UK National Screening Committee

Screening for Bowel Cancer

19 November 2015

Aim

1. To ask the UK National Screening Committee to make a recommendation, based upon the evidence presented in this document, on whether to replace guaiac occult blood testing (gFOBt) with the faecal immunochemical testing (FIT).

2. This document provides background on the items addressing the proposed modification to the NHS Bowel Cancer Screening programme.

Current programme policy and area impacted by the proposed change

3. Screening for bowel cancer is offered every two years to all men and women aged 60 to 74 in England, Wales and Northern Ireland; and to all men and women aged 50 to 74 in Scotland

4. Current policy is to send eligible people the gFOBt sampling card and test for the presence of blood using a simple test which is read by eye.

5. The proposal is to replace gFOBt with FIT. Key reasons supporting this proposal:

    a. FIT is subject to less analytical interference and can be measured more reliably using an automated analyser.

    b. FIT is sensitive to much lower concentrations of blood than gFOBt and therefore can detect cancers more reliably and at an earlier stage. The increased sensitivity enables FIT to detect more pre-cancer lesions (advanced adenomas)

    c. FIT requires a single faecal sample and is more acceptable to invited subjects which markedly increases participation rates.

    d. FIT is a cost effective alternative to FOBt

Consultation

6. A three month consultation was hosted on the UK NSC website. 26 organisations were contacted directly. Stakeholders were invited to comment on any aspect of the supporting documents and on whether they agree or disagree with the proposed modification. Annex A

7. Responses were received from the following 12 stakeholders: Association for Clinical Biochemistry and Laboratory Medicine (ACB), Association of Coloproctology of Great Britain and Ireland, Bowel Cancer UK, British Society of Gastroenterology (BSG), Cancer Research UK, Institute of Biomedical Science, NHS Bowel Cancer Screening Programme – Quality Manager the London Hub, NHS Bowel Cancer Screening Programme – National Radiology QA group, Royal College of Physicians and Surgeons of Glasgow, Royal College of Pathologists, Royal College of Radiographers, Society & College of Radiographers.

   Most press for a change as soon as possible and with a simple nationwide switch. An appreciation was shown in many responses of the endoscopy capacity as a limiting factor in setting the FIT sensitivity level as high as technically possible. A major theme was the urgency and importance of increasing endoscopy resource. The BSG stated clearly that implementation of FIT initially must not increase current colonoscopy referral rates. One consultee pointed out that pressure on CT colonography may also rise.

   The merits of using screening algorithms were supported in many responses with recommendations to ensure the programme(s) gather relevant data to enable these algorithms to be developed. Close working with Scotland was recommended particularly for pooling data to help with the process enhancing the screening algorithm. Many consultees recommended looking at those aspects of the whole programme, including bowel scope, which might enable more cancers and pre-cancers to be detected without exerting pressure on existing diagnostic services.

   All comments are in Annex B.

Recommendation

8. The Committee is asked to approve the following modification to Bowel Cancer Screening Programmes:

   The UK NSC recommends a change to the test used in the Bowel Cancer Screening Programmes. The use of Faecal Immunochemical Test as the primary test for bowel cancer should replace guaiac Faecal Occult Blood Test.

   As colonoscopy capacity grows or screening uptake increases, the UK NSC and programmes should review and recommend alteration of the cut offs to increase the number of cancers detected.

Annex A

List of organisations contacted:

1. The Association of Coloproctology of Great Britain and Ireland
2. Beating Bowel Cancer
3. Bladder & Bowel Foundation
4. Bowel Cancer UK
5. Bowel Cancer Wales
6. The British Association for Cancer Research
7. British Association of Surgical Oncology
8. British Association of Urological Nurses
9. The British Association of Urological Surgeons
10. British Society of Gastroenterology
11. Cancer Research UK
12. Faculty of Public Health
13. Lynn's Bowel Cancer Campaign
14. Macmillan
15. Medical Research Council
16. Primary Care Urology Society
17. Radiology: National Clinical Director for Diagnostics NHSE
18. Royal College of General Practitioners
19. Royal College of Pathologists
20. Royal College of Physicians
21. Royal College of Physicians and Surgeons of Glasgow
22. Royal College of Physicians of Edinburgh
23. Royal College of Surgeons
24. Samantha Walsh (NHSE)
25. Society and College of Radiographers
26. Urostomy Association

List of organisations who submitted a response without prior contact from the NSC Evidence Team:

1. Association for Clinical Biochemistry and Laboratory Medicine (The ACB)
2. Institute of Biomedical Science
3. NHS Bowel Cancer Screening Programme – London hub
4. NHS Bowel Cancer Screening Programme – National Radiology QA group
5. Royal College of Radiographers

Name:	Prof H Scott (in consultation with experts in colorectal surgery)	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Royal College of Physicians and Surgeons of Glasgow		
Role:	**Honorary Secretary**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ The name should be that of the organisation as above

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
	need for applicability in Scotland	Scotland has already 1. Completed a 6 month feasibility trial of FIT in 2 health boards - Ayrshire and Tayside 2. Submitted a Business Case to Scottish Government which has been accepted and funded 3. Appointed a FIT Implementation Group, which is working towards implementation of "FIT as a First Line test" in Scotland from the Spring of 2016.
	Concerns regarding the proposed cut-off level	The proposal to tailor the cut-off point for a positive test at a level (180ug/g of faeces) is based on that which would not increase current colonoscopy utilisation by the screening programme. However, we are concerned that patients will be falsely reassured by such a high 'negative' result. Efforts to increase availability of colonoscopy to investigate positive screening tests should be a priority and the screening programme should decrease the cut off level (to 20ug/g) as rapidly as possible to maximise the benefits of screening.

