

Flexible Sigmoidoscopy: 2nd Supplement to 2nd Watching Brief

This document provides results from the fourth international flexible sigmoidoscopy (FS) trial (the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial) publishing long-term mortality outcomes of screening. It is the second addendum to the 2nd Watching Brief (WB) on flexible sigmoidoscopy, which was published in 2010. The first addendum, released in October 2011 addressed the colorectal cancer (CRC) mortality results from the fall 2011 publication of the SCORE trial.

This supplement can be used by provincial cancer agencies to put the trial results into context with the mortality results from the other three international FS trials. Shortly following the release of this document, a comprehensive Watching Brief incorporating the outcomes from all four FS randomized trials will be distributed.

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Summary Statement of the Panel

The recently published results from the U.S. PLCO trial, along with the U.K., Italy, and Norway trial results provide clear evidence that screening with flexible sigmoidoscopy reduces both CRC mortality and incidence in average risk individuals.

The PLCO study reported a significant reduction of 26% and 21% in CRC mortality and incidence respectively in the screening arm (compared to the control usual care arm) in average risk individuals aged 55-74. The results from three of the trials show a statistically significant reduction in incidence of colorectal cancer and two of the trials found statistically significant reductions in colorectal cancer mortality. Flexible sigmoidoscopy for CRC screening needs to be considered as an option in organized CRC screening programs in Canada; FOBT has already been implemented as the main program screening test.

Published Randomized Controlled Trials of Flexible Sigmoidoscopy

Table 1: Mortality Results for the NORCCAP, U.K. FS, SCORE and PLCO Flexible Sigmoidoscopy Trials

Trial	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		
NORCCAP ^{1†}	0.73 (0.47-1.13)	0.41 (0.21-0.82) [‡]
U.K. FS ²	0.69 (0.59-0.82)	0.57 (0.45-0.72)
SCORE ³	0.78 (0.56-1.08)	0.62 (0.40-0.96)
PLCO ⁴	0.74 (0.63-0.87))	NR
RECTOSIGMOID CANCER MORTALITY		
NORCCAP ^{1†}	0.63 (0.34-1.18)	0.24 (0.08-0.76) [‡]
U.K. FS ²	NR	NR
SCORE ^{3**}	0.73 (0.47-1.12)	0.48 (0.24-0.94)
PLCO ^{4**}	0.50 (0.38-0.64)	NR
ALL-CAUSE MORTALITY		
NORCCAP ^{1†}	1.02 (0.98-1.07)	NR
U.K. FS ²	0.97 (0.94-1.00)	0.95 (0.91-1.00)
SCORE ³	Hazard ratio not reported; only rates (660.26/100,000 person-years in control vs. 640.96/100,000 in intervention group)	NR
PLCO ^{4***}	0.98 (0.96-1.01)	NR

NR = Not Reported.

*Sub-analysis of the effect of screening in participants.

**Distal colon - includes rectum, sigmoid, descending colon and splenic flexure.

***Deaths from other causes, excluding prostate, lung, colorectal and ovarian cancers.

†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: Colorectal Cancer Incidence Results from Flexible Sigmoidoscopy Trials (intervention vs. control groups, relative risk (95% confidence interval))

Trial	Incidence Results		
	All Colorectal Cancers	Distal Cancers	Proximal Cancers
NORCCAP ¹	134.5 vs. 131.9/100,000 person years (no difference)	NR	NR
U.K. FS ²	0.77 (0.70-0.84)	0.64 (0.57-0.72)	0.98 (0.85-1.12)
SCORE ³	0.82 (0.69-0.96)	0.76 (0.62-0.94)	0.91 (0.69-1.20)
PLCO ⁴	0.79 (0.72-0.85)	0.71 (0.64-0.80)	0.86 (0.76-0.97)

NR = Not Reported

References

¹ Hoff G, Grotmol T, Skovlund E, Bretthauer M. Risk of colorectal cancer seven years after flexible sigmoidoscopy screening: randomised controlled trial. *BMJ* 2009;338:b1846.

² Atkin WS, Edwards R, Kralj-Hans I, Wooldrage K, Hart AR, Northover JMA, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomized controlled trial. *Lancet* 2010;375(9726):1624-33.

³ Segnan N, Armaroli P, Bonelli L, Risio M, Sciallero S, Zappa M, et al. Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian randomized controlled trial—SCORE. *JNCI* 2011;103(17):1310-22.

⁴ Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Church T, Laiyemo AO, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. *NEJM* 2012. Published online May 21, 2012. 10.1056/NEJMoa1114635.