UK Flexible Sigmoidoscopy Screening Trial

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

Wendy Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andy Hart,
John Northover, Max Parkin, Jane Wardle, Stephen Duffy, Jack Cuzick
& UK Flexible Sigmoidoscopy Trial Investigators
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:
  \[ \geq 3, \geq 10 \text{ mm}, \geq 25\% \text{ villous, high grade dysplasia} \]
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
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

Trial recruitment

368,142
Sent questionnaire

194,726 (53%)
Responded ‘yes interested’

170,432
Randomised 2:1

113,195
Control

No contact

57,237
Intervention

Invited for screening

24,294
Excluded

Atkin et al. Lancet. 2010;375: 1624-33
Baseline results of screening

40,674 (71%)
Flexible Sigmoidoscopy screening

- 29,406 (71%)
  No polyps
  38,525 (95%)
  Discharged

- 9,119 (21%)
  Low risk polyps

- 2,149 (5%)
  High risk polyps
  2,149 (5%)
  Colonoscopy

Atkin et al. Lancet. 2010;375: 1624-33
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
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
   - Effectiveness in those undergoing the screening
## Intent-to-treat analysis

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Intervention group</th>
<th>Intervention vs. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>112,939</td>
<td>57,099</td>
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<tr>
<td></td>
<td>Cases N</td>
<td>Rate /100,000 py</td>
<td>Cases N</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>1,192</td>
<td>98</td>
<td>386</td>
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<td>Proximal</td>
<td>628</td>
<td>51</td>
<td>311</td>
</tr>
<tr>
<td>Colorectal cancer all sites</td>
<td>1,818</td>
<td>149</td>
<td>706</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>538</td>
<td>44</td>
<td>189</td>
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Atkin et al. Lancet. 2010;375: 1624-33
## Screened vs control groups (adjusted*)

<table>
<thead>
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*Atkin et al. Lancet. 2010;375: 1624-33*
Cumulative incidence distal cancer (%)
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.
# All-cause mortality

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<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All-cause</td>
<td>13,768</td>
<td>4,062</td>
<td><strong>0.95 (0.91 - 1.00)</strong></td>
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<tr>
<td>Rate /100,000 py</td>
<td>1,124</td>
<td>909</td>
<td></td>
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**Cumulative all cause mortality (%)**

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

Efficacy of a once-only flexible sigmoidoscopy

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

<table>
<thead>
<tr>
<th>Name</th>
<th>Number of Examinations</th>
</tr>
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<tbody>
<tr>
<td>Andy Hart</td>
<td>4042</td>
</tr>
<tr>
<td>Andrew Pascoe</td>
<td>3723</td>
</tr>
<tr>
<td>John Painter</td>
<td>3354</td>
</tr>
<tr>
<td>Steve McKain</td>
<td>3305</td>
</tr>
<tr>
<td>Sheikh Ahmad</td>
<td>3301</td>
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<tr>
<td>John Martin</td>
<td>3237</td>
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<tr>
<td>Clare Adams</td>
<td>3140</td>
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<tr>
<td>Mark Watson</td>
<td>3139</td>
</tr>
<tr>
<td>Chris Macklin</td>
<td>3057</td>
</tr>
<tr>
<td>Nagi Iskander</td>
<td>2986</td>
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<tr>
<td>Tom Cecil</td>
<td>2949</td>
</tr>
<tr>
<td>Jon Hanson</td>
<td>2924</td>
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<tr>
<td>Richard Evans</td>
<td>2754</td>
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<tr>
<td>Roger Aubrey</td>
<td>309</td>
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<tr>
<td>Peter McIntyre</td>
<td>240</td>
</tr>
</tbody>
</table>

Number of examinations performed:

Atkin et al. Lancet. 2010;375: 1624-33
UK Flexible Sigmoidoscopy Trial Investigators

Bolton Hospital/Christie Hospital, Manchester: J E Painter, J H Hobbiss, A J M Watson, S T O'Dwyer, S Wells, J H Shanks, N Y Haboubi, D Bisset, R Jones, N Warburton, M Parkinson, D Butler, B F Warren, L Lane, C Cunningham

Business Services Organisation, GRO, Northern Ireland: S Fitzpatrick

Eastern Cancer Registration and Information Centre (ECRIC): J Rashbass, K Wright

Gartnavel General / Western Infirmary, Glasgow: F Duthie, L Swan

Glasgow Royal Infirmary: N Y Iskander, C S McArdle, I Finlay, T G Cooke, J H Anderson, A K Foulis, R Mckee

Good Hope Hospital/ Birmingham Heartlands Hospital: S Stewart, P Colloby

John Radcliffe Hospital, Oxford: A L Pascoe, N J Mortensen, B F Warren

Leeds General Infirmary: C P Macklin, P J Finan, P Quirke, P Senior, P M Sagar, D Jayne, N S Ambrose, A Ghanouni

Leicester General Hospital: A R Hart, J F Mayberry, A C B Wicks, W M Thomas, E H Mackay, R Harrison (and all the histology secretaries), D Hemingway, A Scott, J de Caestecker, D Sharpec

NHSIC: P Wall, J Gray


North West Cancer Intelligence Service (NWCIS): T Moran, C Jones, S Bishop, G Flatt, L Shack

Northern and Yorkshire Cancer Registry & Information Service (NYCRIS): D Forman, P Deer, M Day, E Morris, J Thomas

Northern Ireland Cancer Registry (NICR): A Gavin, R Middleton

ONS: P Goldblatt, A Loveday, S Dewane

Oxford Cancer Intelligence Unit (OCIU): M Roche, N Kennedy

Queen Alexandra Hospital, Portsmouth: T D Cecil, M R Thompson, A Senapati, N J E Marley

Queen Elizabeth Hospital, Birmingham: C Adams, D G Morton, M R B Keighley, D S A Sanders, J Moore, J Bradbury

Queen Elizabeth Hospital, Gateshead/Newcastle General Hospital: J M Hanson, W J Cunliffe, C D M Griffiths, J Varma, M K Bennett, J A Henry, S M Plusa

Queen Elizabeth II Hospital, Welwyn Garden City: P B McIntyre, R Aubrey, A Fattah, M Al Izzè

Royal Gwent Hospital, Newport/Llandough Hospital: S S Ahmad, K D Vellacott, A G Radcliffe, I W Thompson, N S Dallimore, E Pilley, M Jones, J Torkington

Royal Liverpool Hospital: R C Evans, M S Green, J M Rhodes, F Campbell, P Reid

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

South West Cancer Intelligence Service (SWCIS): J Verne, A Pring, M Illes

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

Welsh Cancer Intelligence & Surveillance Unit (WCISU): J Stewart, L Vipond

West Midlands Cancer Intelligence Unit (WMCIU): G Lawrence, V Madurasinge, R Oakes, G Barrett

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

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