Name:	Dr Rachel Harris	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	The Society and College of Radiographers		
Role:	**Professional and Education Manager**		

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Yes ☐X No ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
General		The Society and College of Radiographers believes this is a sensible modification as uptake rates and sensitivity will be improved by the change and thereby patient outcomes.
General		The impact on already stretched colonoscopy services is of concern until the levels for further assessment are better defined.
General		There may be some, although minimal, impact on CTC services as the numbers referred for CTC may slightly increase. This of course, raises the need for workforce availability and training programmes.

Name:	Ann Wood	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	NHS BCSP London Hub		
Role:	Deputy and Quality Hub Manager, Biomedical Scientist		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ✓☐ No ☐

Section and / or page number	Text or issue to which comments relate	Comment
3	FIT	FIT has been shown to be more effective in screening for CRC as it will detect more positives depending on cut-off level used.
	FIT	Ethically I am assuming that it would be a country wide cut off so that there could not be accusations of 'postcode lottery'
4	Staffing: Endoscopy	In successive rounds less individuals will hopefully be detected with CRC so the demands on the endoscopy service will be less. Is it envisaged that the cut off could be lowered as the Programme progressed?
		Would it not be possible in the future to offer FIT instead of FlexiSig at 55? This would screen out all the people not at risk in a non-invasive way and the uptake may be better amongst this, generally, still working age group.
Economic Evaluation (Draft)		The overall impact, both financially and quality of life, with FIT appears to have a positive effect

Name:	Dominic Blunt	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	National BCSP Radiology QA group		
Role:	**Chair**		

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Yes X **No** ☐

Section and / or page number	Text or issue to which comments relate	Comment
Page 4 Consultation summary	Section on stafing	I note the proposal to tailor the cut off in sensitivity of FIT to match capacity in colonoscopy. While colonoscopy is the 'default' investigation, Computed tomography colography is used in between 5 and 10% of cases, and capacity in this investigative test also needs to be factored into the plan. Nationally CTC is stretched, the QA process lags behind those well established in other branches of screening, and there are parts of the country with no access to CTC. Our group looks to improve services and quality and help make the case for capacity planning. We would be happy to support the proposals with this caveat, and offer any help in planning.

Name:	Chris Chaloner	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Association for Clinical Biochemistry and Laboratory Medicine (The ACB)		
Role:	**Director of Scientific Affairs**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes x☐ **~~No~~** ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
General	General	The ACB welcomes this evidence review of testing in the Bowel Cancer Screening Programme
Consultation Summary Page 4	Table: Quantitative FIT performance	The ACB recognises that the evidence is overwhelming that the FIT test is diagnostically superior to the existing gFOB test
Consultation Summary Page 5/6	Acceptability	The ACB recognises that the FIT test is more acceptable to patients in general and previously hard-to-reach groups in particular and that this is a major advantage supporting increased equity of access and an enhanced patient experience
Consultation Summary Page 7	Analytical Interferences	The ACB notes that the absence of analytical interferences in the FIT test is an important advance towards maximising the number of reportable results and minimising wasted diagnostic opportunities

Consultation Summary Page 7	Analytical throughput: Analytical throughput gFOBt 50/hr/person vs FIT 260/hr/analyser	The ACB recognises the importance of building capacity in the laboratory arm of the screening system so as to increase productivity and enhance value for money
Consultation Summary Page 7	EQA: gFOBt - EQAS difficult IQC positivity monitoring; FIT - EQAS difficult Good analyser IQC	The ACB would underline the importance of developing a robust EQA scheme to underpin commutability of results across the regions served by each screening hub
General	General	The ACB agrees that, when taken together, the evidence presented represents an overwhelming argument in favour of changing the test system from gFOBt to FIT
General	General	The ACB strongly supports the proposal to change to measurement of FIT for the National Bowel Cancer Screening programme

Name:	Asha Kaur	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Bowel Cancer UK		
Role:	**Policy Manager**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ **No** ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
n/a	General – key message	Bowel Cancer UK strongly recommends the rapid implementation of the faecal immunochemical test (FIT) as a replacement to the guaiac faecal occult blood test (gFOBt). FIT has been shown to be a more accurate and easy to complete test than the current gFOBt. The introduction of FIT could have a double benefit of more accurately detecting bowel cancer and increasing the number of people participating in the screening programme. The Expert Review documents provide a comprehensive case for the adoption of FIT to aid the early detection of bowel cancer.
n/a	Introduction	Bowel cancer remains a significant health problem in the UK. Over 41,000 people are diagnosed with it each year and 16,000 people die from it. It is the fourth most common cancer and the second biggest cancer killer in the UK. This is despite bowel cancer being preventable, treatable and curable. The introduction of FIT into the screening programme provides us with further opportunity to detect and prevent more cancers. The evidence outlined in the consultation document on the comparative diagnostic yield for FIT vs gFOBT demonstrates that FIT has clear advantages over the gFOBT. Based on the strength of this evidence and the clear need to improve survival rates for bowel cancer we would strongly recommend that FIT is introduced as a matter of urgency, particularly as we know

