

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Quantitative faecal immunochemical tests to assess symptomatic people who are at low risk of colorectal cancer in primary care

Final scope

March 2016

1 Introduction

The medical technologies advisory committee identified faecal immunochemical tests to triage low risk symptomatic populations in primary care as potentially suitable for evaluation by the diagnostics assessment programme on the basis of a briefing note. The revised scope was informed by discussions at the scoping workshop on 16 February 2016 and the assessment subgroup meeting on 2 March 2016.

A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by companies and experts and on information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

There are a number of symptoms which can suggest colorectal cancer; these include rectal bleeding, a change in bowel habits, weight loss, anaemia, abdominal pain and blood in stools (faeces). Sometimes, blood in stools is not visible (faecal occult blood) so tests are used to detect its presence. These faecal occult blood tests can be used in primary care to assess people who are at a low risk of colorectal cancer and help determine if they should be referred for further investigations. The low risk symptomatic population for whom faecal occult blood testing is recommended is outlined in NICE's guideline on [suspected cancer: recognition and referral](#), and is described in

further detail in section 4.2.1 below. Colonoscopy is required for further assessment and to diagnose colorectal cancer because the presence of faecal occult blood can be caused by conditions other than colorectal cancer, so a positive faecal occult blood test cannot alone be used for diagnosis.

Faecal immunochemical tests are a type of faecal occult blood test and are designed to detect small amounts of blood in stool samples using antibodies specific to human haemoglobin. They have been developed as an alternative to guaiac-based faecal occult blood tests which involve using chemicals that react with the haem component of haemoglobin in the blood and produce a blue colour change if blood is detected. Sometimes, this colour change can happen because the chemicals react with food in a person's diet or with medications that a person is taking; this can lead to false test results. Because the faecal immunochemical tests are designed to specifically detect human haemoglobin, they may provide more accurate test results than the guaiac-based faecal occult blood tests. Further, the faecal immunochemical tests target the globin component of haemoglobin, which is said to be degraded as it travels through the gastrointestinal tract, and are therefore less likely to detect globin resulting from upper gastrointestinal bleeding. The improved accuracy of faecal immunochemical tests could lead to a reduced number of inappropriate referrals for colonoscopy, and reduce the length of time taken for people to be seen by a specialist.

2.2 Product properties

Two types of faecal immunochemical tests are available:

- quantitative faecal immunochemical tests which typically use immunoturbidimetric methods to measure the concentration of haemoglobin in faecal samples, that is the tests measure light scattered from haemoglobin particles present in the sample.
- qualitative faecal immunochemical tests which typically use immunochromatographic test devices to detect the presence of haemoglobin in faecal samples, that is the tests detect haemoglobin present in the sample using an immunochemical reaction which results in a colour change (Tinmouth et al. 2015).

During the development of the scope, stakeholders informed NICE that there was a clinical preference for using quantitative tests to triage people presenting to primary care with symptoms. This preference is because the quantitative tests offer the possibility of using a range of test cut-off values for subgroups of people who are anticipated to have higher baseline levels of

faecal haemoglobin such as people who are older and men. Therefore this assessment focusses on quantitative tests.

Quantitative tests typically report results as the concentration of haemoglobin per millilitre of sampling device buffer (ng/ml), however the World Endoscopy Organization has called for standardisation in reporting units to aid the comparison of results between systems which collect different sample masses and use different volumes of buffer ([World Endoscopy Organization](#) 2012). The organization recommends that results are reported as micrograms of haemoglobin per gram of faeces ($\mu\text{g Hb/g}$), where the mass of faeces sampled and the volume of sample buffer are known. Results can be converted from ng/ml using the formula:

$$\mu\text{g Hb/g} = (\text{ng haemoglobin/ml}) \times (\text{volume of buffer in ml}) / (\text{mass of faeces in mg})$$

The properties of the quantitative faecal immunochemical tests included in this assessment are described in more detail below and are summarised in table 1.

