Results from the NHSBCSP, Flexisigmoidoscopy trial and EU guidelines

Phil Quirke

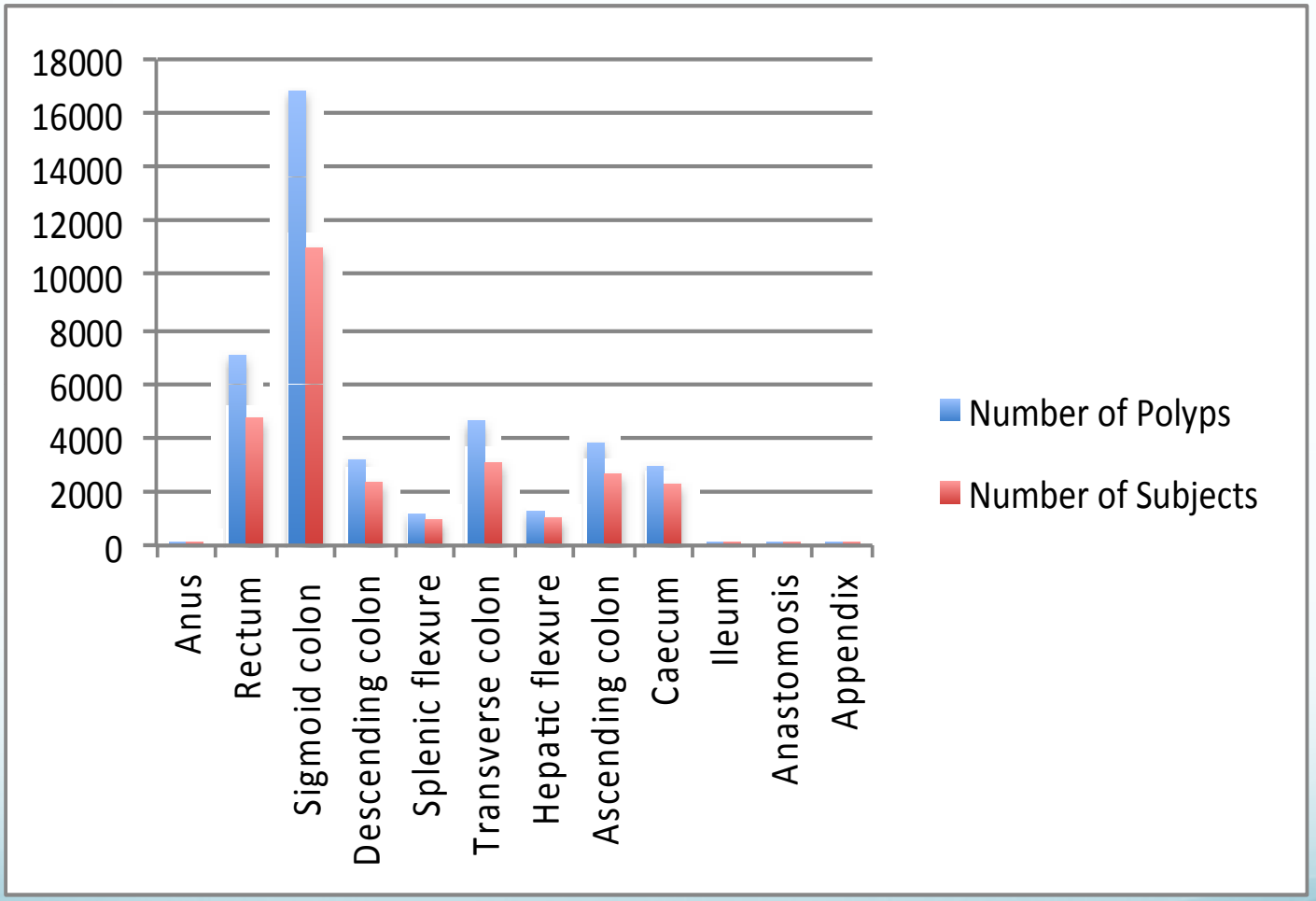
NHS Bowel Cancer Screening Programme

NCIN national cancer intelligence network

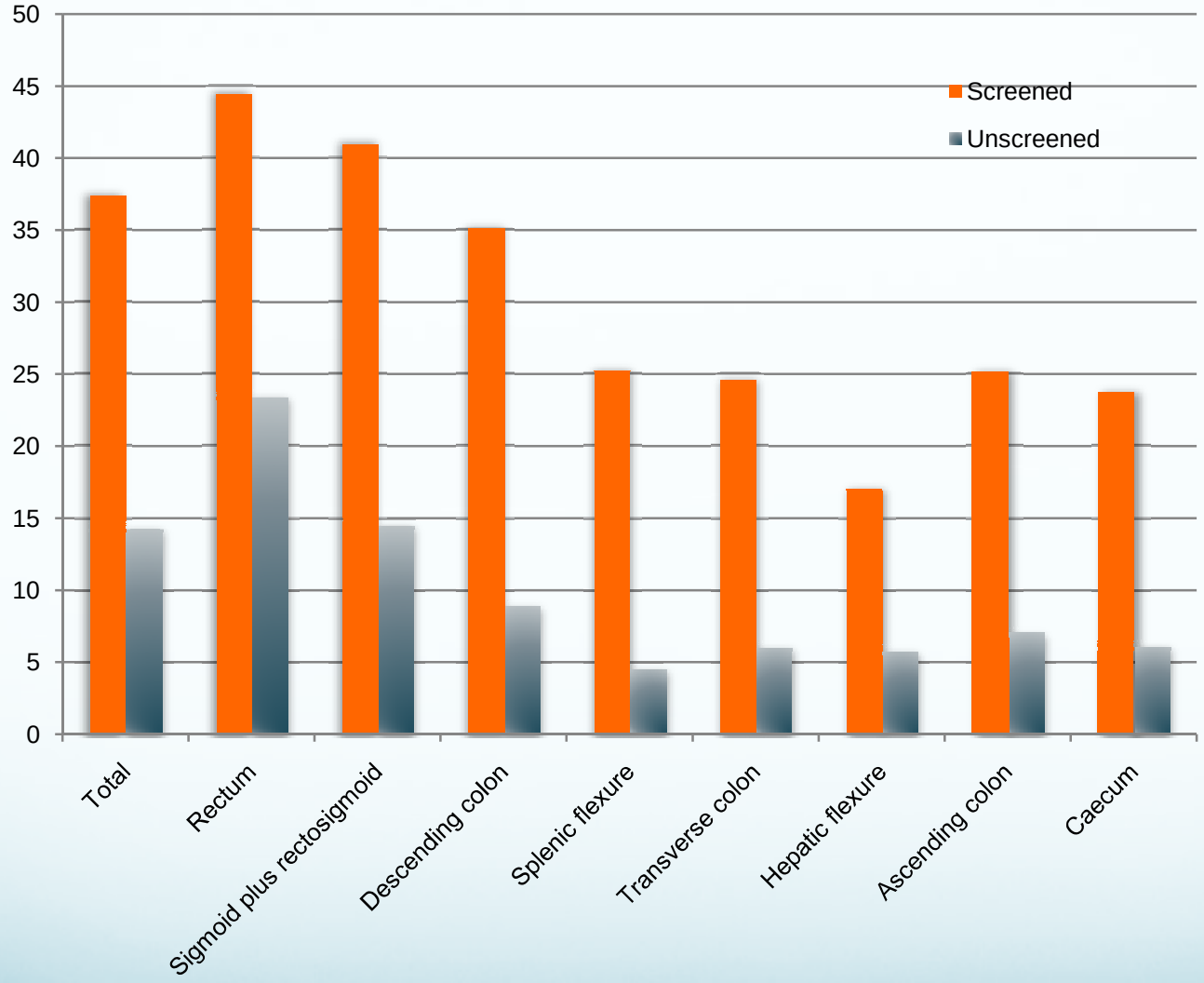
NHSBCSP

- April 2010
- 2% positive FOBT
- 44,520 adenomas
- 30,517 people
- > 4,000 cancers

