	240

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UK Flexible Sigmoidoscopy Trial Investigators

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Royal Victoria Infirmary, NC: L Tweedy

Scottish Cancer Registry: D Brewster, C Storey, A McDonald, R Taylor

Singleton Hospital, Swansea: E S McKain, J Beynon, N D Carr, S Howell, N Williams, E Thomas, S John

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Southern General / Victoria Infirmary, Glasgow: D R McLellan

St Marks Hospital, Harrow: J P Martin, M R Jacyna, I C Talbot

St Mary's, Portsmouth: K Flashman

Thames Cancer Registry: H Møller, V Mak, J Maddams, C Okello, N Hanchett

Trent Cancer Registry: D Meechan, A Smith

University Hospital Aintree: J Sheard, T Austin, P Skaife

University Hospital of Wales: G Williams

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Whiston Hospital: S Morgan, R S Kiff, A Fitzgerald-Smith

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Thank You

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