Table 1 Summary of interventions*

Test	Test principle	Sample size	Measuring range	Limit of detection	Limit of quantitation	Cut off	Throughput
HM JACKarc	Immunoturbidimetry	2mg	7ng/ml to 400ng/ml	7µg Hb/g (7ng/ml)	1.25µg Hb/g (1.25ng/ml)	10µg Hb/g (10ng/ml)	200 samples per hour
FOB Gold	Immunoturbidimetry	10mg	Varies according to the analyser used	Varies according to the analyser used	Varies according to the analyser used	To be determined by each laboratory	Dependent on analyser used
OC Sensor	Immunoturbidimetry	10mg	10ng/ml to 1000ng/ml	10ng/ml	Not stated	10ng/ml	Dependent on analyser used
RIDASCREEN haemoglobin	ELISA	10mg ^a	Not stated	0.42µg Hb/g	Not stated	2µg Hb/g	NK
RIDASCREEN haemoglobin/haptoglobin	ELISA	10mg ^a	Not stated	0.38µg HbHp/g	Not stated	2µg Hb/g	NK

* Information provided by companies or taken from the test's *instructions for use* document.

^a If using RIDASCREEN Stuhlröhrchen tubes

2.2.1 HM-JACKarc system

The HM-JACKarc system (Kyowa Medex/Alpha Laboratories) is a fully automated quantitative faecal immunochemical test system. The system comprises faecal sample tubes which incorporate a sample collection device (the Extel Hemo-auto MC A device) and can hold 2mg of faeces (Carroll et al, 2014) in 2ml of buffer, and latex agglutination reagent (Extel Hemo-Auto HS) and buffer (Extel Hemo-auto). The reagent contains latex particles which are coated in antibodies specific to human haemoglobin. The antibodies bind to haemoglobin present in the faecal sample creating complexes which are detected using turbidimetry. The test has a measuring range of 7ng/ml to 400ng/ml. The assay is compatible with the HM JACKarc analyser which reports results as ng/ml. The results are required to be converted to $\mu\text{g Hb/g}$ by the user, however because the test uses 2mg of sample and 2ml of buffer results reported as ng/ml convert directly to $\mu\text{g Hb/g}$, that is 10 ng/ml equals 10 $\mu\text{g Hb/g}$. The company suggest a cut off of 10 $\mu\text{g Hb/g}$ for symptomatic populations. The HM JACKarc analyser can process up to 200 samples per hour, with a maximum capacity of 80 samples per run.

2.2.2 FOB Gold

The FOB Gold system (Sentinel/Sysmex) is an automated quantitative faecal immunochemical test system. It comprises faecal sample collection tubes (the Sentifit pierce tube faecal collection device) which collect 10mg of faeces (Carroll et al. 2014) in 1.7ml of buffer, and latex agglutination reagent. The FOB Gold latex agglutination reagent contains polyclonal antibodies specific to human haemoglobin which bind to haemoglobin present in the sample creating complexes that are detected using turbidimetry. The FOB Gold kit has CE marked applications for a range of clinical chemistry analysers including those supplied by Siemens, Beckman Coulter and Abbott. The performance characteristics of the assay vary depending on which analyser is used (see table 2). The company suggest that each laboratory should establish their own test cut-off according to the population the laboratory serves. The throughput of the test is dependent upon the clinical chemistry analyser used to process the samples.

Table 2 Performance characteristics of FOB Gold*

Analyser	Measuring range	Limit of detection	Limit of quantitation
Abbott Architect c4000/c8000/c16000	16 – 735ng/ml	4.7ng/ml	16ng/ml
Modular P / Hitachi 917	14 – 750ng/ml	9.5ng/ml	13.9ng/ml
Beckman Coulter AU series	4.1 – 700ng/ml	4.1ng/ml	Not stated
Siemens Dimension	20 – 760ng/ml	5.0ng/ml	20.0ng/ml
Siemens Advia 2400	30 – 840ng/ml	19.5ng/ml	28.5ng/ml
BioMajesty JCA-6010/C	10ng/ml to highest calibrator concentration	Not stated	10ng/ml
SENTiFIT 270	10ng/ml to highest calibrator concentration	7.6ng/ml	10ng/ml