Adenomas by site



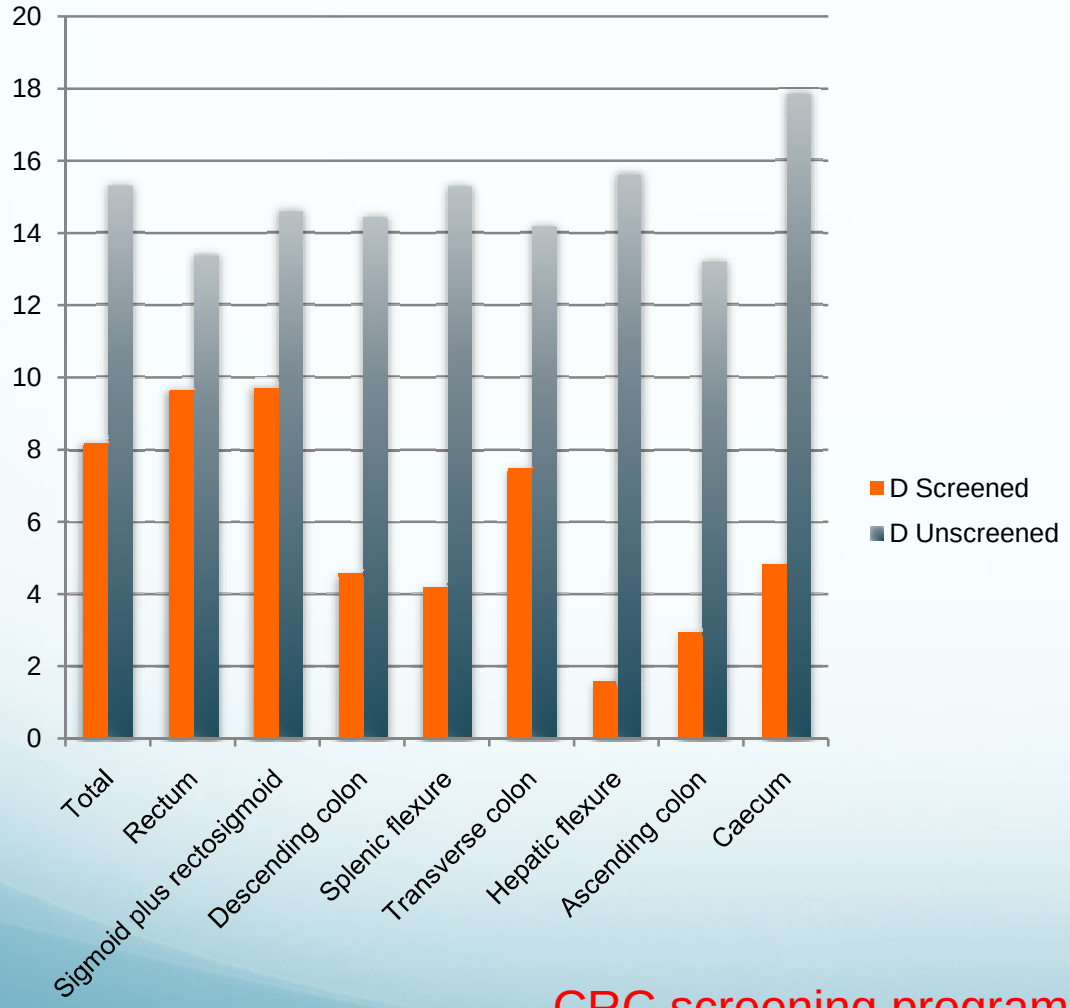
Total Stage A and by site



CRC screening programme n= 3,744 (Stage A n = 1401)

CRC outside programme n = 49,193 (Stage A n = 7136)

Total Stage D and site



	Screened	Unscreened
Total	8.2	14.8
Rectum	9.6	13.4
Sigmoid plus rectosigmoid	9.7	14.6
Descending colon	4.6	14.4
Splenic flexure	4.2	15.3
Transverse colon	7.5	14.2
Hepatic flexure	1.6	15.6
Ascending colon	3.0	13.2
Caecum	4.8	17.8

CRC screening programme n= 3,744 (stage D n = 307)

CRC outside programme n = 49,193 (stage D n =7279)

Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial

UK Flexible Sigmoidoscopy Screening Trial Investigators*

Lancet 2002; **359:** 1291–300
See Commentary page 1266

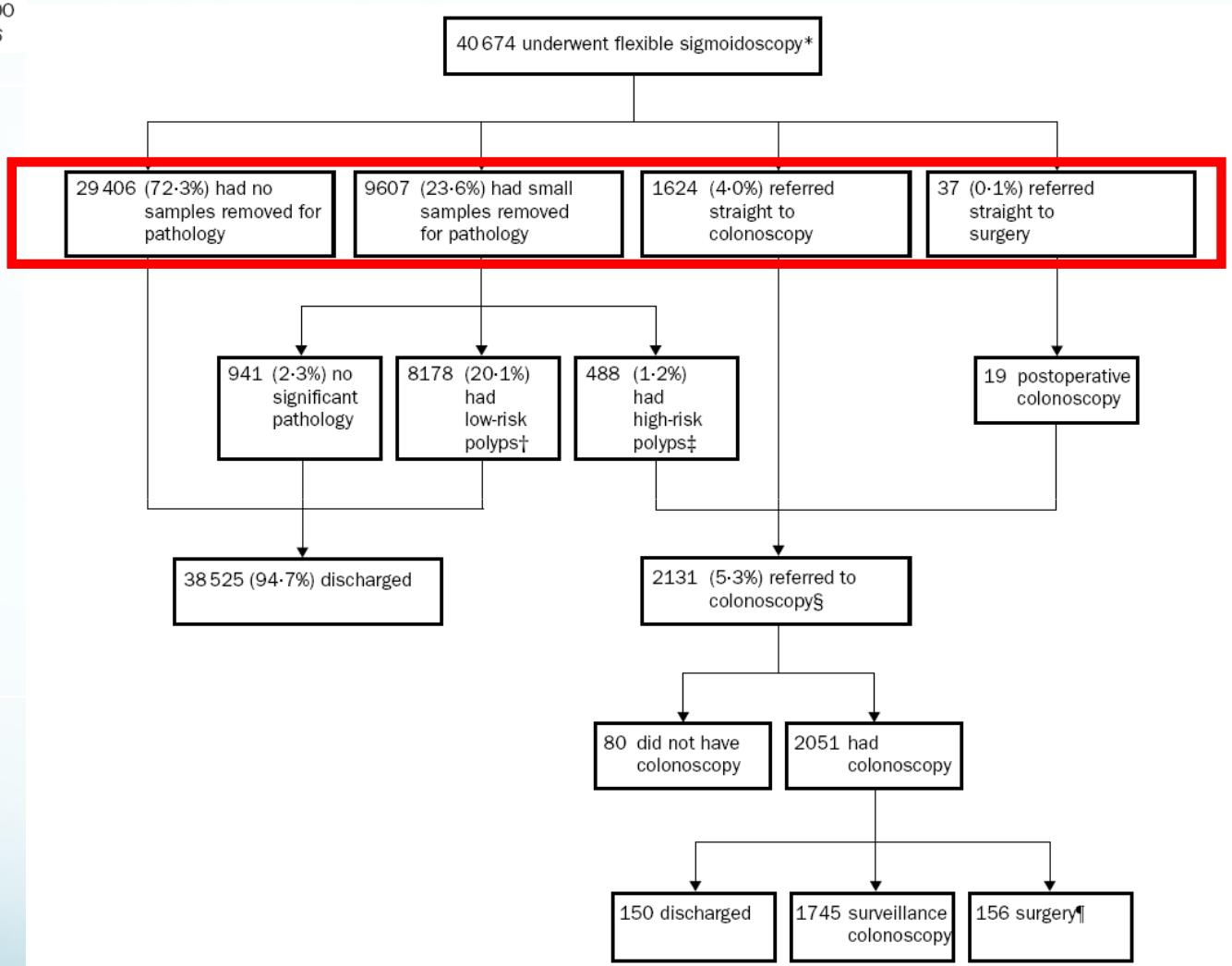


Figure 2: **Management of trial participants**

Percentages are of the total screened. *Includes 342 people who underwent colonoscopy in the family history study; their management is reported here on the basis of distal findings only. †Polyps defined as: adenoma, hyperplastic polyp, serrated adenoma, leiomyoma, inflammatory, inverted, carcinoid tumour, juvenile polyp, regenerative polyp, hamartomatous polyp, fibroepithelial polyp, lipoma, inflammatory cap polyp, lymphoid polyp. ‡Participants were defined as at high risk if any of the following were found in the distal colon: ⩾3 adenomas, polyp size ⩾1 cm, tubulovillous or villous histology, severe dysplasia, malignancy, or ⩾20 hyperplastic polyps. §165 participants were referred straight to colonoscopy for reasons other than high-risk polyps (safety of polypectomy 31; family history of cancer 20; suspicious symptoms 16; difficult or incomplete sigmoidoscopy ten; borderline high-risk six; error or confusion about criteria for high-risk 24; other reasons 58); also includes 16 people in the family history study who were found to have high-risk neoplasia in the distal colon. ¶Two people had surgery before and after colonoscopy.

27.7% Pathology material

Flexisigmoidoscopy and colonoscopy

	Men	Women	Relative risk (95%CI)*	Total
Screened	20 519	20 155	..	40 674
Distal polyps*				
* Any	6481 (31·6%)	3777 (18·7%)	1·7 (1·6–1·7)	10 258 (25·2%)
* Three or more	1451 (7·1%)	570 (2·8%)	2·5 (2·3–2·7)	2021 (5·0%)
Largest polyp 1 cm or larger	909 (4·4%)	384 (1·9%)	2·3 (2·1–2·6)	1293 (3·2%)
