Brian D Nicholson, Matthew Thompson, Christopher P Price, Carl Heneghan and Annette Plüddemann

Home-use faecal immunochemical testing:

primary care diagnostic technology update

Clinical Question

What is the evidence base for home faecal immunochemical testing for colorectal cancer?

Brian D Nicholson, MRCGP, clinical fellow; **Christopher P Price**, PhD, FRCPath, visiting professor in clinical biochemistry; **Carl Heneghan**, MA, MRCGP, DPhil, professor of evidence-based medicine; **Annette Plüddemann**, PhD, director, Horizon Scanning Programme, Primary Care Diagnostic Horizon Scanning, Centre for Monitoring and Diagnosis Oxford, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK. **Matthew Thompson**, DPhil, MRCGP, professor of family medicine, Department of Family Medicine, University of Washington, Seattle, WA, US.

Address for correspondence

Annette Plüddemann, Primary Care Diagnostic Horizon Scanning, Centre for Monitoring and Diagnosis Oxford, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford OX2 6GG, UK.

E-mail: annette.plüddemann@phc.ox.ac.uk

Submitted: 14 September 2014; **Editor's response:** 15 October 2014; **final acceptance:** 24 October 2014.

DOI: 10.3399/bjgp15X684229

BACKGROUND AND ADVANTAGES OVER EXISTING TECHNOLOGY

A variety of home-use faecal occult blood testing (FOBt) kits remain commercially available to UK patients despite caution regarding their safety and accuracy.

FOBt is a relatively non-invasive and inexpensive test. The NHS Bowel Cancer Screening Programme (BCSP) and the majority of European screening programmes uses guaiac FOBt (gFOB). A Cochrane Review has shown that biennial population screening with card-based postal laboratory-analysed gFOB can reduce colorectal mortality by 15% (relative risk [RR] 0.85, confidence interval [CI] = 0.78 to 0.92) in people aged 45–74 years.[1] Those who attend screening have a 25% reduction (RR 0.75, CI = 0.66 to 0.84) in their risk of death, but only 40% return all three BCSP gFOB kits, although involving GPs in screening increases uptake.[1,2]

Faecal immunochemical testing (FIT) measures the globin component of human haemoglobin. Unlike gFOB, FIT does not require dietary restriction, is specific to lower gastrointestinal (GI) cancers as upper GI enzymes degrade human globin, and is less affected by concomitant medication use. FIT has started to replace gFOB in some regions (for example, the Czech Republic and Italy) and guidelines (for example, the US) given these gains in diagnostic accuracy.

Home FIT kits are designed to obtain samples from multiple parts of a single stool and use immunochromatography to provide an immediate (qualitative) positive or negative result, avoiding the delay and costs associated with laboratory (quantitative) FIT and gFOB. Patients may present to primary care having used home bowel-testing kits, and so this report outlines the existing evidence detailing the potential accuracy and utility of the home FIT available to the adult consumer.

DETAILS OF TECHNOLOGY

Based on a search conducted in December 2013, Box 1 shows the CE approved FIT kits retailing to the UK consumer for between £5.59 and £15.95, marketed as stand-alone home-test kits for use on a single stool sample with rapid results. The PRIMA home test is included as a stand-alone test that is repeated on three samples. None of these kits currently has FDA approval.

PATIENT GROUP AND USE

Home-based testing of adult patients.

IMPORTANCE

Colorectal cancer is the third most common cancer worldwide after lung and breast; incidence patterns are associated with family history and genetics, and variations in diet, deprivation, body weight, and physical activity. In the UK in 2010, colorectal cancer was the fourth most common cancer, accounting for 40 695 new cases and 10% of cancer-related deaths. Early detection of low-grade colorectal cancer increases the likelihood of curative surgical resection and survival, but systematic review repeatedly shows the predictive value of individual (or combined) symptoms or signs is limited in primary care.[3,4]

PREVIOUS RESEARCH

Accuracy compared with existing technology

No studies evaluating the diagnostic accuracy of any of the home bowel testing kits available to the UK consumer were found.

A systematic review of the value of symptoms and additional diagnostic tests for colorectal cancer detection in primary care reported that qualitative FIT was easy to perform and well tolerated for the investigation of colorectal cancer in symptomatic patients in primary care (sensitivity 50–100%, specificity 71–93%) if compared to gFOB (sensitivity 33–100%, specificity 72–94%).[3] However, five FIT kits the HemeSelect™ test, Hemoblot, iFOBT strip device, Immunohemostick, InSure® FIT™ test) were compared in studies involving symptomatic patients referred to

Box 1. CE marked point of care faecal immunochemical test kits marketed for home use in the UK