* all information taken from the instructions for use for each analyser

2.2.3 OC Sensor

The OC Sensor (Eiken Chemical/MAST Diagnostics) is a quantitative faecal immunochemical test. It comprises faecal sample collection tubes, latex reagent and buffer. The OC Sensor faecal sample collection tubes can hold 10mg of faeces (Carroll et al. 2014) in 2ml of buffer. The OC sensor latex reagent contains latex particles coated with polyclonal antibodies for human haemoglobin. The antibodies bind with haemoglobin present in the faecal sample creating complexes which are detected using turbidimetry. The test has a measuring range of 10ng/ml to 1000ng/ml and the company suggest a cut-off of 10 ng/ml for a symptomatic population. The test can be run on either the OC Sensor Pledia or the OC Sensor IO analyser, which differ in the number of samples they are able to process. The OC Sensor Pledia can process up to 320 samples per hour, with a capacity of 200 samples per run. The OC Sensor IO can process up to 88 samples per hour with a maximum capacity of 20 samples per run.

2.2.4 RIDASCREEN haemoglobin and haemoglobin/haptoglobin

The RIDASCREEN haemoglobin test (R-Biopharm Rhône Ltd) is an enzyme immunoassay (ELISA) for the quantitative determination of human haemoglobin in stool samples. Prior to the use of the test the stool sample is diluted with extraction buffer and mixed. This can be done manually or

automated sample dilution can be done using the DSX automated ELISA system which is a fully automated system and automates the test process including washing, incubation and absorbance detection. The test is run on a microtitre plate using wells coated with polyclonal antibodies for human haemoglobin. Each kit is sufficient for 96 tests. The instructions for use document for the test suggest that it can be used with laboratory equipment other than the DSX automated ELISA system.

The test process incorporates 3 incubations and 2 wash steps. During the first incubation any human haemoglobin present in the sample is captured by the polyclonal antibodies in the sample well. Unbound antigens are removed in the first wash step before peroxidase labelled monoclonal antibodies for human haemoglobin (conjugate) are added which bind to the captured haemoglobin during the second incubation. In the final incubation hydrogen peroxide and TMB (substrate) is added which reacts with the peroxidase creating a colour change which is detected by a plate reader. The values produced by the plate reader are interpreted with the RIDA-SOFT Win.net software which reports results as the concentration of haemoglobin per gram of stool ($\mu\text{g/g}$). The company recommends a cut off value of $>2\mu\text{g/g}$ to determine a positive sample. The test has a limit of detection of $0.42\mu\text{g/g}$.

The company also produce the RIDASCREEN haemoglobin/haptoglobin enzyme immunoassay which can be used in combination with the haemoglobin assay, using the same sample and processing on the same microtitre plate but with the addition of a well coated with polyclonal antibodies for human haptoglobin. Haptoglobin is a protein produced by the liver which binds to haemoglobin making it less likely to break down during transit through the gastrointestinal tract. The detection of haptoglobin is claimed to increase the likelihood of detecting lesions in the ascending and transverse colon. The company recommends a cut off value of $>2\mu\text{g/g}$ to determine a positive test using the haemoglobin/haptoglobin assay.

3 Description of the comparator

The first comparator used in this assessment is guaiac based faecal occult blood testing. Guaiac based tests detect the pseudoperoxidase activity of the haem component of haemoglobin in stool samples using guaiac test paper and hydrogen peroxide developer. Unlike faecal immunochemical tests, they are not specific to human haemoglobin which may cause false positive results in the presence of ingested animal haemoglobin and plant peroxidases. False positive guaiac faecal occult blood tests can be caused by:

- Substances or conditions that cause bleeding such as bleeding gums or medications that are known to cause gastrointestinal bleeding such

as anticoagulants, aspirin, steroids and iron preparations ([Lab Tests Online](#) UK, 2015). Upper gastrointestinal bleeding may be detected because haem is not broken down during gastrointestinal transit.