Distal adenomas				
Any	3294 (16·1%)	1637 (8·1%)	2·0 (1·9–2·1)	4931 (12·1%)
Three or more	208 (1·0%)	42 (0·2%)	4·9 (3·5–6·8)	250 (0·6%)
Tubulovillous or villous histology†	647 (3·2%)	317 (1·6%)	2·0 (1·8–2·3)	964 (2·4%)
Severe dysplasia†	216 (1·1%)	85 (0·4%)	2·5 (1·9–3·2)	301 (0·7%)
High-risk lesions	1317 (6·4%)	588 (2·9%)	2·2 (2·0–2·4)	1905 (4·7%)
Cancer	90 (0·5%)	35 (0·2%)	2·7 (1·8–4·0)	131 (0·3%)

342 people underwent colonoscopy instead of flexible sigmoidoscopy, but only the distal findings are included in this table. *Men vs women. †Most advanced histology or dysplasia per person. ‡Participants were defined as at high risk if any of the following were found in the distal colon: ≥3 adenomas, polyp size ≥1 cm, tubulovillous or villous histology, severe dysplasia, malignancy, or ≥20 hyperplastic polyps. §Distal polyps are lesions at sigmoidoscopy or from the rectum or sigmoid colon at colonoscopy.

Table 1: **Numbers of people with polyps or cancer detected in distal colon**

5% 3 or more Lesions

	Men	Women	Relative risk (95% CI)	Total
Underwent colonoscopy*	1396	655	..	2051
Proximal polyps†				
* Any	369 (26·4%)	93 (14·2%)	1·9 (1·5–2·3)	462 (22·5%)
* Three or more	82 (5·9%)	20 (3·1%)	1·9 (1·2–3·1)	102 (5·0%)
Largest polyp 1 cm or larger	71 (5·1%)	22 (3·4%)	1·5 (0·9–2·4)	93 (4·5%)
Proximal adenomas				
Any	316 (22·6%)	70 (10·7%)	2·1 (1·7–2·7)	386 (18·8%)
Three or more	64 (4·6%)	11 (1·7%)	2·7 (1·4–5·1)	75 (3·7%)
Tubulovillous/villous histology‡	54 (3·9%)	16 (2·4%)	1·6 (0·9–2·7)	70 (3·4%)
Severe dysplasia‡	19 (1·4%)	4 (0·6%)	2·2 (0·8–6·5)	23 (1·1%)
Advanced adenomas§	83 (5·9%)	24 (3·7%)	1·6 (1·0–2·5)	107 (5·2%)
Cancers	8 (0·6%)	1 (0·2%)	3·8 (0·5–29·9)	9 (0·4%)

