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Should data from diagnostic case-control studies be included in systematic reviews alongside diagnostic cohort studies?

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Background

- Diagnostic case-control studies are prone to bias and are thought to overestimate diagnostic accuracy.[1, 2]
- Evaluating data from diagnostic cohort and diagnostic case-control studies in one review can be problematic, particularly where the two study designs are used disproportionately to address different questions
- We undertook a systematic review comparing the accuracy of faecal occult blood tests (FOBTs)
- Two types of FOBT were evaluated (guaiac and immunochemical):
  - Guaiac FOBTs detect the haem moiety of haemoglobin molecules by making use of the pseudoperoxidase activity of haem
  - Immunochemical FOBTs use monoclonal or polyclonal antibodies raised against the globin moiety of human haemoglobin to detect intact haemoglobin or its early degradation products
- Both diagnostic cohort studies and diagnostic case-control studies were included in the review

Objective

- To assess the impact of including diagnostic case-control studies upon estimates of diagnostic accuracy of FOBTs and upon the overall conclusions of the review. The validity of using indirect comparisons to assess relative accuracy was also considered.

Methods

- Systematic review of diagnostic accuracy studies
- We included diagnostic cohort and diagnostic case-control studies that compared guaiac and/or immunochemical FOBTs to any reference standard, for the detection of colorectal cancer in an average risk adult population, and which reported sufficient data to construct a 2 x 2 table
- Studies evaluating flushable FOBTs, stool markers currently being developed such as detection of mutated DNA, tests for albumin, and calprotectin were excluded
- Data from the treatment (screened) arms of RCTs of the effectiveness of screening programs were used to derive additional diagnostic cohorts
- Few direct comparisons of the accuracy of guaiac vs. immunochemical FOBTs were available and indirect comparisons were attempted

Results

- Thirty three studies evaluated guaiac FOBTs, of which 23 were diagnostic cohort studies
- Thirty five studies evaluated immunochemical FOBTs, of which 17 were diagnostic cohort studies
- The apparent impact of study design was primarily on sensitivity

Figure 1:

Results of diagnostic accuracy studies of guaiac FOBTs for the detection of all neoplasms plotted in ROC space. Blue symbols are results from diagnostic cohort studies, and red symbols from diagnostic case-control studies