- Other sources of haemoglobin such as eating red meat ([Lab Tests Online](#) UK, 2015)
- Other substances that can react with the test such as eating fish, turnips or horseradish or medications such as colchicines and oxidising drugs ([Lab Tests Online](#) UK, 2015).

The second comparator is clinical assessment and referral for colonoscopy based on lower gastrointestinal symptoms alone.

4 Target conditions

4.1 Colorectal cancer

Colorectal cancer is one of the most common cancers, and in 2012, 41,855 people in the UK were diagnosed with the disease and 16,187 people died from the disease ([Cancer Research UK](#) 2014). Risk factors for colorectal cancer include older age, a family history of the disease, having familial adenomatous polyposis or Lynch Syndrome, having colorectal polyps, and having ulcerative colitis and Crohn's disease. In addition, Jewish people of central and eastern European family origin are thought to be at increased risk of colorectal cancer ([Cancer Research UK](#) 2016).

Colorectal cancer is typically diagnosed when people present with symptoms and are referred to a specialist for further investigations. The symptoms of colorectal cancer include rectal bleeding, a change in bowel habits, weight loss, anaemia and abdominal pain. Blood in stools can also be a symptom of colorectal cancer, and may be visible or hidden. Blood in the stool which is not visible is known as faecal occult blood, and can be detected by faecal occult blood tests, which are designed to detect small amounts of blood from stool samples. These tests are currently used within the NHS Bowel Cancer Screening Programme in England where people aged 60 to 74 are invited to take a faecal occult blood test every 2 years with the aim of detecting colorectal cancer at an early stage or to prevent it developing by detecting high risk colorectal polyps which also cause bleeding and can be removed during a colonoscopy ([NHS Bowel Cancer Screening Programme](#) 2015).

4.2 Diagnostic and care pathway

4.2.1 Testing for faecal occult blood in primary care

Quantitative faecal immunochemical tests to assess symptomatic people who are at low risk of colorectal cancer in primary care
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NICE's guideline on [suspected cancer: recognition and referral](#) includes advice on assessing people presenting to primary care with certain clinical signs and symptoms that may be indicative of colorectal cancer. It makes the following recommendations:

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if:

- they are aged 40 and over with unexplained weight loss and abdominal pain or
- they are aged 50 and over with unexplained rectal bleeding or
- they are aged 60 and over with:
 - iron-deficiency anaemia or
 - changes in their bowel habit, or
- tests show occult blood in their faeces

A suspected cancer referral (for an appointment within 2 weeks) should also be considered for:

- People with a rectal or abdominal mass
- Adults aged under 50 with rectal bleeding and any of the following unexplained symptoms or findings:
 - Abdominal pain
 - Change in bowel habit
 - Weight loss
 - Iron-deficiency anaemia

The faecal occult blood tests are recommended to triage referral to secondary care. The tests are intended to be used in selected groups of people who have symptoms which could indicate colorectal cancer, but in whom a definitive diagnosis of cancer is unlikely, that is they have a low probability of having colorectal cancer (their age and symptoms have a positive predictive value within the range of 0.1% to 3% for colorectal cancer). Faecal occult blood tests to assess for colorectal cancer should be offered to adults without rectal bleeding who:

- are aged 50 and over with unexplained:
 - abdominal pain or
 - weight loss, or
- are aged under 60 with:
 - changes in their bowel habit or
 - iron-deficiency anaemia, or
- are aged 60 and over and have anaemia even in the absence of iron deficiency

In 2014-15 94.2% of patients who were urgently referred for suspected cancer by their GP were seen by a specialist within 14 days ([NHS England 2015a](#)). In total 1,549,694 people were seen by a specialist following an urgent suspected cancer referral, 240,767 of which were referrals for a suspected lower gastrointestinal cancer (93.5% of whom were seen within 14 days) ([NHS England 2015a](#)).