*Excludes 326 people who underwent colonoscopy as part of the family-history study and were not found to have high-risk lesions in the distal colon. †Proximal polyps are lesions removed from sites proximal to the sigmoid colon at colonoscopy. ‡Most advanced histology or dysplasia per person. §≥1 cm, tubulovillous or villous histology, severe dysplasia.

Table 2: **Numbers of people with polyps or cancer detected in proximal colon**

Colonoscopies 22.5%+ Lesions 5% 3 or more

CLINICAL–ALIMENTARY TRACT

Wide Variation in Adenoma Detection Rates at Screening Flexible Sigmoidoscopy

WENDY ATKIN,* PAULINE ROGERS,* CHRISTOPHER CARDWELL,* CLAIRE COOK,*
JACK CUZICK,*‡ JANE WARDLE,*§ and ROB EDWARDS*‖
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GASTROENTEROLOGY 2004;126:1247–1256

- Flexisigmoidoscopy detection rates vary between observers

Table 1. Endoscopists' Detection Rates of Polyps, Adenomas, and Polyps >1 cm in Diameter, Specialty, and Background Incidence Rate of CRC

		Screening results, n (%)				
Endoscopist (ranked by ADR)	No. of people screened (n)	At least one polyp	At least one adenoma (ADR)	At least one polyp >1 cm	Medical specialty	Incidence rate of CRC per 100,000 population
1	3015	* 1263 (41.9)	478 (15.9)	101 (3.3)	Surgery	50.2
2	2646	865 (32.7)	390 (14.7)	69 (2.6)	Gastroenterology	50.5
3	3178	1014 (31.9)	468 (14.7)	75 (2.4)	Gastroenterology	48.0
4	2907	917 (31.5)	421 (14.5)	71 (2.4)	Surgery	40.1
5	2905	976 (33.6)	408 (14.0)	68 (2.3)	Surgery	47.5
6	3085	788 (25.5)	390 (12.6)	45 (1.5)	Gastroenterology	40.1
7	2987	907 (30.4)	353 (11.8)	92 (3.1)	Surgery	44.6
8	2902	657 (22.6)	327 (11.3)	71 (2.4)	Surgery	44.9
9	2970	774 (26.1)	325 (10.9)	44 (1.5)	Surgery	45.9
10	2948	617 (20.9)	288 (9.8)	78 (2.6)	Surgery	46.5
11	2482	437 (17.6)	239 (9.6)	51 (2.1)	Gastroenterology	61.2
12	3902	1206 (30.9)	355 (9.1)	83 (2.1)	Gastroenterology	41.4
13	2674	* 418 (15.6)	230 (8.6)	68 (2.5)	Surgery	57.6
Total	38,601	10,839 (28.1)	4672 (12.1)	916 (2.4)		48.0

Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

- 113,195 controls
- 57,237 flexisigmoidoscopy
- 40,621 underwent it
- Age 60

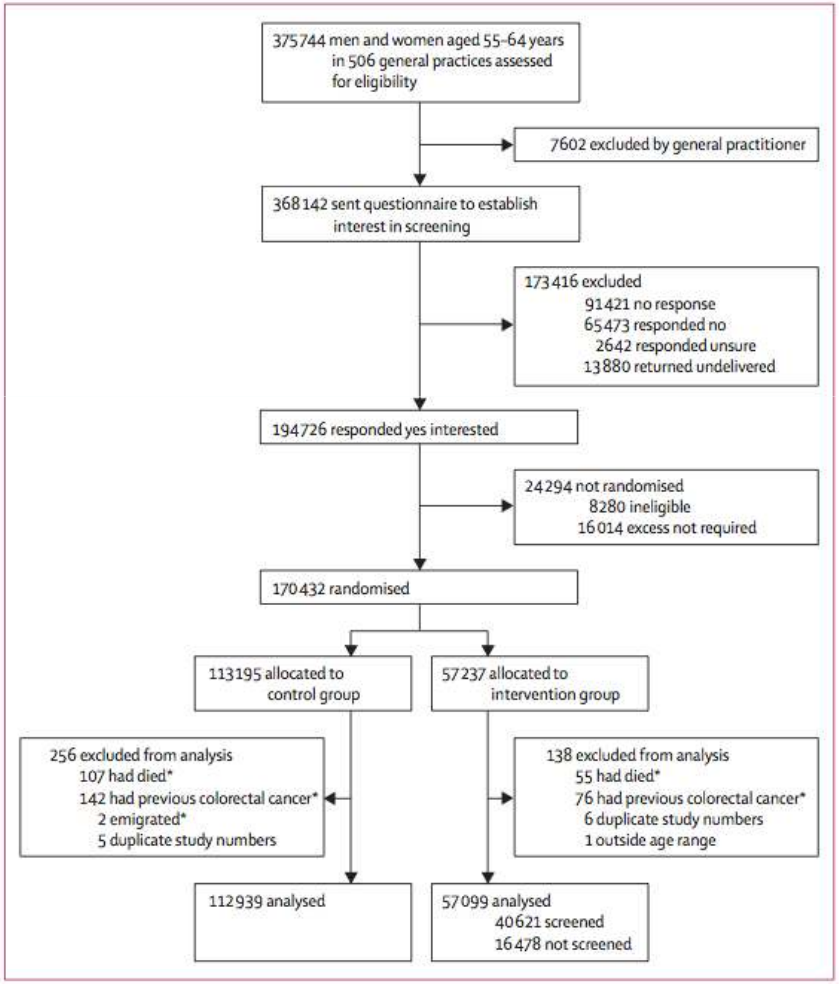
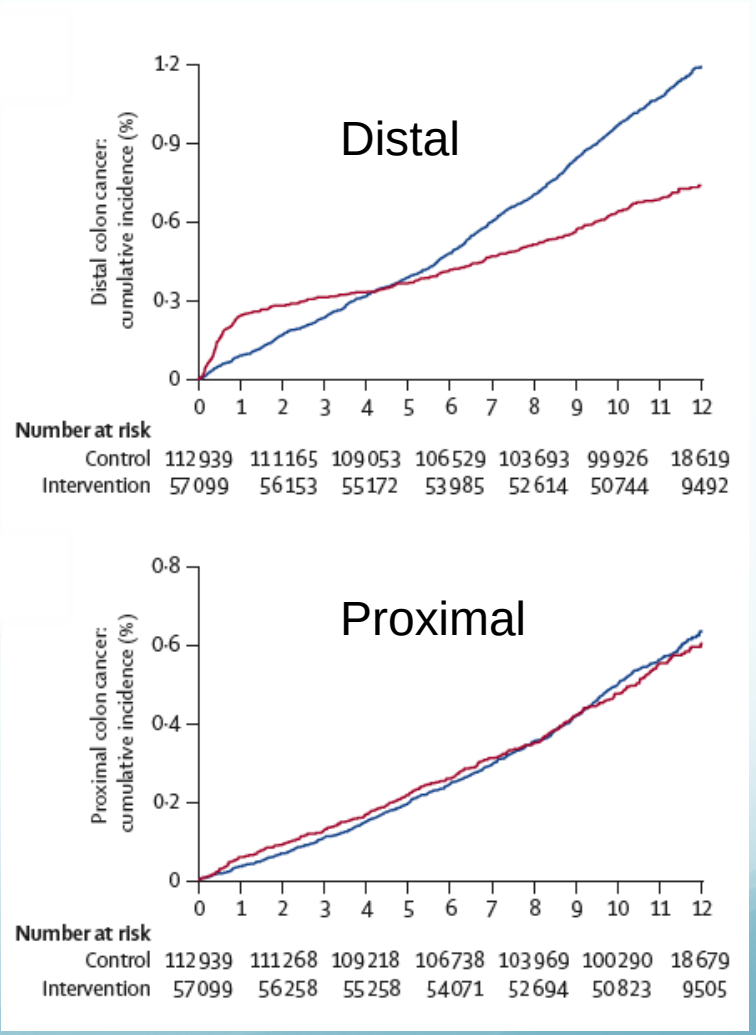


Figure 1: **Trial profile**
*Prerandomisation events.

www.thelancet.com **Published online April 28, 2010 DOI:10.1016/S0140-6736(10)60551-X**

Results

- Incidence 23% (33%) drop
- Mortality 31% (43%)drop
- Left sided/rectal cancer 50% incidence drop



3 pilots April 2011 and roll out April 2012

Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

	Control group (n=112 939)		Intervention group				Number of events expected in intervention group	Number of events prevented in intervention group	Number needed to screen to prevent one event (95% CI)
			Total (n=57 099)		Screened (n=40 621)				
	n	Rate (per 1000; 95% CI)	n	Rate (per 1000; 95% CI)	n	Rate (per 1000; 95% CI)			
Colorectal cancer diagnosis	1818	16·1 (15·4–16·9)	706	12·4 (11·5–13·3)	445	11·0 (10·0–12·0)	919	213	191 (145–277)
Colorectal cancer death*	538	4·8 (4·4–5·2)	189	3·3 (2·9–3·8)	111	2·7 (2·3–3·3)	272	83	489 (343–852)
Colorectal cancer death (verified†)	637	5·6 (5·2–6·1)	221	3·9 (3·4–4·4)	127	3·1 (2·6–3·7)	322	101	402 (291–647)

*Deaths certified by the Office for National Statistics as colorectal cancer as underlying cause of death by automatic coding. †Assignment of colorectal cancer as underlying cause of death by independent expert coder.