		that gFOBT can miss at least 50 per cent of cancers. We would like to comment on the following issues in relation to the move from FOBt to FIT as the screening test of choice: 1. Sensitivity threshold 2. Colonoscopy capacity 3. Roll-out and implementation 4. Procurement of providers 5. Risk stratification 6. Sharing of best practice
	Sensitivity threshold	The consultation document "*Moving from guaiac faecal occult blood test (gFOBT) to a faecal immunochemical test for haemoglobin (FIT) in the bowel screening programme: A consultation*" states that a high clinical sensitivity at the analytical level of around 20 µg Hb/g faeces gives the highest detection of colorectal cancer and adenoma. Thus, clinical sensitivity is highest at the lowest possible faecal haemoglobin concentration cut-off. Furthermore, not only is FIT more clinically sensitive it is also, according to the Expert Review documents, cost-effective at every sensitivity level. If the full benefits of FIT are to be achieved then it is essential the test is brought in at a more sensitive level.
	Colonoscopy capacity	We understand and appreciate the impact that a low threshold could have on colonoscopy services, particularly as many centres are currently struggling to deal with increasing demand. We would therefore support the introduction of FIT at the same analytical level as the guaiac faecal occult blood test of 150 µg Hb/g to ensure a similar positivity yield and therefore minimise the impact on colonoscopy services. If FIT is to be brought in at a higher threshold, to maintain current positivity rates, there needs to be a

		clear and planned programme to increase capacity in endoscopy units to ensure the sensitivity can be adjusted to detect more cancers. We know that as screening progresses, round by round, the positivity rate decreases as disease is culled from the population choosing to participate in the screening programme. In this case we would expect the cut-off of faecal haemoglobin concentration to be lowered to fully occupy the available colonoscopy resource. This strategy is a much noted advantage of using quantitative FIT in a bowel cancer screening programme. We therefore welcome the consultation summary statement that UKNSC will recommend alteration of the cut-offs to maximise the number of cancers detected as colonoscopy capacity grows. The ultimate ambition of UKNSC should be to have lowered the sensitivity level to 20 µg Hb/g. We strongly recommend that any planned approach to reducing the cut-off should be made publicly available for both transparency and accountability purposes. Bowel Cancer UK would be happy to work with the UKNSC to produce this. We would also like to bring to the attention of the committee a recently published paper on the assessment of faecal haemoglobin concentration distributions which recommends the following strategy: • Examine the f-Hb distributions in pilot participants, or very early in the programme, by age and sex. • Determine positivity at different f-Hb cut-off(s) by age and sex. • Assess the characteristics of the invited population in determining the f-Hb cut-off(s) to be used to obtain the positivity required. • Change the f-Hb cut-off(s) where necessary, using the f-Hb distributions to set these objectively.

		• Use examination of the f-Hb to investigate problems. • Perform this assessment regularly as the programme evolves and change the f-Hb cut-off with screening round to fully occupy the available colonoscopy resource. Ref. Fraser C.G. *Assessment of faecal haemoglobin concentration distributions is vital for faecal immunochemical test (FIT)-based colorectal cancer screening programmes*. J Med Screen. 2015 Jul 20.[Epub ahead of print].
	Risk Stratification	FIT has the advantage of being a quantitative test and therefore offers flexibility. As a result different haemoglobin cut-off concentrations can be set depending on patient characteristics. It is well-documented that faecal haemoglobin concentrations rise with age, are higher in men than women, as well as in certain deprivation groups. The UKNSC must explore the introduction of risk stratification in the bowel cancer screening programme, particularly as the current BCSP has the software to support a programme of this kind. The UKNSC should also consider applying different criteria to participants in different episodes. Fraser CG, Rubeca T, Rapi S, Chen LS, Chen HH. *Faecal haemoglobin concentrations vary with sex and age, but data are not transferable across geography for colorectal cancer screening*. Clin Chem Lab Med. 2014;52:1211-6. Fraser CG, Auge JM; PROCOLON Group. *Faecal haemoglobin concentrations do vary across geography as well as with age and sex: ramifications for colorectal cancer screening*. Clin Chem Lab Med. 2015;53:e235-7. Digby J, McDonald PJ, Strachan JA, Libby G, Steele RJ, Fraser CG. *Deprivation and faecal haemoglobin: implications for bowel cancer screening*. J Med Screen 2014 ;21:95-7.
	Risk scoring	The UKNSC must consider combining various patient characteristics and the FIT level into a risk