4.2.2 Detecting faecal occult blood

Faecal occult blood can be detected using either guaiac based tests or faecal immunochemical tests. A positive faecal occult blood test indicates that bleeding is occurring in the gastrointestinal tract ([Lab Tests Online UK 2015](#)). This could be caused by ulcers, diverticulitis, inflammatory bowel disease such as Crohn's disease or ulcerative colitis, haemorrhoids, vascular malformations such as angiodysplasia, benign or malignant polyps, or tumours. Further investigation by colonoscopy is therefore required after a positive faecal occult blood test to determine the underlying cause of the bleeding and establish whether colorectal cancer is present. False positive faecal occult blood tests can occur because of dietary or medication interactions, particularly where guaiac based tests are used.

People who have a negative faecal occult blood test in primary care can be reassured that colorectal cancer is unlikely at present and have further testing for alternative diagnoses where advised by their General Practitioner. However, false negative faecal occult blood tests can also occur. In most instances this may be because some lesions and polyps may only bleed intermittently, although guaiac based tests can be falsely negative where a person has been taking high doses of vitamin c which can interfere with the chemical reaction and prevent colour formation that should occur in the presence of haemoglobin ([Lab Tests Online UK 2015](#)). To reduce the impact

of false negative faecal occult blood tests NICE's guideline on [suspected cancer: recognition and referral](#) notes that clinicians should be aware of the possibility of false-negative results for faecal occult blood tests and recommends safety netting is used for instances where a false-negative result is suspected. Safety netting is defined as the "active monitoring in primary care of people who have presented with symptoms" and NICE's guideline on [suspected cancer: recognition and referral](#) makes the following recommendation:

"Consider a review for people with any symptom that is associated with an increased risk of cancer, but who do not meet the criteria for referral or other investigative action. The review may be:

- planned within a time frame agreed with the person or
- patient-initiated if new symptoms develop, the person continues to be concerned, or their symptoms recur, persist or worsen."

4.2.3 Further testing following a positive faecal occult blood test

Following a positive faecal occult blood test, people in England should be referred using a suspected cancer referral to establish a diagnosis ([NICE guidelines 12](#)). Colonoscopy is considered to be the gold standard for diagnosing colorectal cancer as the entire colon can usually be visualised and biopsies can be taken to assess the tissue in a laboratory to determine whether the sample contains benign or malignant cells. For people with co-morbidities which mean colonoscopy is unsuitable, CT colonography can be offered as an alternative. Colonoscopy is most frequently performed as an outpatient procedure with people undergoing the procedure being offered sedation or painkillers. In 2014-15 the rate of colonoscopy and flexible sigmoidoscopy procedures ranged from 93.1 to 231.6 per 10,000 population across clinical commissioning groups in England ([NHS England 2015b](#)), although these figures also include people referred to colonoscopy for reasons other than a positive faecal occult blood test.

The most common finding during a colonoscopy is colorectal polyps, which can be removed using cauterisation or a snare. Sometimes, these polyps develop into cancer and in cases where colorectal cancer is confirmed further imaging tests such as CT or MRI will be done to stage the cancer and determine what treatment is required ([NICE clinical guideline 131](#)). Colorectal cancer can also develop from abnormal cells in the lining of the colon or rectum and this would also be detected during a colonoscopy. Colonoscopy may also find other bowel diseases such as Crohn's disease, ulcerative colitis and diverticulosis which may require further treatment and follow-up. People

who have a positive faecal occult blood test but no abnormalities detected during colonoscopy may be referred for further testing where a clinician judges this to be necessary.

4.2.4 Treatment of colorectal cancer

Following diagnosis and staging, colorectal cancer may be treated with surgery, chemotherapy and radiotherapy, or in some cases with biological agents such as cetuximab. Treatment is dependent upon the stage of the cancer and is described in more detail in NICE's guideline on [colorectal cancer diagnosis and management](#).

