Accuracy of fecal immunochemical tests for colorectal cancer: systematic review and meta-analysis

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CRD summary
This review found that faecal immunochemical tests had high overall accuracy for detecting colorectal cancer, but their performance depended on the cut-off value for a positive result. This was a well-conducted review and the conclusions appear to be reliable.

Authors' objectives
To evaluate the accuracy of faecal immunochemical tests for colorectal cancer, and to identify the factors affecting the performance of these tests.

Searching
All studies identified in a previous report (see Other Publications of Related Interest) were included. This was updated by searching MEDLINE, EMBASE, DARE, HTA database, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials (CENTRAL) for publications in English from January 2008 to August 2013. Bibliographies and reference lists of eligible papers and reviews were searched, and experts and authors of the included studies were contacted. The search terms were provided.

Study selection
Studies were included if they evaluated the diagnostic accuracy of faecal immunochemical tests for colorectal cancer. They had to report or make available diagnostic data for a 2x2 table; have a randomised trial or cohort design; assess asymptomatic patients aged over 18 years, with a mean age of over 40 years; and report an appropriate reference standard (colonoscopy, or two years or more of follow-up of control patients by their medical records or cancer registry).

In the included studies, the mean age of the participants ranged from 45.2 to 62.7 years, where reported. Some studies included patients younger than 40 years or older than 80 years. Studies usually excluded patients with a history of any medical condition that increased the risk of colorectal cancer. Eight different faecal immunochemical tests were assessed. The cut-off value for a positive result varied from 6.1 to 300 micrograms of haemoglobin per gram of stool (μg/g); most studies used a cut-off between 10μg/g and 20μg/g. Most studies used colonoscopy as the reference standard for all patients.

Two reviewers independently assessed studies for eligibility.

Assessment of study quality
Two reviewers independently assessed quality using the QUADAS 2.

Data extraction
Data were extracted to calculate the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio, with 95% confidence intervals. For studies reporting several cut-off values or different numbers of samples for the same population, the cut-off value or number of samples that was most common in US practice, or recommended nationally or by experts, was used. Where necessary, units were converted into μg/g.

Two reviewers independently extracted the data. Authors were contacted for missing data.

Methods of synthesis
The sensitivity and specificity of the tests for colorectal cancer were pooled using a bivariate random-effects model. The positive and negative likelihood ratios, with 95% confidence intervals, were pooled. The area under the hierarchical summary receiver operating characteristic curve was calculated. Heterogeneity was assessed using Cochran’s Q and I².
Studies were grouped based on the number of samples (one, two or three); the pre-specified cut-off value for a positive result; the brand of test; and the reference standard used to follow up patients with negative results. Analyses excluding older test types were conducted, and further pre-specified sources of heterogeneity were investigated in meta-regression.

**Results of the review**

Nineteen cohort studies were included in the review (113,360 participants). Sample sizes ranged from 80 to 27,860 patients. There were risks of bias in the flow and timing of patients, and reference standards – seven studies used different standards depending on the test results, and endoscopists were not blinded to the test results. Patient selection was open to bias.

The overall pooled sensitivity of the faecal immunochemical tests for colorectal cancer was 0.79 (95% CI 0.69 to 0.86; $I^2=68.45\%$). Specificity was 0.94 (95% CI 0.92 to 0.95; $I^2=98.5\%$). The positive likelihood ratio was 13.10 (95% CI 10.49 to 16.35) and the negative likelihood ratio was 0.23 (95% CI 0.15 to 0.33). The overall accuracy of the tests was 95% (95% CI 93 to 97).

Sensitivity improved with lower cut-off values for a positive result, but specificity decreased. A single sample had similar sensitivity and specificity to several samples, independent of the test brand. The results of other subgroup and sensitivity analyses were reported.

**Authors' conclusions**

Faecal immunochemical tests were moderately sensitive, highly specific and had high overall diagnostic accuracy for detecting colorectal cancer. The performance of the tests depended on the cut-off value for a positive result.

**CRD commentary**

This review had clear inclusion criteria to underpin the research question. Searching covered a range of resources but the limitation to English-language studies could have missed relevant evidence. Study quality was assessed using an appropriate tool. Two reviewers were involved in study selection, data extraction and quality assessment, which helps to minimise bias. The methods of analysis and synthesis appear to have been appropriate, with extensive subgroup analyses and investigation of heterogeneity.

This was a well-conducted review and, despite the restriction on language, the conclusions appear to be reliable.

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

**Practice:** The authors suggested that the test type (qualitative or quantitative) could be customised to different care settings, without significant variability in accuracy. To optimise a quantitative test, the trade-off between increasing sensitivity, by lowering the cut-off for a positive test, and the resulting increase in the number of positive tests should be considered.

**Research:** The authors did not state any implications for research.

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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.