		score to further inform referral. There is considerable literature on risk-scoring in the detection of bowel cancer and a number of well-validated methods are available, although few have incorporated faecal haemoglobin concentration. This recent paper from Spain shows an example of how risk scoring could be performed (Ref. Auge JM, Pellise M, Escudero JM, Hernandez C, Andreu M, Grau J, Buron A, López-Cerón M, Bessa X, Serradesanferm A, Piracés M, Macià F, Guayta R, Filella X, Molina R, Jimenez W, Castells A; PROCOLON Group. *Risk stratification for advanced colorectal neoplasia according to fecal hemoglobin concentration in a colorectal cancer screening program*. Gastroenterology. 2014;147:628-636). This strategy would divide participants into risk groups using factors such as age and gender, BMI, and any other variable seen or proved as important such as smoking and deprivation, along with the faecal haemoglobin concentration levels. An algorithm could be developed to facilitate this process to generate an individual risk score, which could then be used to determine referral. A cut-off risk score, appropriate for the colonoscopy resource available, could be calculated and modified with time as screening rounds progresses and as colonoscopy resources increases. In addition, there is the consideration that those with low risk could be invited at longer screening intervals than every two years allowing either more frequent invitation to those at highest risk or lowering of the risk-score cut-off that triggers referral.
	Roll-out	Our preferred option for roll-out would be an immediate switch from gFOBt to FIT, rather than an incremental roll-out.
	Procurement	The selection should be done objectively using a detailed and clear specification in the procurement process. It is vital that such a specification is prepared with significant input from professionals in laboratory medicine, as well as others involved in the organisation and management of the BCSP. The UKNSC needs to ensure that weightings are appropriate for each criterion to avoid procuring a

		test that is cheap but unsafe. A discussion document prepared by The Expert Working Group on FIT for Screening of the World Endoscopy Organisation could be used as a basis for the detailed specification required. http://www.worldendo.org/fit-for-screening-discussion-documents.html A comparative evaluation of FIT devices should take place to ensure a swift response when a procurement decision has been made.
	Sharing of best practice	Learning from Scotland, who are in the process of implementing FIT into the screening programme, will be key. In particular the screening programme should seek to share data and implementation plans. The programmes should also seek to ascertain data that could inform an enhanced screening algorithm which would allow for more effective use of limited colonoscopic resource.

Name:	Dr Richard Tighe	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	On behalf of the British Society of Gastroenterology		
Role:	**Clinical expert**		

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Yes x☐ No ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
n/a	General comments	There is clear evidence that FIT is a superior test for occult faecal blood when compared to guaiac testing, and the BSG would support a move to FIT testing for the bowel cancer screening programme. FIT not only improves uptake of FOBT screening but also has a greater sensitivity for detecting colorectal cancer at low cut-off values.
n/a	General comments	The BSG shares the concerns of others with regard to colonoscopy capacity, though this alone should not influence decisions about the right testing method for patients. The rate limiting step in the FOBT screening programme is colonoscopy capacity. The FOBT bcsp screening centres are currently funded for a 2% FOBT positivity rate (those requiring colonoscopy)and for a 60% uptake. Any changes to the programme affecting colonoscopy referrals would need policy and financial support – not only to cover funding for additional colonoscopy work, but also to establish additional colonoscopy capacity in a service which is already struggling with increasing workload. For example, a change from guaiac testing at a screening centre covering a population of 1 million to FIT at the cut-off of 20mcg/g as used in the pilot, would result in a 4 fold increase in positivity and a 10% increase in uptake. In practical terms,

		this would increase colonoscopy demand from FOBT bcsp from 7 lists per week to 28 lists per week for the increased positivity with a further 10% increase for improved uptake to 31 lists per week. This would require construction of 2 additional endoscopy suites, training of colonoscopists and supporting endoscopy staff. All of these are possible with policy backing but would require long term forward planning and would not be amenable to tweaking down the cut-off level year-by-year without adequate planning. Another consideration is that, by setting the cut-off rate for FIT too high (at 150-180mcg/g), FIT is not hugely better in detecting colorectal cancer than guaiac although uptake is 10% higher. The pilot analysis includes advanced adenomas in its case for a FIT of 150-180mcg/g – but the bcsp is a cancer detection programme and any adenomas detected are largely fortuitous. The discussion on cut-off values should therefore be focussed on colorectal cancer detection rates rather than all neoplasia.
n/a	General comments	The key to adopting FIT for the bowel cancer screening programme will be the cut-off level and forward planning of colonoscopy capacity and funding (likely need to prime-pump) to avoid swamping an already stretched service. Without additional colonoscopy capacity being commissioned, the BSG would expect the transition to FIT to be pitched at a cut-off level which achieves positivity 10% less than guaiac to allow for the estimated 10% increase in uptake – so that referral numbers for colonoscopy are unaffected.
n/a	General comments	Our consultation has also raised two other interesting points. 1. Would it be more advantageous to conduct FIT FOBT screening with a lower cut-off but less often so that colonoscopy demand is unaffected – at perhaps 5 yearly intervals, rather than a high cut-off 2 yearly. Perhaps this is something NICE could model.