4.3 Patient issues and preferences

Faecal immunochemical tests typically require fewer samples than guaiac based faecal occult blood tests which can require up to 6 samples (2 samples per day on 3 consecutive days). Some faecal immunochemical tests may also have sample collection devices which are easier to use, and this, combined with the requirement for fewer samples may make patients prefer the tests over guaiac based card-test-devices (Young et al. 2014). Guaiac based faecal occult blood tests also detect haemoglobin from ingested red meat and the peroxidase reaction may be falsely triggered by substances in foods such as such as melon, raw turnips and radishes and people are advised to restrict these foods from their diet for up to 72 hours in advance of guaiac based testing ([Lab Tests Online UK](#)). Faecal immunochemical tests are less susceptible to false positive results from foods and therefore there is no requirement for dietary restrictions prior to testing which may make them more acceptable to patients (Young et al. 2014).

Use of faecal immunochemical tests may also result in more accurate identification of people who need colonoscopy, and reduce the number of people referred because of false positive faecal occult blood tests.

Colonoscopy is an invasive procedure with associated complications, therefore reducing unnecessary referrals is preferable. Complications associated with colonoscopy include the possibility of heavy bleeding that needs further assessment (1 in 250 chance) and perforation of the bowel (1 in 1,000 chance) ([NHS Bowel Cancer Screening Programme 2012](#)).

Colonoscopy can also result in death in rare cases (1 in 10,000) ([NHS Bowel Cancer Screening Programme 2012](#)).

5 Scope of the evaluation

Table 3: Scope of the evaluation

Decision question	What is the clinical and cost effectiveness of using quantitative faecal immunochemical tests to triage low risk symptomatic populations for suspected colorectal cancer referrals?
Populations	<p>People presenting to primary care who have symptoms but are considered at low risk of colorectal cancer (that is people for whom faecal occult blood tests are recommended in NICE guideline 12).</p> <p>Where evidence is available subgroups may include :</p> <ul style="list-style-type: none"> • Age • Sex • People taking medications which increase the risk of gastrointestinal bleeding <p>Faecal haemoglobin levels are thought to differ according to age and sex, and in people taking medications which increase the risk of gastrointestinal bleeding. Different cut-off values may be needed for these subgroups.</p>
Interventions	<ul style="list-style-type: none"> • HM-JACKarc • FOB Gold • OC Sensor • RIDASCREEN haemoglobin + haemoglobin/haptoglobin
Comparator	<ol style="list-style-type: none"> 1. Guaiac based faecal occult blood tests 2. Clinical assessment and referral for colonoscopy based on lower gastrointestinal symptoms alone (referral to colonoscopy without triage) <p>The reference standard for assessing the accuracy of both the faecal immunochemical tests and the guaiac based faecal occult blood tests is colonoscopy. People with negative faecal occult blood tests may be followed up in primary care.</p>
Healthcare setting	Primary care
Outcomes	<p>Intermediate measures for consideration may include:</p> <ul style="list-style-type: none"> • Diagnostic accuracy • Test failure rates • Prognostic implications of false negative results • Uptake of testing by patients

	<ul style="list-style-type: none"> • Proportion of people referred to secondary care • Proportion of people followed up in primary care • Number of colonoscopies • Number of colorectal cancer diagnoses • Number of people with advanced adenomas detected and treated • Number of people with other bowel pathologies diagnosed • Time to colonoscopy and diagnosis
	<p>Clinical outcomes for consideration may include:</p> <ul style="list-style-type: none"> • Morbidity including adverse events associated with colonoscopy • Mortality
	<p>Patient-reported outcomes for consideration may include:</p> <ul style="list-style-type: none"> • Health related quality of life • Anxiety associated with testing, waiting for results and further diagnostic work up
	<p>Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:</p> <ul style="list-style-type: none"> • Cost of equipment, reagents and consumables • Cost of staff and associated training • Medical costs arising from testing and care including further follow up and safety netting in primary care • Medical costs arising from adverse events which arise from testing or further diagnostic work up, including those associated with false test results and inappropriate treatment.
	<p>The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.</p>
Time horizon	<p>The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p>