Kit/Manufacturer/Distributor	Method	Haemoglobin threshold
SELF-SURE™ Epitope Diagnostics Inc., San Diego, US Distributed by Personal Diagnostics, UK	Plastic stool collection device stabs stool at 'two or more sites', is then twisted into sealed sampling tube containing developing suspension and shaken. Test strip is screwed into other end of sealed sampling tube and result given.	Not specified
FOBCHECK© NanoRepro, Marburg, Germany Distributed through Amazon.co.uk	Plastic stool collection device stabs stool at 'various locations', is then twisted into sealed sampling tube containing developing suspension and mixed. Top is unscrewed and three drops are dropped into the sample well of the test device and result given.	40 µg/l
Certain Bowel Health Test Koroglu Medical Devices Ltd, Turkey Distributed through Amazon.co.uk	Sampling device incorporated into the lid of the developing solution bottle is used to stab stool at 'three different locations', then is fastened and shaken. Tip of top is snapped off and three to four drops are dropped into the dropping hole of the test device and result given.	30 µg/l
SELFCheck: Bowel Health Kit CARE Diagnostica, Austria Distributed by1st Health Products Ltd, UK through Amazon.co.uk	Sampling device incorporated into the lid of the developing solution bottle is used to stab stool, taking '3–6 samples at different locations' then is fastened and shaken. Tip of top is snapped off and two drops are dropped into the dropping hole of the test cassette and result given in 5 minutes.	Not specified
BOWEL HOME TEST Kit The Boots Company PLC, Nottingham, England Boots Pharmaceuticals.	Sampling device incorporated into the lid of the developing solution bottle is used to stab stool, taking '3-6 samples at different locations' then is fastened and shaken. Tip of top is snapped off and two drops are dropped into the dropping hole of the test cassette and result given in 5 minutes.	Not specified
PRIMA®Home Test: Bowel Test — FOB Healthy Europe s.r.l., Milan, Italy Distributed through Amazon.co.uk	Unscrew the syringe cap and dip the stick about 2 cm into the faeces at three separate locations, replace the collection stick to the collection device and shake well repeating this procedure three times on separate stools keeping the device in the fridge in between. Snap off the tip and drop six drops to the sample well and read the result after 10 minutes	Not specified

secondary care for investigation, and so no direct evidence was found from primary care populations. The studies included were highly heterogeneous, and validation of the findings using larger studies is needed in primary care, but subgroup analyses suggested that FIT was more sensitive for cancer at all sites and for detecting earlier-stage disease than gFOB.[3]

One subsequent study was found evaluating an additional FIT (OC-Light 'Eiken', Nagase, Japan) in 112 symptomatic patients referred to a rapid-access colorectal service without overt rectal bleeding who underwent lower GI endoscopy or barium enema. For colorectal cancer the sensitivity was 100% and specificity 86.3%, positive predictive value 56.6%, and negative predictive value 100% (confidence intervals not reported).[5] It remains unclear whether this accuracy would remain if the test was used in primary care or at home.

Overall, no studies were found that evaluated the accuracy of qualitative FIT kits in asymptomatic patients at home. However, data available from laboratory (quantitative) FIT suggest that home testing may have a potential role in diagnosis, although confirmatory studies in primary care populations are required.

Accuracy of laboratory FIT versus gFOB

A Dutch randomised controlled trial detected advanced neoplasia in a screening population at significantly higher rates using laboratory-based quantitative FIT (OR 2.4, 95% CI = 1.3 to 4.1) compared with laboratory-analysed gFOB,[6] and a large study of 85 149 average-risk individuals from the French colorectal cancer screening programme showed superior accuracy of automated quantitative FIT over manual laboratory-analysed gFOB.[7] Numerous diagnostic accuracy studies support that laboratory-based quantitative FIT has higher sensitivity and specificity when screening colorectal cancer than gFOB, especially for detecting high-risk adenomas.[8]

Laboratory FIT versus qualitative FIT

A large German study combined data from asymptomatic patients undergoing screening (n = 1492) and symptomatic patients prior to colonoscopy (n = 62) to compare accuracy between six point-of-care qualitative FITs (ImmunoCARE-C®, FOB advanced, PreventID® CC, bioNexia® FOBplus, QuickVue® iFOB, bioNexia Hb/Hp Complex®) and three laboratory-based quantitative FITs (RIDASCREEN® Hb, RIDASCREEN® Hb/Hp Complex, OC-SENSOR).[9] The FITs showed good inter-test agreement using similar thresholds. However, trained investigators in the laboratory setting performed the tests, and no similar evidence was found for FITs performed by primary care practitioners or by patients at home.

Single versus repeat sampling

Whereas single sampling detects large heavily bleeding lesions, repeat sampling is more suited to the intermittent bleeding

seen with smaller lesions. Depending on the haemoglobin threshold used, up to two-thirds of advanced neoplasms can be missed by single or double FIT sampling.[10] Increasing sensitivity at the cost of specificity by lowering the threshold value used for a single FIT test (instead of improving specificity by using two or more samples) risks overburdening colonoscopy services. If an appropriate threshold is chosen in relation to the population tested, single-sample FIT testing may perform as accurately as repeated sampling. Several studies have indicated that a single sample using 7.5 µg/l represents a good trade-off between sensitivity and specificity, but great variation in (and poor reporting of) the thresholds used by manufacturers still remain a problem (Box 1).

Impact compared with existing technology

FOBt has greater uptake than flexible sigmoidoscopy in screened populations, and screening uptake is significantly higher using FIT compared with gFOB (RR 1.21, 95% CI = 1.09 to 1.33).[11] Despite greater convenience due to simplified test procedure, there is no clear evidence currently that home (qualitative) FIT would further improve screening uptake at a population level. FIT could alternatively be used as a second line to reduce false positives from borderline gFOB.

