Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies

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CRD summary
This review assessed the effectiveness of screening sigmoidoscopy and colonoscopy in prevention of colorectal cancer occurrence and mortality and concluded that the evidence consistently showed that both methods prevented the majority of deaths from distal colorectal cancer. This was a generally well-conducted review, the authors discussed some limitations of the evidence and their conclusions are likely to be reliable.

Authors' objectives
To assess the effectiveness of screening sigmoidoscopy and screening colonoscopy in the prevention of colorectal cancer occurrence and mortality.

Searching
PubMed, EMBASE and Web of Science were searched for articles published in English up to August 2012 (EMBASE) or November 2013. Search terms were reported. Reference lists of relevant articles were screened manually.

Study selection
Randomised controlled trials (RCTs) and observational studies were eligible. Studies had to compare the effects of endoscopy (screening sigmoidoscopy or screening colonoscopy) versus no endoscopy on incidence of colorectal cancer and/or mortality. The population of interest was the general population at average risk for colorectal cancer. Abstracts were excluded from the review.

Half of the studies were in the USA; others were in Canada or Europe (one UK). The age of participants in the RCTs ranged from 55 to 74 years; ages were not reported in the observational studies. RCTs offered once only flexible sigmoidoscopy with or without additional faecal occult blood test or second sigmoidoscopy after three to five years. Controls in the RCTs received lower gastrointestinal endoscopy during or after the screening phase. Controls in the observational studies were mostly participants receiving/not receiving endoscopy.

Two reviewers independently screened studies for inclusion; disagreements were resolved through consensus or referral to a third reviewer.

Assessment of study quality
Two reviewers independently assessed the quality of RCTs based on recruitment process, adherence, contamination in control group and adjustment for contamination, follow-up and reporting analysis on an intention-to-screen and per protocol basis. Observational studies were assessed according to recruitment, relevant comparison, adequate follow-up, controlling for confounders and reporting of results.

Any discrepancies between reviewers were resolved through discussion.

Data extraction
Two reviewers independently extracted data according to site of colorectal cancer (any, proximal or distal to the colon) and outcome. Relative risks and 95% confidence intervals for individual studies were calculated. Data from RCTs were extracted on an intention-to-screen and per protocol basis.

Any disagreements between reviewers were resolved through discussion.

Methods of synthesis
A random-effects model was used to pool relative risks and 95% confidence intervals stratified by study design and type of endoscopy. Statistical heterogeneity was assessed using $I^2$ and Cochran’s Q.
Subgroup analyses were conducted according to type of intervention (sigmoidoscopy or colonoscopy), cancer site and for RCTs by type of analysis (intention-to-screen or per protocol). Sensitivity analysis was performed by removing the most heterogeneous studies. Indirect comparisons were made using the Bucher method (adjusts according to the results from direct comparisons with a common control).

Publication bias was assessed using funnel plots.

**Results of the review**

Four RCTs (437,600 participants, range 55,736 to 170,432) and 12 observational studies (four cohort studies and eight case control studies; number of patients not reported) were included in the review. Median follow-up ranged from seven to 12 years in the RCTs. Participation rates in the RCTs ranged from 58.3% to 86.6%. RCTs fulfilled eight or nine out of 11 quality criteria; none reported estimates adjusted for contamination of the control group. One RCT had a short follow-up duration and one RCT did not report per protocol analyses. Observational studies met between four and nine out of nine quality criteria.

**RCTs**: Screening with flexible sigmoidoscopy statistically significantly reduced the incidence of cancer in participants compared to controls on an intention-to-screen basis at any site (RR 0.82, 95% CI 0.75 to 0.89; I²=52%; four RCTs), proximal (RR 0.91, 95% CI 0.83 to 0.99; I²=0%; three RCTs) and distal (RR 0.69, 95% CI 0.63 to 0.74; I²=24%; three RCTs).

Screening with flexible sigmoidoscopy statistically significantly reduced mortality (RR 0.72, 95% CI 0.65 to 0.80; I²=0%; four RCTs). When subgroup analyses were performed by cancer site, the results remained statistically significant for distal sites (RR 0.54, 95% CI 0.42 to 0.67; I²=0%; three RCTs) but were no longer statistically significant for proximal sites (RR 0.95, 95% CI 0.77 to 1.17; I²=0%; two RCTs). Sensitivity analysis reduced heterogeneity but did not significantly alter the estimates of effect. Results on a per protocol basis showed considerably stronger effect estimates.

**Observational studies**: Sigmoidoscopy reduced cancer incidence (RR 0.51, 95% CI 0.39 to 0.65; three studies; I²=0) and mortality (RR 0.53, 95% CI 0.30 to 0.97; three studies; I²=68%). Colonoscopy also reduced cancer incidence (RR 0.31, 95% CI 0.12 to 0.77; five studies; I²=94%) and mortality (RR 0.32, 95% CI 0.23 to 0.43; three studies; I²=0). Results for distal and proximal incidence and mortality were reported and showed that reductions were no longer statistically significant for proximal mortality with sigmoidoscopy or proximal and distal cancer incidence with colonoscopy.

Results from indirect comparisons were reported. There was no evidence of significant publication bias.

**Authors’ conclusions**

Consistent evidence from RCTs and observational studies showed that screening sigmoidoscopy and screening colonoscopy prevented the majority of deaths from distal colorectal cancer.

**CRD commentary**

The review question and supporting inclusion criteria were clearly stated. Three electronic databases were searched for relevant publications. The authors acknowledged that restrictions were applied and so potentially relevant data may have been missed. Each stage of the review process was conducted in duplicate, thereby minimising potential for reviewer error and bias. Study quality was assessed and the limitations were discussed by the authors.

Only a small number of RCTs were included but they included large numbers of participants. Appropriate methods were used to combine and explore the data. The authors acknowledged some of the limitations of the evidence such as substantial contamination due to controls receiving sigmoidoscopy or colonoscopy screening and insufficient length of follow-up. They also suggested that the evidence base was somewhat limited and heterogeneous, and some studies were conducted many years ago, which may impact on the performance of endoscopies.

This was a generally well-conducted review and the authors discussed some of the limitations of the evidence. The authors’ conclusions reflect the evidence and are likely to be reliable.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.
Research: The authors stated that continued follow-up of the large RCTs was essential. They also stated that further research was needed to assess the impact and relative effectiveness of screening colonoscopy compared with screening sigmoidoscopy and weighed against costs, complexity, discomfort, complication rates, capacities required and possible differences in compliance. Particular attention should be paid to possible underestimation of screening.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.