Table 3: **Cumulative incidence of and mortality from colorectal cancer, and the number needed to screen to prevent one event in the present follow-up period**

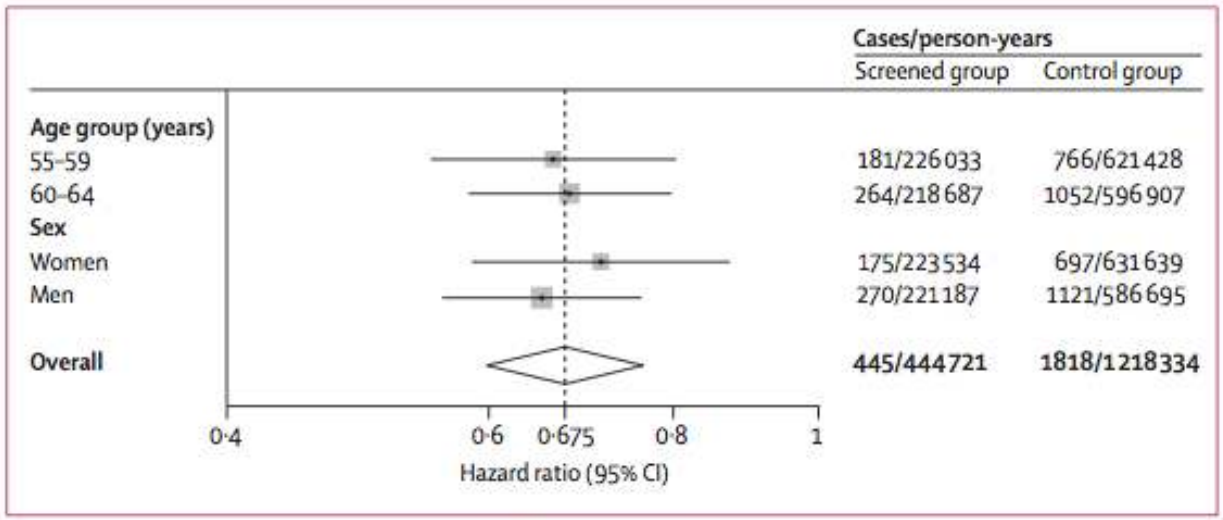


Figure 4: **Hazard ratios for colorectal cancer (all sites) in screened versus control groups by age group and sex**
Hazard ratios are adjusted for non-compliance with screening.

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EU guidelines for bowel cancer screening

Virchows Arch
DOI 10.1007/s00428-010-0997-6

REVIEW AND PERSPECTIVE

Quality assurance in pathology in colorectal cancer screening and diagnosis—European recommendations

Phil Quirke · Mauro Risio · René Lambert · Lawrence von Karsa · Michael Vieth

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Abstract In Europe, colorectal cancer is the most common newly diagnosed cancer and the second most common cause of cancer deaths, accounting for approximately 436,000 incident cases and 212,000 deaths in 2008. The potential of high-quality screening to improve control of the disease has been recognized by the Council of the European Union who issued a recommendation on cancer screening in 2003. Multidisciplinary, evidence-based European Guidelines for quality assurance in colorectal cancer screening and diagnosis have recently been developed by experts in a pan-European project coordinated by the International Agency for Research on Cancer. The full guideline document consists of ten chapters and an extensive evidence base. The content of the chapter dealing with pathology in colorectal cancer screening and diagnosis is presented here in order to promote international discussion and collaboration leading to improvements in colorectal cancer screening and diagnosis by making the principles and standards recommended in the new EU Guidelines known to a wider scientific community.

Keywords Colorectal cancer screening · Multidisciplinary evidence-based guidelines · Quality assurance · Histopathology · Classification · Precursor lesions

Introduction

Colorectal cancer is a significant health problem, the importance of which will increase substantially in the coming years [1]. In Europe, colorectal cancer is the most common newly diagnosed cancer and the second most common cause of cancer deaths, accounting for approximately 436,000 incident cases and 212,000 deaths in 2008 [2]. Randomized trials have shown that systematic screening of a target population of suitable age can reduce colorectal cancer (CRC) by detecting asymptomatic lesions [3–5]. Early treatment is more effective and has a lower morbidity and mortality. Moreover, the endoscopic removal of adenomas reduces the incidence of CRC by stopping the progression of precursor lesions to cancer. The potential of high-quality screening to improve control of CRC has been recognized by the Council of the European Union who issued a recommendation on cancer screening in 2003 [6]. The recommendation encourages the EU Member States to implement population-based screening programmes using evidence-based tests for breast, cervical and colorectal cancer, according to European Quality Assurance Guidelines where they exist. Comprehensive European Guidelines for quality

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REVIEW AND PERSPECTIVE

Annex to Quirke et al. Quality assurance in pathology in colorectal cancer screening and diagnosis: annotations of colorectal lesions

Michael Vieth · Phil Quirke · René Lambert · Lawrence von Karsa · Mauro Risio

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Abstract Multidisciplinary, evidence-based European Guidelines for quality assurance in colorectal cancer screening and diagnosis have recently been developed by experts in a pan-European project coordinated by the International Agency for Research on Cancer. The full guideline document includes a chapter on pathology with pan-European recommendations which take into account the diversity and heterogeneity of health care systems across the EU. The present paper is based on the annex to the pathology chapter which attempts to describe in greater depth some of the issues raised in the chapter in greater depth, particularly details of special interest to pathologists. It is presented here to make the relevant discussion known to a wider scientific audience.