		2. Several BSG members have raised the question of replacing Bowelscope in 55 year olds with FIT – so freeing up endoscopy capacity. Our view would be that the two programmes are different. FOBT is a cancer detection programme which does not reduce the numbers of cancers but may detect some at an earlier stage and so improves survival from CRC. Bowelscope is an adenoma detection programme which prevents the development of cancer and so lowers CRC incidence. A comparison was published in Gut in 2010 which demonstrated the flexible sigmoidoscopy compared with FIT (100mcg/g) detected 3 times the number of advanced adenomas and 10 times the number of non-advanced adenomas. Furthermore Atkins original study demonstrated that flexible sigmoidoscopy screening resulted in a greater reduction in colorectal cancer mortality compared to FOBT screening programmes and abandoning Flexible sigmoidoscopy screening for an enhanced FOBT screening does not seem logical Screening for colorectal cancer: randomised trial comparing guaiac-based and immunochemical faecal occult blood testing and flexible sigmoidoscopy. Dekken et al. Gut 2010 59:62-68

Name:	Sarah May	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Institute of Biomedical Science		
Role:	Deputy Chief Executive		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes X☐ No ☐

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3	Comparisons with gFOBT	The new test is clearly better than the current FOB test for both specificity and sensitivity and also ease of use for both patients and laboratory staff. The evidence for use of FIT is strong, and there is also evidence that faecal haemoglobin concentrations are age and sex dependent (McDonald et al, Clin Chem Lab Med. 2011) which makes the use of a quantitative method important
4	Costs	The economic modelling looks sound and clearly supports the new test 3.
5	Laboratories	More detailed information is needed on the costings and timelines for IT system development and technological solutions for

		automating the pre-analytics in the laboratory. At present they are somewhat generalised statements of intent rather than having any real substance to them

Cancer Research UK response to the UK National Screening Committee consultation: moving from guaiac faecal occult blood test (FOBT) to a faecal immunochemical test for haemoglobin (FIT) in the bowel screening programme - October 2015

Cancer Research UK welcomes the opportunity to respond to this consultation.

Summary

Cancer Research UK supports the adoption of the faecal immunochemical test for haemoglobin (FIT) into the bowel screening programme, as a replacement for the guaiac faecal occult blood test (FOBT). We support the timely replacement of FOBT with FIT because for each month that the introduction of FIT is delayed, around 30 people will miss their opportunity for an earlier diagnosis of their cancer.[i] Early diagnosis is incredibly important as the earlier someone's cancer is diagnosed, the better their outcomes – for example, regarding bowel cancer, nine out of ten people will survive their cancer for at least ten years if diagnosed at stage one, whereas this drops to just one in ten people when diagnosed at stage four.[ii]

Introducing FIT should be prioritised and in an ideal scenario it would be implemented at a low cut-off concentration. However, we understand that current limitations with endoscopy capacity mean a pragmatic approach is more likely to be successful. The introduction of FIT should follow a clearly defined, transparent and monitored timetable for the decrease in cut-off concentration, so we can be sure that the potential of this new technology is realised. This should take into account ongoing programmes of work and commitments from the Department of Health to address endoscopy capacity. Further details and a decrease in cut-off concentration should be included as part of a phased implementation, rather than delaying its introduction.

To ensure a smooth introduction of FIT into the bowel screening programme, the following should be considered:

1. Phased reduction of cut-off concentration
2. Detail on the test itself
3. Processes for subsets of patients – further research
4. Wider changes to the bowel screening programme
5. Cross-border sharing of information

We look forward to working with the National Screening Committee to ensure a smooth implementation process.

1. Phased reduction of cut-off concentration

The cut-off concentration for FIT should be carefully considered to maximise the detection of cancers and advanced adenomas, whilst appreciating the current capacity of endoscopy services. The papers provided through the consultation show that FIT is clearly more effective as it detects more neoplasms. It is also cost-saving compared with FOBT, especially at the lowest cut-off concentration (20ug haemoglobin per gram (Hb/g)). However, endoscopy demand increases as the cut-off is reduced, and current endoscopy capacity prohibits the use of lower cut-offs.

We appreciate that there are ongoing programmes of work to address endoscopy capacity. Whilst these are in progress, it is justifiable that the introduction of FIT is phased in according to a clearly defined, detailed and monitored timetable for reducing the cut-off concentration. The plan for phased introduction of cut-off should be publically available to ensure full accountability of the screening programme. The published timetable to reduce the cut-off concentration must coincide with increases in endoscopy capacity[iii]. The Department of Health has stated its ambition for 500,000 extra endoscopies to be delivered by 2020 and we welcome these efforts: as they begin to deliver increases in capacity, this should be reflected in a reduction in the cut-off concentration.

However, further capacity above these extra endoscopies is likely to be needed – as modelling suggests that around 750,000 additional endoscopies (250,000 more than the 500,000 already committed to) will be required over the next five years, *without* factoring in the decrease in cut-off concentration that is possible with FIT.[iv] Effort must be made to address this continuing capacity shortage.

A phased introduction should start in 2016 with a ≤150ug Hb/g threshold. The Independent Cancer Taskforce recommended that roll out should start 'as soon as possible'.[v] We estimate that the pilot results so far suggest that 150ug Hb/g would detect around 1600 more advanced adenomas every year compared to 180ug Hb/g. 150ug Hb/g has also been chosen in London as their cut-off threshold for their forthcoming pilot. The final ambition for the screening programme should be to maximise effectiveness, and reducing the cut-off concentration to 20ug Hb/g plays an important role in achieving this.

We also believe it is important that consideration is given to how the screening programme can use FIT more smartly, as well as more sensitively, to save more lives. FIT offers potentially much more than a simple binary test, by introducing different thresholds for different groups (e.g. by screening round or gender) there is the potential to concentrate resource where it is most needed. There is also the possibility of using the Hb concentration along with other factors to create a composite risk score. All such approaches would require an evidence base and we encourage the NSC, and the screening programmes, to consider this in planning for future development of the programme and to consider how useful data collection and analysis can be built in.

