

The prevention of colorectal cancer by colonoscopic surveillance in individuals with a family history of colorectal cancer: a sixteen year prospective follow-up study.

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# Aim

- Do individuals with moderate risk familial colorectal cancer benefit from colonoscopic surveillance?

# Methods

- Cancer Research UK Family Cancer Clinic at St Mark's Hospital established in 1986
  - March 1987 – December 2003
  - Previous description of clinic and results published (Houlston et al Br Med J 1990, Gaglia et al Gut 1995)
  - Colonoscopic surveillance if empiric lifetime mortality risk  $\geq 10\%$
  - Individuals flagged with NHS Central Register

# Methods

- Colonoscopy outcome (most advanced lesion):
  - High risk adenomas
  - Colorectal cancer

**Advanced neoplasia**
- Family History
  - HNPCC
  - 3FDR
  - 2FDR
  - 1FDR

**MRFCC**

# Statistical methods

- Standardised for age, sex and FH
  - Expected cancers = published cancer registry rates from England x RR (lowest, best, highest)
  - Expected cancer deaths based on published incidence and survival figures
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- $SIR/SMR = O/E \%$

# Results

- Initial colonoscopy
- N=1,678
  - F= 1,055 M=623
- Median age 41yrs

## Results: Colonoscopic findings at initial surveillance colonoscopy for MRFCC (% of risk-age group)

Risk Gp	Age gp		Normal %	MP %	LR Ad %	Multiple Ad %	HR Ad%	CRC %
HNPCC	20-34	n=213	83.2	5.9	6.4	0.9	2.7	0.9
	35-44	n=158	72.8	6.3	14.5	0.6	5.1	0.6
	45-64	n=164	53.8	16.0	19.1	3.1	7.4	0.6
	≥65	n=19	55.8	5.5	16.6	0.0	17.0	5.1
Overall			68.7	9.3	15.4		6.6	
3FDR	<45	n=177	83.6	6.2	9.6	0.0	0.6	0.0
	45-64	n=190	57.9	8.1	25.9	3.2	4.9	0.0
	≥65	n=24	54.2	16.6	0.0	8.3	16.6	4.2
	Overall		72.9	7.2	16.5		3.3	
2FDR	<45	n=316	80.9	7.7	9.6	0.3	1.5	0.0
	45-64	n=201	72.1	8.8	12.7	2.5	3.9	0.0
	≥65	n=19	33.3	20.5	35.9	5.3	5.0	0.0
	Overall		76.2	8.5	12.8		2.5	
1FDR	<45	n=139	87.9	8.3	3.0	0.0	0.8	0.0
	45-64	n=53	74.4	9.9	15.7	0.0	0.0	0.0
	≥65	n=5	57.1	22.0	0.0	20.9	0.0	0.0
	Overall		81.8	9.8	7.8		0.6	

Most advanced neoplastic lesion per examination  
Results are age standardised

# Results: follow-up colonoscopy

- 1,143 individuals from 740 families
- 8,865 person years
  - 3,020 in HNPCC      5,845 in MRFCC
- Median intervals (years)

HNPCC	3.3
3FDR	4.6
2FDR	5.1
1FDR	5.1

## Results: rates of advanced neoplasia per 1000 person yrs (person years)

### No advanced neoplasia on 1<sup>st</sup> surveillance colonoscopy

Age at next colonoscopy	MRFCC	HNPCC
20-34	0.0 (462)	3.6 (561)
35-44	1.2 (1646)	5.0 (803)
45-64	2.3 (3045)	6.7 (1351)
65+	4.0 (500)	19.7 (101)

### Advanced neoplasia present on 1<sup>st</sup> colonoscopy

	MRFCC	HNPCC
All ages	27.6 (144.8)	56.5 (124)

# Results: observed vs expected cancers and deaths

	No. individuals	Pers- yrs	Observed	Lowest risk estimate		Best risk estimate		Highest risk estimate	
				Expected	O/E%	Expected	O/E%	Expected	O/E%
1. Analysis of deaths from CRC (followed up to 31/12/2002)									
MRFCC	1124	9169	<b>2</b>	5.3	38	<b>10.7</b>	<b>19**</b>	19.33	10***
HNPCC	554	4004	<b>3</b>	5.05	59	<b>10.90</b>	<b>28*</b>	15.15	20***
2. Analysis of CRC in individuals followed for at least 3 years (up to 31/12/2001)									
MRFCC	894	7805	<b>4</b>	9.84	41	<b>19.93</b>	<b>20***</b>	35.92	11***
HNPCC	385	3285	<b>11</b>	8.92	123	<b>19.24</b>	<b>57</b>	26.76	41***
3. Analysis of CRC in individuals followed for at least 3 years (followed up to 31/12/2003)									
MRFCC	1028	10075	<b>4</b>	13.16	30.4**	<b>26.53</b>	<b>15.1***</b>	47.71	8**
HNPCC	467	4341	<b>11</b>	12.37	88.9	<b>26.63</b>	<b>41.3**</b>	37.11	30***

\* Twice 1-sided p<.05

\*\* Twice 1-sided p<.01

\*\*\* Twice 1-sided p<.001

† %O/E = 100 x Observed divided by Expected. It is often called the standardized mortality (or incidence) ratio

# Conclusions

- Surveillance effective in preventing CRC and decreasing mortality in MRFCC (and HNPPC)
- MRFCC
  - Start surveillance after 45 yrs (even 50?)
  - Consider longer surveillance intervals if no evidence of advanced neoplasia on initial colonoscopy
- HNPPC confirm need for short intervals

# Discussion

- Large cohort with long follow-up
- Substantial number of individuals from MRFCC families
- Prospective results of individuals normally undergoing surveillance compared O vs E

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