6 Modelling approach

6.1 Existing models

NICE's guideline on [suspected cancer: recognition and referral](#) included an [economic model](#) which aimed to assess the cost effectiveness of diagnostic

tests to diagnose colorectal cancer for patients aged 40 and over with a change in bowel habit in primary care. The model comprised a decision tree with combined Markov states to capture the diagnosis and subsequent staging of colorectal cancer and was run with one year cycle lengths and a lifetime time horizon. The population entering the model were people aged 40 years or over with a change in bowel habit presenting to their GP for the first time. The following diagnostic tests were included in the model: faecal occult blood tests (guaiac based), barium enema, flexible sigmoidoscopy, CT colonography, and colonoscopy. Faecal immunochemical tests, using data from one study which reported a sensitivity of 74.7% and a specificity of 88.0%, were included in a supplementary analysis.

7 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Older people and Jewish people of central and eastern European family origin are at increased risk of colorectal cancer. These potential equality issues are functions of the clinical condition and not the technologies under assessment. People with cancer are protected under the Equality Act 2010 from the point of diagnosis.

Faecal haemoglobin concentrations may be greater in men than women, and may also increase with age. Test cut-offs may therefore vary according to age and sex (Fraser 2012).

The tests may not be suitable for use in people with an existing diagnosis of inflammatory bowel disease, some of whom may be covered by the disability provision of the Equality Act 2010. Disabled people may need support to obtain and submit a stool sample, and to understand the purpose of the test and the implications of the test results.

Cultural preferences may influence the acceptability of tests that require collection of a stool sample.

8 Potential implementation issues

There will need to be agreement between primary care, gastric surgery, gastroenterology and laboratories about suitable local pathways, in addition to training about use of these pathways, to support adoption of faecal immunochemical tests and appropriate care for patients. Information for

patients may also have to be developed to explain both the purpose of the test and the most effective way to collect a sample.

Laboratories reporting faecal immunochemical tests will need to take part in recognised quality assurance schemes.

Appendix A Glossary of terms

Colchicine

A medication which is used to treat gout

Colonoscopy

An investigation that allows doctors to examine the lining of the colon (large intestine) using a flexible tube that contains a camera and light source (colonoscope).

Faecal immunochemical test

A test which detects faecal occult blood using antibodies against human haemoglobin.

Flexible sigmoidoscopy

An investigation that allows doctors to examine the lining of the lower section of the colon (sigmoid) using a flexible tube that contains a camera and light source (sigmoidoscope).

Guaic faecal occult blood test

A test which detects faecal occult blood using a test device containing guaiac paper. Hydrogen peroxide developer is added to the guaiac paper which reacts with the alpha-guaiaconic acid on the paper creating a blue colour change. Where haemoglobin is present in the sample, the haem speeds up the reaction creating a rapid colour change.

Haemoglobin

A protein molecule found in red blood cells. Its presence in faecal samples indicates that gastrointestinal bleeding may be occurring.

Haptoglobin

A protein which binds to haemoglobin making it less susceptible to breaking down as it passes through the gastrointestinal tract.

Appendix B Abbreviations

CT	Computed tomography scan
ELISA	Enzyme-linked immunosorbent assay
MRI	Magnetic resonance imaging scan

Appendix C Related guidance

Published NICE guidance

[Gastrointestinal cancers](#) (2016) NICE Pathway

[Suspected cancer: recognition and referral](#) (2015) NICE guidelines 12

[Low-energy contact X-ray brachytherapy \(the Papillon technique\) for early-stage rectal cancer](#) (2015) NICE interventional procedure guidance 532

[Preoperative high dose rate brachytherapy for rectal cancer](#) (2015) NICE interventional procedure guidance 531

[Transanal total mesorectal excision of the rectum](#) (2015) NICE interventional procedure guidance 514

[Combined endoscopic and laparoscopic removal of colonic polyps](#) (2014) NICE interventional procedure guidance 503