Detail on the phased introduction:
To ensure the introduction of FIT can be successful, it is important to consider that the transition to FIT will require different technology and organization of resources. The hubs involved in the pilot will already have the required equipment to analyse the kits in place. London will also have access to these analysers as they are conducting a pilot. Other hubs should consider bulk purchasing to increase cost-effectiveness.

The implementation plans, working across Public Health England and NHS England, should consider the following questions to deliver roll-out:

a. Should invitations be sent initially to specified age groups, people in different screening rounds or with different screening histories i.e. previous non-responders?

b. How to create the right balance of incentives and levers to ensure services provide a high-quality screening, which considers the drive to increase uptake and reduce health inequalities?
c. What is the level of required investment to ensure optimal roll-out?
d. Would the current infrastructure be able to cope with stratification (e.g. by age, gender etc)? If not, what updates or alterations to infrastructure would be required to support stratification?

2. **Detail on the test itself**

There are many manufacturers producing FIT kits and analysers. The OC-SENSOR system used in the pilot is likely to be the most suitable[vi] given its prior use in the England population. Consideration should be made for bulk purchasing across the screening hubs, to ensure the screening programme achieves the best possible value for money through potential discounts.

As demonstrated in the pilot, the collection of one sample leads to advantages in uptake. We therefore recommend that one sample should be collected for each participant. We recognise that collecting multiple samples may have merits, particular with early screening rounds, but the increased uptake because providing just one sample is simpler, remains an advantage that FIT has over FOBT.

3. **Processes for subsets of patients – further research**

Further research should be conducted to ensure that there are clearly defined processes and sensitivity thresholds in place for management of the following subsets of patients:

a. Where the result comes in just under the threshold
b. For those having their first versus a repeat screen
c. Men/women
d. Age groups
e. Different deprivation groups
f. Whether they have taken part in bowel scope screening
g. Those with other risk factors, combined with their FIT score to provide a referral

The phased implementation plan should outline how and when these questions can be explored which will not disrupt the introduction of FIT.

Communications, Patient and Public Information

We understand that information has been produced as part of piloting FIT and feel it would be important to have this reviewed and evaluated, ensuring that there is patient and public involvement and engagement during this process. Cancer Research UK would be happy to assist with this.

4. **Wider changes to the bowel screening programme**

Bowel scope

Although the National Screening Committee are not considering changing other aspects of the programme such as bowel scope, follow-up diagnosis, treatment or surveillance, these should be considered in tandem with the introduction of FIT, as well as cost-effectiveness of these two tests in

combination. This should include consideration of the optimal combination of FIT and bowel scope, including potential changes to the age range, and the screening interval for FIT.

Surveillance will need further attention: as the introduction of FIT will pick up more advanced adenomas, more people will enter surveillance. This will have a big impact on endoscopy capacity.

Data

FIT provides a quantitative result: consideration should be made as to the recording, use and communication of this, as it may have clinical utility (in addition to just recording whether someone had a 'positive or negative' result according to the cut-off concentration specified at the time). It is also important to continue collecting data on the efficacy of the whole bowel cancer screening programme in combination with bowel scope.

Data from FIT and the bowel cancer screening programme more generally, including coverage, uptake and positivity rate, should be made available in a timely manner. This should be available as an aggregated performance measure to the public, for example as part of the Public Health Outcomes Framework (as cervical and breast are already) as well as in appropriate forms to researchers and analysts.

5. **Cross-border sharing of information**

As Scotland has already announced that it will be implementing FIT, it would be pertinent to ensure that all nations are sharing information which may enable a smooth introduction of FIT to their respective bowel screening programmes.

About us

Cancer Research UK is the world's largest independent cancer charity dedicated to saving lives through research. The charity's pioneering work has been at the heart of the progress that has already seen survival rates in the UK double in the last forty years. In 2014/15, Cancer Research UK spent £434 million on research in institutes, hospitals and universities across the UK. The charity supports research into all aspects of cancer through the work of over 4,000 scientists, doctors and nurses.

For more information, please contact Sara Bainbridge,

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[i] Estimated by extrapolating the pilot results to the number of people invited to FOBT bowel screening in England 2012-13 (source: www.publications.parliament.uk/pa/cm201314/cmhansrd/cm140401/text/140401w0001.htm#1404026000015)

[ii] Bowel Cancer (C18 – C20) Ten-year relative survival rates by diagnosis, Former Anglia Cancer Network, 1996 - 2000

[iii] https://www.gov.uk/government/news/from-2020-people-with-suspected-cancer-will-be-diagnosed-faster

[iv] Scoping the Future: a evaluation of endoscopy capacity across the NHS in England (2015) Health Services Management Centre at the University of Birmingham and the Strategy Unit at NHS Midlands and Lancashire Commissioning Support Unit, on behalf of Cancer Research UK

[v] Achieving World-Class Cancer Outcomes: a strategy for England, 2015 – 2020 (2015) Independent Cancer Taskforce

[vi] Lamph, SA; Bennitt, WE; Brannon, CR and Halloran, SP, *Evaluation report: immunochemical faecal occult blood tests* Centre for Evidence-based Purchasing (2009)

