Flexible Sigmoidoscopy: Supplement to 2nd Watching Brief

This document provides results from the follow-up findings of the SCORE trial and is an addendum to the 2nd Watching Brief (WB) on flexible sigmoidoscopy (FS). The first WB examined colorectal cancer (CRC) mortality results from the NORCCAP trial, which was published in June 2009. The second WB examined CRC mortality results from the U.K FS trial, which was published online in April 2010.

This supplement to the second WB provides information that can be used by provincial cancer agencies to put the trial results into context. The Expert Panel will continue to monitor and review trial evidence as it becomes available.

Summary Statement of the Panel

New evidence from the SCORE trial supports one-time FS screening for CRC in average risk individuals 55-64 years of age. This study reported CRC incidence and mortality according to both intention-to-treat and per-protocol analyses. In the intention-to-treat analysis, CRC incidence and mortality were reduced by 18% and 22%, respectively. The reduction in CRC mortality was not statistically significant. However, in the per-protocol analysis, CRC incidence and mortality were statistically significantly reduced by 31% and 38%, respectively.

These results, together with those of the U.K. FS trial highlight the need to consider the role of FS in organized CRC screening programs in Canada.

Published Randomized Controlled Trials of Flexible Sigmoidoscopy

Table 1: Mortality results for the SCORE[1], U.K.[2] and NORCCAP[3] Flexible Sigmoidoscopy Trials

Mortality Results	Intervention vs. control group (intent-to-treat analysis), hazard ratio (95% CI)	Screening vs. non-screening* (per protocol analysis), hazard ratio (95% CI)
ALL CRC MORTALITY		
SCORE	0.78 (0.56-1.08)	0.62 (0.40-0.96)
NORCCAP†	0.73 (0.47-1.13)	0.41 (0.21-0.82)‡
U.K.	0.69 (0.59-0.82)	0.57 (0.45-0.72)
RECTOSIGMOID CANCER MORTALITY		
NORCCAP†	0.63 (0.34-1.18)	0.24 (0.08-0.76)‡
U.K.	Not reported	Not reported

Mortality Results	Intervention vs. control group (intent-to-treat analysis), hazard ratio (95% CI)	Screening vs. non-screening* (per protocol analysis), hazard ratio (95% CI)
ALL-CAUSE MORTALITY		
SCORE	Hazard ratio not reported; only rates (660.26/100,000 person-years in control vs. 640.96/100,000 in intervention group)	-
NORCCAP†	1.02 (0.98-1.07)	Not reported
U.K.	0.97 (0.94-1.00)	0.95 (0.91-1.00)

*Sub-analysis of the effect of screening in participants.
†Results are for FS and FS + FIT groups combined.
‡Note that the NORCCAP screening vs. non-screening analysis does not adjust for self-selection bias; therefore, caution is advised when interpreting these results.

Table 2: Key Features of Flexible Sigmoidoscopy Randomized Controlled Trials

FEATURES	NORCCAP[3]	U.K. FS[2,4]	SCORE[5]	PLCO[6]
STUDY				
Country	Norway	U.K.	Italy	U.S.
Lead investigator	Hoff, G.	Atkin, W.S.	Segnan, N.	Weissfeld, J.
Recruitment period	1999-2000	1996-1999	1995-1999	1993-2001
POPULATION				
Number randomized	55,736	170,432	34,272	154,000
Setting	2 areas: 1 city, 1 country	14 centres	6 trial centres: Arezzo, Biella, Genoa, Milan, Rimini, Turin	10 cities
Sources	Population registry	General practice registry	1. General practice patient registry (Arezzo, Rimini, Turin) 2. Volunteer practices (Milan) 3. Health services registry (Biella, Genoa)	Public, commercial, screening centre mailing lists
Age (years)	55-64	55-64	55-64	55-74

