Comparison of immunochemical and guaiac-based fecal occult blood test in screening and surveillance for advanced colorectal neoplasms: a meta-analysis

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CRD summary
This review concluded that immunochemical faecal occult blood tests could perform better in increasing the detection rate of advanced colorectal neoplasm than guaiac-based tests. There was substantial clinical variation across the included studies. The authors’ cautious conclusions and recommendations for research seem appropriate, although it is worth noting that the estimates of diagnostic accuracy for both tests were generally low.

Authors’ objectives
To evaluate whether immunochemical faecal occult blood tests (iFOBT) could improve clinical performance and test accuracy in screening and surveillance for advanced colorectal neoplasms.

Searching
PubMed, EMBASE, Science Citation Index, Cochrane Central Register of Controlled Trials (CENTRAL) and Chinese Biomedical Database were searched to August 2009 for studies published in English or Chinese or studies in other languages for which a translation was available; search terms were reported. Reference lists of included studies were screened. Abstracts of two gastroenterology conferences were searched. Authors of trials contacted for additional studies.

Study selection
Randomised controlled trials (RCTs) of comparisons between a guaiac FOBT (gFOBT) and iFOBT were eligible for inclusion as were diagnostic cohort studies where samples were tested with both a gFOBT and an iFOBT. Studies needed to be of adults. Diagnostic cohorts had to use colonoscopy or sigmoidoscopy as the reference standard. Studies that included patients with visible rectal bleeding, haematuria, menstruation, history of colonic cancer, history of colorectal surgery or a positive family history of colorectal cancer were excluded.

A wide range of gFOBTs and iFOBTs were evaluated; most comparisons between two specific tests were evaluated in single studies only. Studies were conducted in screening populations or people with known or suspected colorectal disease. Most participants in the RCTs with a positive FOBT had their diagnosis confirmed by colonoscopy or sigmoidoscopy.

Two reviewers selected studies for the review; disagreements were resolved by a third reviewer.

Assessment of study quality
Study quality was assessed using QUADAS criteria.

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Data extraction
Numbers of neoplasms detected with each test were extracted from the RCTs to produce odds ratios (OR) and 95% confidence intervals (CIs); a high odds ratio indicated a higher rate of detection with iFOBT than gFOBT. Data were extracted from the diagnostic cohort studies to construct 2x2 tables of test performance from which sensitivity, specificity and positive predictive value were calculated.

Methods of synthesis
Pooled odds ratios and 95% CIs were calculated using a random-effects model. Heterogeneity was investigated using the Cochrane Q and I². Pooled estimates of sensitivity and specificity and diagnostic odds ratios (DOR) with 95% CIs were calculated using a fixed-effect model where no significant heterogeneity was observed (Cochrane Q<0.05 and
A random-effects model was used where there was heterogeneity. Summary receiver operating characteristic curves (SROC) were produced. Subgroup analyses were conducted for the different types of FOBT. Publication bias was investigated using a funnel plot and Egger's regression.

**Results of the review**

Sixteen studies met the inclusion criteria: five RCTs (n=22,709, range 1,219 to 10,993) and 11 diagnostic cohort studies (n=49,840, range 135 to 20,322). Four of the cohort studies were in screening (average risk) populations, five were in people known to have or suspected of having colorectal disease (at risk) and two were in both populations. The RCTs were considered good quality in terms of randomisation, allocation concealment and comparability at baseline. All the diagnostic cohort studies were considered good quality in terms of the patient spectrum, reference standard, incorporation bias and reporting of withdrawals. Nine studies were prone to partial and differential verification bias.

**RCTs:** The detection rate of advanced colorectal neoplasm was greater with iFOBTs than with gFOBTs, but the result did not reach statistical significance (OR 1.50, 95% CI 0.94 to 2.39); statistically significant heterogeneity was observed ($I^2=70.7\%$).

**Cohort studies:** When data from screening and at-risk populations were combined, iFOBT detected significantly more advanced colorectal neoplasm than gFOBTs (OR 1.77, 95% CI 1.31 to 2.39); statistically significant heterogeneity was observed ($I^2=75.6\%$). This significant superiority of iFOBT over gFOBT was observed in screening (OR 2.90, 95% CI 2.50 to 3.36) and at-risk (OR 1.27, 95% CI 1.01 to 1.60) populations; no statistically significant heterogeneity was observed for either analysis. Across all diagnostic cohort studies the positive predictive value ranged from 2% to 50%.

In patients scheduled for colonoscopy, sensitivity for gFOBTs ranged from 29% to 91% and specificity ranged from 59% to 93%. iFOBT sensitivity ranged from 42% to 86% and specificity from 62% to 98%.

Results were reported for a range of subgroup analyses, which included the impact of dietary restrictions. Data were limited for most subgroup analyses.

Funnel plots showed some asymmetry, but the Egger regression test detected no significant asymmetry.

**Authors' conclusions**

iFOBT could perform better in increasing the detection rate of advanced colorectal neoplasm than gFOBT.

**CRD commentary**

The review addressed a clear review question supported by appropriate inclusion criteria. Several relevant sources were searched. Unpublished studies were sought. Language bias could not be ruled out. Study selection and quality assessment were conducted in duplicate; it was unclear whether similar methods to reduce error and bias were employed during data extraction. Study quality was assessed with appropriate criteria and the results were reported in detail. Few study and population characteristics were reported. From the details reported, there was substantial clinical heterogeneity across the studies in terms of the tests evaluated and the populations studied. The pooling of these studies may not have been appropriate and it could be difficult to generalise the pooled results to clinical practice.

Heterogeneity was investigated, but the volume of data available for most of the test/population subgroups was small and this reduced the reliability of these results. Most studies showed a benefit of iFOBT over gFOBT, but the magnitude of this benefit was very variable and differed depending upon the specific gFOBT/population evaluated. Several studies were prone to verification bias. The estimates of positive predictive value, sensitivity and specificity were generally low for both tests.

The generalisability of the results may prove difficult, but the authors' cautious conclusions and recommendations for further research seem appropriate.

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

**Practice:** The authors did not state implications for practice.

**Research:** The authors stated that well-designed RCTs that directly compared gFOBTs and iFOBTs were required.
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