The Royal College of Pathologists
Pathology: the science behind the cure

UK National Screening Committee Bowel Cancer Consultation

The Royal College of Pathologists' written submission

October 2015

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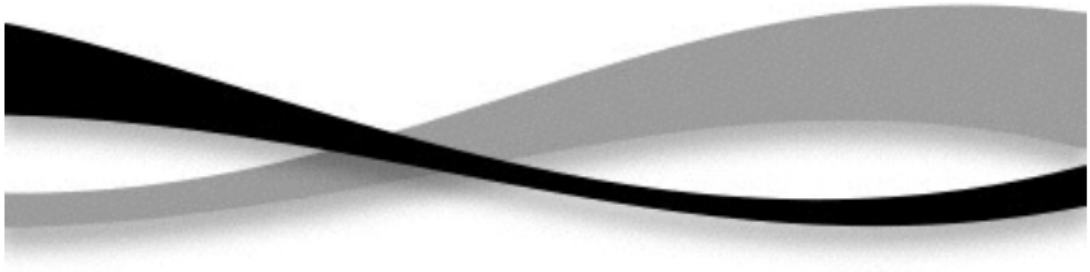

1 About the Royal College of Pathologists

1.1 The Royal College of Pathologists (RCPath) is a professional membership organisation with charitable status. It is committed to setting and maintaining professional standards and to promoting excellence in the teaching and practice of pathology. Pathology is the science at the heart of modern medicine and is involved in 70 per cent of all diagnoses made within the National Health Service. The College aims to advance the science and practice of pathology, to provide public education, to promote research in pathology and to disseminate the results. We have over 10,000 members across 19 specialties working in hospital laboratories, universities and industry worldwide to diagnose, treat and prevent illness.

1.2 The Royal College of Pathologists comments on the UK National Screening Committee Bowel Cancer Consultation. The following comments were made by Fellows of the College during the consultation which ran from 21st August until 16th July 2015.

2 General consultation responses:

2.1 RCPath Fellows overwhelmingly supported the recommendations and considered that the case for the CRC screening programme to move from gFOBt to FIT was simple and clear. This was for several reasons.

2.2 Problems with the currently used guaic-based test were cited. The FOBt produces a colour change based on peroxidase if the globin part of Hb is present in the stool and comes as a 3 sample test kit which is unpleasant to use and may need to be repeated. It is also not specific to human Hb. A manual and subjective method of measuring the haem moiety of Hb and therefore it is nonspecific and the simple redox reaction used for detection is crude and subject to a myriad of potential dietary and drug interfering substances. Specifically it gives false positives due to peroxidise in the diet.

2.3 In contrast FIT is an automated objective means of measuring the quantity of Hb in faeces. It uses an antibody against the globulin moiety of Hb and, as such, is specific for human haemoglobin.

2.4 RCPath Fellows cited the literature published on the topic including a large number of clinical trials which compare FIT with gFOBt. These have been greatly supported by the evidence from the FIT pilot performed during 2014/5 in England. All of these studies demonstrate predictable improvement in the detection of bleeding due to CRC but importantly also from the precursor lesions, advanced adenomas both at high and intermediate risk. These studies demonstrate that FIT can be both diagnostic and preventative in its role as a screening biomarker.

2.5 Additional benefits of the FIT test were mentioned. FIT provides additional opportunities not possible with gFOBt because it provides quantitative results. This important enhancement means that the cut-off concentration can be selected to ensure the programme works within its endoscopy capacity but of equal importance, it means that FIT can be be used as one of several risk factors for CRC and that it can be used similarly to how cholesterol is used in the assessment of CHD. The other risk factors can be age, sex, screening history all of which are held in the screening database but others like BMI, smoking, drinking and family history could also enhance a multivariate risk algorithm with FIT at the centre. This development is now under investigation in the UK and several other countries.

2.6 In regard to future developments in the field it was noted that whilst much work has been done, and continues to be done, in the search for other biomarkers, the only development of proven significance has been with combining a panel of DNA markers in faeces with FIT. This test is being marketed as Cologuard, it currently requires a full stool sample, costs about £500 and has a much higher false positive rate than we have with gFOBt. It points the way for the future but it is a long way away from it having value in a population-based screening programme. No blood marker has been found which is as sensitive and specific as FIT but the search continues.

2.7 Therefore the response from the College is that we believe that FIT is clearly the way forward for CRC screening in the UK, that if we are to benefit from its full potential the positivity rate (referral to colonoscopy) needs to be greater than that used currently for gFOBt and to do so the NHS needs to increase its endoscopy capacity closer to that enjoyed in most other developed countries.

2.8 With regard to implementation, it was noted by the Fellows of the RCPath that the change to FIT in the Scottish Bowel Screening Programme had already been approved and announced by the Scottish Health Secretary in February 2015. Work was on-going to progress this change over the next 18 months or so in Scotland and the Welsh and Northern Irish programmes had yet to announce any changes to their screening programmes.

2.9 Finally, the Fellows remarked that the value of FIT to CRC screening is such that early implementation will bring substantial clinical benefit and should therefore be considered a high priority.