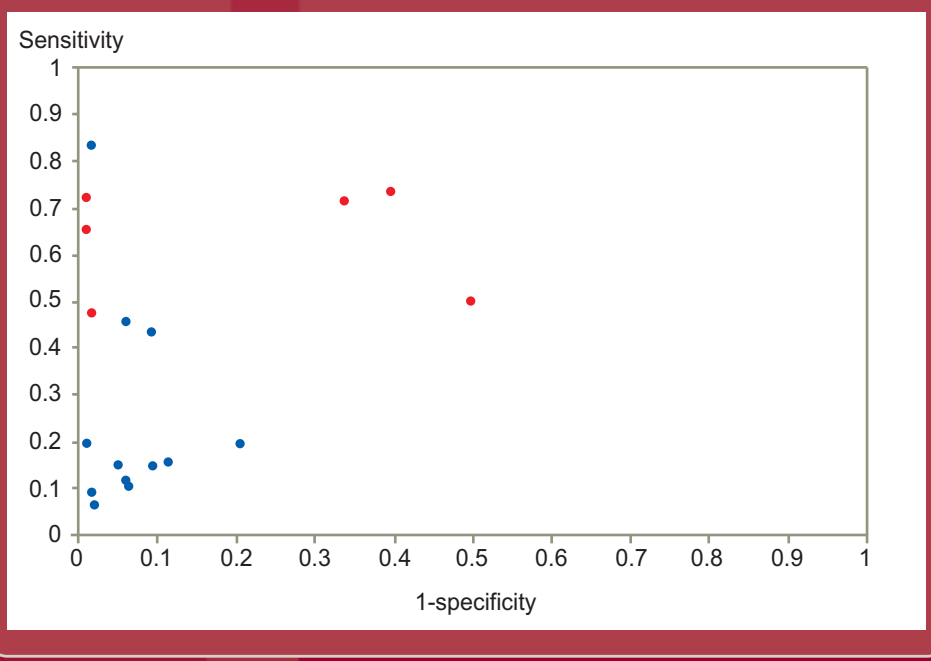
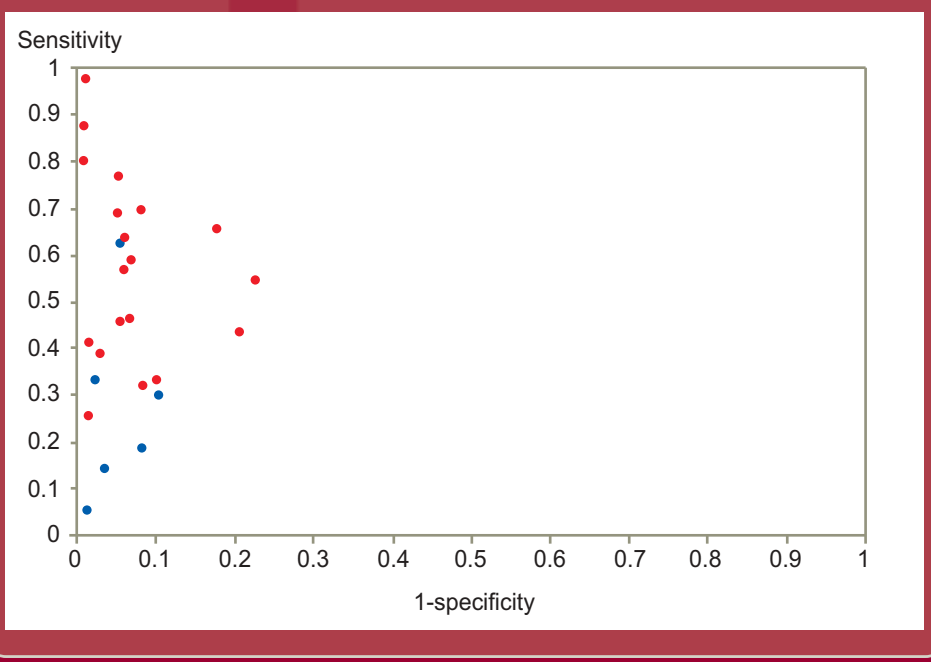


Figure 2:

Results of diagnostic accuracy studies of immunochemical FOBTs for the detection of all neoplasms plotted in ROC space. Blue symbols are results from diagnostic cohort studies, and red symbols from diagnostic case-control studies



- Overall, studies of diagnostic case-control design reported higher sensitivities for the detection of all neoplasms for both guaiac (Figure 1) and immunochemical FOBTs (Figure 2)
- One guaiac FOBT (Haemoccult) and two immunochemical FOBTs (OC Light and Imudia HemSp) were evaluated using both diagnostic cohort and diagnostic case-control study designs. For the detection of all neoplasms:
  - The sensitivity of Haemoccult (guaiac FOBT) ranged from 4.3% to 45% in diagnostic cohort studies; diagnostic case-control studies reported sensitivities between 50% and 71%
  - Two diagnostic cohort studies evaluating OC Light (immunochemical FOBT) reported sensitivities of 5.4% and 18%; sensitivities from diagnostic case-control studies ranged from 39% to 69%
  - The one diagnostic cohort study evaluating Imudia HemSp (immunochemical FOBT) reported a sensitivity of 63%; sensitivities from diagnostic case-control studies ranged from 43% to 98%
- 51% of studies evaluating immunochemical FOBTs were of diagnostic case-control design, compared to 30% of those evaluating guaiac FOBTs
- Heterogeneous data ruled out pooling exacerbating the difficulty of comparing FOBTs
- There was insufficient evidence to investigate the validity of indirect comparisons

Conclusions

- The data presented consolidate the view that the diagnostic case-control design tends to produce inflated estimates of test accuracy
- In our review, this overestimation was evident for both guaiac and immunochemical FOBTs
- For diagnostic accuracy questions, a prospective diagnostic cohort is the preferred study design
- Those conducting systematic reviews of test accuracy should be wary of including both diagnostic cohort and diagnostic case-control studies
- If both study designs are included in a review, the results of the two study designs should be analysed separately and the implications for the conclusions of the review discussed fully

References

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2. Westwood ME, Whiting PF, Kleijnen J. How does study quality affect the results of a diagnostic meta-analysis? *BMC Med Res Methodol* 2005;5:20.

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