The diagnostic value of symptoms for colorectal cancer in primary care: a systematic review

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CRD summary
This review concluded that investigation of rectal bleeding or anaemia in primary patients was warranted irrespective of other symptoms. These conclusions should be interpreted with caution due to possible bias and errors in the review process, limitations in the analysis and heterogeneity across studies.

Authors' objectives
To determine the diagnostic value of symptoms associated with colorectal cancer.

Searching
MEDLINE, EMBASE, The Cochrane Library and CINAHL were searched to February 2010. There were no language restrictions. Search terms were reported and included a diagnostic filter. Ongoing studies were identified by searching relevant cancer websites. Reference lists of included studies were screened and authors were contacted.

Study selection
Studies of at least 100 primary care patients that evaluated the accuracy of symptoms (index test) for diagnosis of adenocarcinoma of the colon or rectum (target condition) against a reference standard of histology, colonoscopy, double-contrast barium enema, computerised tomography (CT) colonography or at least one years' clinical follow-up were eligible for inclusion. Studies of asymptomatic patients, patients already referred to secondary care and patients with recurrent colorectal cancer were excluded.

Most studies were conducted in Europe; single studies were in USA and Australia. Most studies were multicentre (only three were single-centre). Where reported, symptom data were collected using a questionnaire or template for patients or doctors, routine general practitioner (GP) processes/records or retrieved from NHS databases. Prevalence of colorectal cancer ranged from 0.4% to 23.2%; most studies reported a prevalence of 10% or less.

One reviewer screened the results of the searches for relevance; a second reviewer checked those identified as potentially relevant. It was unclear how full-text studies were assessed for inclusion.

Assessment of study quality
One reviewer assessed study quality using the 14-item QUADAS tool. Items for blinding of the reference standard and availability of clinical information to the person interpreting the index test were removed. An item on description of symptoms was added to the tool.

Data extraction
One reviewer extracted data to populate 2x2 tables of test performance and a second reviewer checked. Data were used to calculate sensitivity specificity, positive and negative likelihood ratios and positive predictive values and likelihood ratios.

Methods of synthesis
Summary sensitivity, specificity and positive and negative likelihood ratios were calculated together with 95% confidence intervals (CIs). Summary positive predictive values were calculated for symptoms evaluated in cohort studies. Heterogeneity was assessed using \( I^2 \) and \( X^2 \). Subgroup analysis was conducted to investigate the influence of age, sample size, single centre versus multicentre, study design, data collection by template or questionnaire versus consultation, quality criteria and studies of first-onset only rectal bleeding versus all times of onset.

Results of the review
Twenty-three studies were included in the review (81,464 participants, range 112 to 43,791). The main potential source of bias in the included studies was potential for partial (48% of studies) and differential (26% of studies) verification.
Only three studies reported sufficient data to calculate 2x2 tables for the accuracy of individual symptoms to suggest a diagnosis of colon cancer. The symptom with the greatest utility in ruling in a diagnosis was rectal bleeding (summary positive likelihood ratio 5.31, 95% CI 1.65 to 17.07, I²=98.7%; three studies). Summary positive likelihood ratios for other single symptoms (abdominal pain, weight loss, diarrhea, constipation, anaemia, change in bowel habit, bloating) ranged from 0.88 (95% CI 0.63 to 1.15; one study) for bloating to 3.98 (95% CI 2.81 to 5.64) and 4.62 (95% CI 3.03 to 7.06) for the two studies that assessed anaemia. Negative likelihood ratios were all close to one (range 0.75 to 0.86 for symptom evaluated in at least three studies).

Six studies reported data on the accuracy of rectal bleeding combined with a second symptom. The only pair of symptoms to suggest a greater potential for ruling in colon cancer than rectal bleeding alone was rectal bleeding combined with anaemia (LR+ 7.88, 95% CI 2.65 to 23.4) but this was only assessed in a single study.

Data on predictive values were reported in the other studies (results available in the paper).

**Authors' conclusions**

The findings suggested that investigation of rectal bleeding or anaemia in primary patients was warranted irrespective of other symptoms. Risks from other symptoms were lower. Multiple symptoms warranted investigation.

**CRD commentary**

The review addressed a clear question. Inclusion criteria were defined. The literature search was adequate and included some steps to locate unpublished data. Use of a methodological filter may have resulted in some relevant studies being missed. Most stages of the review were conducted by a single author and this raised the possibility of bias and errors in the review process. Study quality was assessed using appropriate criteria, but results were reported only as a summary across all studies. Individual study details were limited and so it was not possible to determine the reliability of the three studies that contributed to most of the summary estimates.

Methods used to pool data were not based on the most robust methods. Much of the analysis focused on summary estimates of positive predictive values. Pooling such measures was not appropriate when disease prevalence varied across studies as these are strongly dependent on the prevalence of disease. There was substantial variation in prevalence of colon cancer in the included studies and so these values should be interpreted with caution. Only a small number of studies provided sufficient data to construct a 2x2 contingency table of test performance and there was substantial heterogeneity across these studies, so the summary likelihood ratios reported should be interpreted with caution.

The authors' conclusions regarding rectal bleeding and anaemia were supported by the results, but should be interpreted with caution due to possible bias and errors in the review process, limitations in the analysis and heterogeneity across studies.

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

**Practice:** The authors stated that investigation of rectal bleeding or anaemia in primary patients was warranted irrespective of whether other symptoms were present. Risks from other symptoms were lower. Multiple symptoms warranted investigation.

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

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