[Fluorouracil chemotherapy: The My5-FU assay for guiding dose adjustment](#) (2014) NICE diagnostics guidance 16

[Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy](#) (2014) NICE technology appraisal guidance 307

[Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel](#) (2013) NICE diagnostics guidance 11

[Ulcerative colitis: management](#) (2013) NICE guidelines CG166

[Crohn's disease: management](#) (2012) NICE guidelines CG152

[Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy](#) (2012) NICE technology appraisal guidance 242

[Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer](#) (2012) NICE technology appraisal guidance 212

[Selective internal radiation therapy for non-resectable colorectal metastases in the liver](#) (2011) NICE interventional procedure guidance 401

[Colonoscopic surveillance for preventing colorectal cancer in adults with ulcerative colitis, Crohn's disease or adenomas](#) (2011) NICE clinical guideline 118

[Colorectal cancer: diagnosis and management](#) (2011) NICE clinical guideline 131

[Endoscopic submucosal dissection of lower gastrointestinal lesions](#) (2010) NICE interventional procedure guidance 335

[Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis](#) (2010) NICE interventional procedure guidance 331

[Cetuximab for the first-line treatment of metastatic colorectal cancer](#) (2009) NICE technology appraisal guidance 176

[Radiofrequency ablation for colorectal liver metastases](#) (2009) NICE interventional procedure guidance 327

[Irritable bowel syndrome in adults: diagnosis and management](#) (2008) NICE guidelines CG61

[Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer](#) (2007) NICE technology appraisal guidance 118

[Laparoscopic surgery for colorectal cancer](#) (2006) NICE technology appraisal guidance 105

[Capecitabine and oxaliplatin in the adjuvant treatment of stage III \(Dukes' C\) colon cancer](#) (2006) NICE technology appraisal guidance 100

[Preoperative high dose rate brachytherapy for rectal cancer](#) (2006) NICE interventional procedure guidance 201

[Computed tomographic colonography \(virtual colonoscopy\)](#) (2005) NICE interventional procedure guidance 129

[Wireless capsule endoscopy for investigation of the small bowel](#) (2004) NICE interventional procedure guidance 101

[Improving outcomes in colorectal cancer](#) (2004) NICE guidelines CSG5

[Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer](#) (2003) NICE technology appraisal guidance 61

NICE guidance underdevelopment

[Suspected cancer](#) NICE Quality Standard. Publication expected May 2016.

[Colorectal cancer \(metastatic\) - cetuximab \(review TA176\) and panitumumab \(part review TA240\) \(1st line\) ID794](#). NICE technology appraisal guidance. Publication expected: April 2016

[Colorectal cancer \(metastatic\) - trifluridine \(with tipiracil hydrochloride, after standard therapy\) \[ID876\]](#). NICE technology appraisal guidance. Publication expected October 2016

[Microsatellite instability testing \(and alternative technologies identified during scoping\) for Lynch syndrome in people diagnosed with colorectal cancer.](#)

NICE diagnostics guidance. Publication expected January 2017

[Virtual chromoendoscopy for real-time assessment of colorectal polyps during colonoscopy.](#) NICE diagnostics guidance. Publication expected February 2017

NICE pathways

The faecal immunochemical tests guidance will be included in several NICE pathways, for example: suspected cancer recognition and referral pathway (published), gastrointestinal cancers pathway (published) and colorectal cancer pathway (published).

In some of these pathways, it may be appropriate to include the full recommendations of the guidance, in others it will only be necessary to give a link to the guidance.

Relevant guidance from other organisations

Association of Coloproctology of Great Britain and Ireland (2013)

[Management of the malignant colorectal polyp: ACPGBI position statement](#)

National Cancer Intelligence Network (2012) The characteristics of individuals with colorectal cancer who die rapidly after their diagnosis

SIGN (2011) Diagnosis and management of colorectal cancer

British Society of Gastroenterology (2011) The management of gastric polyps

British Society of Gastroenterology (2010) Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002)

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Appendix D References

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