FEATURES	NORCCAP[3]	U.K. FS[2,4]	SCORE[5]	PLCO[6]
STUDY GROUPS				
Randomization	Before invitation	After invitation	After invitation	After invitation
Study arms	1. FS 2. FS & FIT 3. No screening	1. FS 2. No screening	1. FS 2. No screening	1. FS 2. No screening
POWER CALCULATION ASSUMPTIONS				
Screening arm(s) (n)	7,000 FS 7,000 FS & FIT	65,000	20,000	74,000
Control arm (n)	42,000	130,000	20,000	74,000
Compliance (%)	70	55 (5% contamination in control arm)	70	85
CRC incidence reduction (intent to treat) (%)	30	20 between study arms, 40 in each subgroup: < 60 years, ≥ 60 years	21	NA
CRC mortality reduction (intent to treat) (%)	NA	20 between study arms, 40 in each subgroup: < 60 years, ≥ 60 years	NA	20
Follow-up (incidence) (years)	5	10	6	NA
Follow-up (mortality) (years)	5	15	11	10
Significance level (%)	5 (two-sided)	5 (two-sided)	5 (one-sided)	5 (one-sided)
Power (%)	90	90	80	90
UPTAKE				
Interested in screening (invited)* (%)	NA	55	16	NA
Attended screening (randomized)† (%)	67	71	58	83
Attended screening (invited)‡ (%)	67	39	9	NA
SIGMOIDOSCOPY				

FEATURES	NORCCAP[3]	U.K. FS[2,4]	SCORE[5]	PLCO[6]
Instrument	140 cm colonoscope	60 cm videoscope	4 centres: 140 cm colonscope 1 centre: "sigmoidoscope"	60 cm flexible sigmoidoscope
Endoscopist	Not given	Registrar-level gastroenterologists & surgeon	Gastroenterologists	Physicians, nurse practitioners'
Screen frequency	Once only	Once only	Once only	Baseline, year 5
Criteria for colonoscopy	1. Any polyp ≥ 10 mm 2. Any neoplasia	1. Any polyp ≥ 10 mm 2. ≥ 3 adenomas 3. Any polyp with villous component or severe dyplasia 4. Any cancer 5. ≥ 20 hyperplastic polyps above distal rectum	Any polyp ≥ 5 mm 1. Any polyp + inadequate bowel prep 2. ≥ 3 adenomas 3. Any polyp with villous component ≥ 20 or severe dyplasia 4. Any cancer 5. ≥ 5 hyperplastic polyps above distal rectum	Any polypoid lesion or mass
Proportion requiring colonoscopy (%)	20.4	5.2	5.3	23.4

FS = flexible sigmoidoscopy; FIT = immunochemical fecal occult blood test
*Proportion of individuals interested in screening from those with a delivered invitation.
†Proportion of those with a delivered invitation who were interested in screening and attended for FS.
‡Proportion of those with a delivered invitation who were interested in screening and attended for FS (Product of Interested in Screening and Attended Screening – Randomized).

Table 3: Proportion of Individuals in whom Colorectal Adenoma or CRC were Detected by FS or colonoscopy Screening

	Flexible Sigmoidoscopy					Colonoscopy			
Key Features	**NORCCAP[3] (total cohort)**	**NORCCAP[3] (FS only cohort)**	**U.K. FS[2]**	**SCORE[5]**	**PLCO[6]**	**Lieberman[7] 2000**	**Imperiale[8] 2000**	**Schoenfeld[9] 2005**	**Regula[10] 2006**
Country	Norway	Norway	U.K.	Italy	U.S.	U.S.	U.S.	U.S.	Poland
Study Design	RCT	RCT	RCT	RCT	RCT	Cohort study	Cross-sectional study	Cohort study	Cross-sectional study
RESULTS									
No polyps (%)	83.0	83.0	75.0	82.0	66.0	61.0	78.0	80.0	NR
Any adenoma (%)	17.0	NR	NR	NR	31.0	37.0	22.0	20.0	13.0
Distal adenoma (%)	NR	NR	12.0	10.0	23.0	23.0	8.0	6.0	NR
Any advanced lesion (%)	NR	NR	NR	NR	NR	11.0	5.0	5.0	6.0
Distal advanced lesion (%)	NR	NR	NR	NR	NR	7.0	3.0	NR	NR
Proximal advanced lesion (%)	NR	NR	NR	NR	NR	5.0	3.0	NR	NR
Any cancer (%)	0.3	0.3	NR	0.5	0.4	1.0	0.6	0.1	0.8
Distal cancer (%)	NR	NR	0.3	0.5	0.2	0.6	0.3	NR	NR
Proximal cancer (%)	NR	NR	NR	NR	NR	0.4	0.4	NR	NR

RCT = Randomized Control Trial
NR = Not Reported

References

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