Keywords Colorectal cancer screening · Multidisciplinary evidence-based guidelines · Quality assurance · Histopathology · Classification · Precursor lesions

Introduction

In 2004 and 2006 the European Union (EU) was expanded to include 12 new Member States. This has added greater diversity and heterogeneity in health care systems, including professional and technical standards and capacities. The authors and editors of the European guidelines for quality assurance in colorectal cancer screening and diagnosis have been conscious of the importance of raising and maintaining standards across the EU. While recommending standards and procedures that are of prime importance for mortality reduction, an equitable balance of best practice and ease of service delivery that can be achieved across a wide spectrum of cultural and economic healthcare settings has been sought. Care was taken to avoid promotion of recent research findings before their putative benefit has been demonstrated in clinical practice.

In preparing the guidelines chapter with pan-European recommendations dealing with pathology [1], the authors were aware that the rapid pace of developments in the field and the diversity in the EU would not permit a discussion of some of the issues in greater depth, even though a more detailed discussion would be welcomed by a number of readers, particularly regarding items of special interest to pathologists. All of the guideline recommendations for quality assurance in pathology are therefore presented in the preceding paper and in the pathology chapter in the full guidelines document [1], on which the preceding paper is based.

The present paper is based on the annex to the chapter on pathology in the full guidelines document [2]. It attempts to address the limitations of the discussion in the

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Published online: 09 November 2010

Acknowledgements Some of the materials contained in these guidelines is reproduced with permission of the UK bowel cancer screening programme pathology screening committee (Carey F, Mapstone N, Quirke P (Chair), Shepherd N, Warren B, Williams G) and the Royal College of Pathologists minimum dataset for colorectal cancer reporting (Williams G, Quirke P, Shepherd N).

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EU guidelines website

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Virtual Pathology at the University of Leeds
Quality assurance in pathology in colorectal cancer screening and diagnosis
Authors
Reviewers
Acknowledgements

Virtual Pathology at the University of Leeds
European Union Bowel Cancer Screening Pathology Examples
NHS

Virtual Pathology at the University of Leeds
Hyperplastic polyp - Example 1

Digital EQA results

J Clin Pathol. 2010 Oct;63(10):916-20.

Virtual microscopy for histology quality assurance of screen-detected polyps.

Risio M, Bussolati G, Senore C, Vigna S, Frangipane E, Segnan N, Cassoni P.

Unit of Pathology, IRCC, Candiolo-Torino, Italy.

Table 3 Intraobserver agreement (first diagnosis using optical microscopy, second using virtual microscopy) in 457 screen-detected polyps

A unit	Advanced	High-grade dysplasia	Villous component	Hyperplastic/sessile serrated lesion
Optical	105	40	95	167
Virtual	108	54	81	151
κ statistics (95% CI)	0.76 (0.69 to 0.83)	0.70 (0.59 to 0.81)	0.78 (0.70 to 0.85)	0.87 (0.82 to 0.6491)
B unit	**Advanced**	**High-grade dysplasia**	**Villous component**	**Hyperplastic/sessile serrated lesion**
Optical	112	99	57	153
Virtual	117	101	62	147
κ statistics (95% CI)	0.81 (0.74 to 0.87)	0.78 (0.71 to 0.85)	0.89 (0.83 to 0.96)	0.88 (0.83 to 0.92)

Table 4 Interobserver agreement using either optical or virtual microscopy in 457 screen-detected polyps

Optical	Advanced	High-grade dysplasia	Villous component	Hyperplastic/sessile serrated lesion
A unit	105	40	95	167
B unit	112	99	57	153
κ statistics (95% CI)	0.63 (0.55 to 0.70)	0.42 (0.32 to 0.53)	0.52 (0.41 to 0.62)	0.77 (0.71 to 0.83)
Virtual	**Advanced**	**High-grade dysplasia**	**Villous component**	**Hyperplastic/sessile serrated lesion**
A unit	108	54	81	151
B unit	117	101	62	147
κ statistics (95% CI)	0.65 (0.57 to 0.73)	0.39 (0.28 to 0.49)	0.66 (0.57 to 0.76)	0.79 (0.73 to 0.85)

Summary

- The NHSBCSP appears to be working
- Increase in early stage cancers
- Reduction in Stage IV (D)
- Flexisigmoidoscopy trial shows death reduction
- Introduction April 2011, roll out 2012
- New EU Guidelines similar to UK guidelines
- Validation of digital EQA

Thanks to:

- Reporting pathologists
- Trust leads
- Regional leads
- Pathology committee
- Julietta Patnick

NHS Bowel Cancer Screening Programme

NCIN national cancer intelligence network