Relevant guidelines

The UK 2005 NICE referral guidelines for suspected cancer do not recommend the use of FOBt, stating *'the sensitivity, specificity, and positive predictive values of FOBt are too low to make these tests helpful'*. In contrast, the 2012 Ontario guideline for the *Referral of Patients with Suspected Colorectal Cancer by Family Physicians and Other Primary Care Providers* recommends the use of FOBt in patients with no active rectal bleeding but with unexplained signs and symptoms who do not meet criteria for urgent or semi-urgent referral. The 2015 NICE update consultation document recommends gFOB in cases without rectal bleeding with: abdominal pain; weight loss; iron deficiency (<60 years); or a change in bowel habit (<60 years). FIT is not recommended due to insufficient primary care evidence.

European guidelines for quality assurance in colorectal cancer screening and diagnosis recommend FIT rather than gFOB for screening asymptomatic individuals, noting that positive tests must be followed up with colonoscopy given the low specificity for colorectal neoplasia.

What this technology adds

FIT is more accurate than gFOB for screening, and comparable diagnostic accuracy can be achieved between laboratory based and qualitative FITs (if attention is given to the thresholds used). FIT offers advantages of one-step, single stool, home sampling. GP recommended home FIT could improve screening yield and uptake (as this has worked for gFOB), and home testing could potentially be used as part of diagnostic evaluation in symptomatic patients, but studies in primary care are needed to confirm this. The lack of robust evidence on the comparative accuracy of home bowel testing kits and laboratory methods needs urgent attention in both the asymptomatic and symptomatic patients. For example, a diagnostic accuracy study comparing laboratory (quantitative) FIT with the available home (qualitative) FITs when used at home by patients and in primary care by a GP. At present there is not enough information to confidently say whether a patient who presents to primary care having performed a home test and received a negative (or positive) result should be reassured (or investigated).

Methodology

Standardised methodology was applied in writing this report, using prioritisation criteria and a comprehensive, standardised search strategy, and critical appraisal (full details at www.madox.org). The search for this article was conducted in December 2013.

Funding

This work was supported by the National Institute for Health Research (NIHR) Diagnostic Evidence Co-operative Oxford at Oxford Health NHS Foundation Trust. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

Acknowledgements

We thank Nia Roberts for helpful discussions.

Online version

Read the full-length version of this article online: **bjgp.org**

Discuss this article

Contribute and read comments about this article: **bjgp.org/letters**

REFERENCES

1. Hewitson P, Glasziou P, Irwig L, *et al.* Screening for colorectal cancer using the faecal occult blood test, Hemoccult. *Cochrane Database Syst Rev* 2007; **24 (1):** CD001216.
2. Lo SH, Halloran S, Snowball J, *et al.* Colorectal cancer screening uptake over three biennial invitation rounds in the English bowel cancer screening programme. *Gut* 2015; **64(2):** 282–291.
3. Jellema P, van der Windt DA, Bruinvels DJ, *et al.* Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis. *BMJ* 2010; **340:** c1269.
4. Maringe CWS, Walters S, Rachet B, *et al.* Stage at diagnosis and colorectal cancer survival in six high-income countries: a population-based study of patients diagnosed during 2000–2007. *Acta Oncol* 2013; **52(5):** 919–932.
5. Kaul A, Shah A, Magill FH, *et al.* Immunological faecal occult blood testing: a discriminatory test to identify colorectal cancer in symptomatic patients. *Int J Surg* 2013; **11(4):** 329–331.
6. Hol L, van Leerdam ME, van Ballegooijen M, *et al.* Screening for colorectal cancer: randomised trial comparing guaiac-based and immunochemical faecal occult blood testing and flexible sigmoidoscopy. *Gut* 2010; **59(1):** 62–68.
7. Faivre J, Dancourt V, Denis B, *et al.* Comparison between a guaiac and three immunochemical faecal occult blood tests in screening for colorectal cancer. *Eur J Cancer* 2012; **48(16):** 2969–2976.
8. Allison JE, Fraser CG, Halloran SP, Young GP. Population screening for colorectal cancer means getting FIT: the past, present, and future of colorectal cancer screening using the fecal immunochemical test for hemoglobin (FIT). *Gut Liver* 2014; **8(2):** 117–130.
9. Tao S, Brenner H. Well adjusted qualitative immunochemical faecal occult blood tests promising alternative for inexpensive, high-quality colorectal cancer. *Eur J Cancer Prev* 2013; **22(4):** 305–310.
10. Oort FA, van Turenhout ST, Coupe VMH, *et al.* Double sampling of a faecal immunochemical test is not superior to single sampling for detection of colorectal neoplasia: a colonoscopy controlled prospective cohort study. *BMC Cancer* 2011; **11:** 434.
11. Vart G, Banzi R, Minozzi S. Comparing participation rates between immunochemical and guaiac faecal occult blood tests: a systematic review and meta-analysis. *Prev Med* 2012; **55(2):** 87–92.