



**Editorial: volatile organic compound analysis to improve
faecal immunochemical testing in the detection of colorectal
cancer**

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Editorial: volatile organic compound analysis to improve faecal immunochemical testing in the detection of colorectal cancer

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For Peer Review

The "VOC(F)IT working group" carried out two independent meta-analyses on faecal immunochemical tests (FIT) and volatile organic compounds (VOC), concluding that the combination of FIT and VOC may be a better triage tool for colorectal cancer (CRC) detection in patients with lower gastrointestinal symptoms than FIT alone.¹ The translational impact of their finding is that testing FIT-negative patients for VOCs would reduce missed cancers.

While these meta-analyses are hypothesis generating, the concept of combined FIT and VOC to reduce missed CRCs remains to be tested in a prospective study. The meta-analyses did not include paired FIT and VOC tests in the same population, or VOC data in FIT negative patients, which is the proposed diagnostic tree. We view the results of these meta-analyses with caution, optimism and careful consideration.

The caution arises from inclusion of multiple matrixes of breath, urine, and faeces VOC analysed with different analytical instruments. This variability is heightened by the lack of standardisation of sample collection and transport, VOC analysis, and quality-control measures.² The most critical issue is the lack of large-scale external validation clinical studies. Not surprisingly, the results of the VOC meta-analysis showed significant heterogeneity. Furthermore, there is no substantial data on VOC testing in T1 CRC, hence detecting early cancer in FIT negative patients is an untested hypothesis.

The results should also be viewed with optimism. Achieving a very good area under the receiver operator characteristic curve in the VOC meta-analysis, in spite of the above limitations, is encouraging. The acceptability of VOC tests in primary care will enhance uptake by patients from different backgrounds.³ We also believe that achieving a sensitivity and specificity comparable to that of FIT is not beyond VOC testing. Adequately powered VOC studies with robust quality assurance using quantitative analytical methods will produce reproducible valid results that would exceed the reported data in early VOC studies.

The introduction of a VOC triage test in the diagnostic pathway requires careful consideration. While it is understandable that authors focus on CRC, and hence a VOC sequential test in FIT negative patients, VOC testing is a platform technology currently developed for other abdominal malignancies with non-specific symptoms that are shared with CRCs.⁴ It could be envisaged that if a GP is presented with a FIT-negative patient with non-specific symptoms that could be shared with other malignancies, he/she may offer the breath test to estimate the risk of cancer at various gastrointestinal sites. A negative test for CRC would minimise the need for colonoscopy but a positive result for other abdominal cancers would warrant immediate referral for upper gastrointestinal endoscopy or CT scan.

The authors should be commended for their collaborative approach to innovate the established FIT-based diagnostic pathway with VOC tests. These data support the need for multicentre studies of FIT and VOC testing with inter-laboratory cross validation. The optimal use of multiple non-invasive triage tests is a novel approach that minimises the need for invasive and expensive definitive investigations. Future studies should examine the clinical utility and cost effectiveness of combining FIT with VOC tests.

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