NSC UK National Screening Committee

Name:	Professor RJC Steele on behalf of The Association of Coloproctology of Great Britain and Ireland	**Email address:**	
Organisation (if appropriate):	Association of Coloproctology of Great Britain and Ireland		
Role:	RJC Steele is President of The Association of Coloproctology of Great Britain and Ireland		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☐ yes **No** ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and ad as required.*
1. Sensitivity threshold	What should the sensitivity threshold be on introduction and what would be the optimal sensitivity threshold?	Currently the Guaiac Faecal Occult Blood Test (gFOBT programme operates at a test sensitivity which is equ

	We, ideally, would want the test to be brought in at as sensitive a level as possible but appreciate the colonoscopy constraints.	around 80 µgHb/g faeces, and if the introduction of Quantitative FIT is to have no impact on colonoscopy, then this is the cut off that would have to be used. However, there is incontrovertible evidence that clinical sensitivity rises with analytical sensitivity and it could be argued that the cut off of about 10 µgHb/g faeces would give optimal clinical sensitivity. This, however, would come at a significant reduction in specificity and hence in the negative colonoscopy rate.
	Should there be an incremental increase in sensitivity level over a period of time, with a clear and timetabled programme of action to increase capacity at screening centres. Is this feasible?	From a screening point of view this would certainly be desirable; whether or not it is feasible depends on colonoscopy capacity. There is increasing interest in the use of Quantitative FIT In order to triage symptomatic patients and if this were to be introduced nationally, it could bring about a reduction in the need for colonoscopy in the symptomatic service which could be reinvested in the screening service.
	What would a strategy for incremental increase in sensitivity level look like?	It would probably make sense and cause the least disruption to introduce FIT at a cut off of around 80 µgHb/g faeces but aim to bring this down to 10 µg over a period of approximately 5 years to allow development of colonoscopy services and also to take account of decreasing demand in the symptomatic service as suggested in the last section.
2. Providers	Best option for the screening programme? Same as pilot?	There are now a number of systems available for Quantitative FIT, and it is important that an up to date procurement process is

		employed, taking account of the relevant performance and cost.
	Benefits and drawbacks of test used in pilot? i. OC-SENSOR (Eiken Chemical Co. Ltd., Japan, supplied by Mast Diagnostics UK) _ England Pilot ii. HM-JACKarc, manufactured by Kyowa Medex Co., Ltd, supplied by Alpha Laboratories – Scotland	Both of these systems seem to perform to approximately the same standards with the exception that the detection limit appears to be lower with the HM-JACKarc.
	What strategy should be used to choose type of test?	Formal detailed procurement process.
	Any learning from Scotland?	The FIT Pilot in Scotland was carried out using a cut off for faecal haemoglobin of 80 µgHb/g faeces which provides the same clinical and analytical sensitivity as the current gFOBT. This study, therefore provides precise insight into what might be expected were Quantitative FIT to be introduced at this level. (Reference: Steele *et al* United European Gastroenterology Journal 2013;1:198-205) It would also be possible to obtain the specification used for the Scottish procurement process.
	Technical/operational performance? Are any easier/better for patients to use?	All the Quantitative FIT systems are subtly different but there has not been any high quality research comparing the ease of use of the different systems. It may be useful to use focus group studies to

		explore this area.
3. Roll-out/implementation	Preferred option for roll-out? Immediate switch	Although an immediate switch might represent a risk if there was a problem with the new system which had not been foreseen, this would be our favoured option. Having both systems running in parallel would create operational difficulties and there might be a problem with staff retention in the knowledge that the labour intensive gFOBT was being phased out. In addition the public would understand that a better test was on its way and may choose not to complete the gFOBT with serious consequences for uptake.
	What will the transitional process look like?	As suggested above the ideal would be an immediate switch which would of course require extremely careful preparation and significant modification to the IT System.
	Overlap b/t gFOBT and QFIT?	Although we believe this should be minimised, it would be inevitable to have a short period of overlap as gFOBT kits would still be coming in while the QFIT were being issued.
4. Risk stratification and personalisation of the programme	Would the current BCSP support this and if not what change would need to be made?	The information that would be available to the BCSP on individuals completing the screening test would be the faecal haemoglobin concentration, the subject's age and the subject's gender. As we know that faecal haemoglobin concentration and colorectal cancer risk vary by age and gender, it would make sense to develop a risk score on the

		basis of all three parameters. This would not be supported by the current system but should be quite possible to achieve by means of a significant modification of the IT system.
5. A combined risk score	Should other risk factors as well as FIT inform referral?	As in the last section we would suggest trying to incorporate age and gender into a risk score.
6.Screening age	Should we be calling for screening to start from age 50?	Evidence from the Scottish Screening Programme indicates that between the ages of 50 and 60 there is a substantial yield of pathology from gFOBT. Although we do not have access to the most up to date data, it is understood that the flexible sigmoidoscopy programme introduced at the age of 55 in England does not appear to be associated with a particularly good uptake or with particularly good detection of colorectal neoplasia; it is also logistically and difficult to provide. Our suggestion would be to carry out a critical appraisal of the impact of the current flexible sigmoidoscopy programme and make a decision on the age of starting FIT screening based on the outcome.
7.Learning from Scotland/other nations	How should England work with Scotland and what is the best approach to working together/sharing best practice?	Currently the five English Hubs and the Centres in Scotland, Northern Ireland and Wales meet once per year in order to share ideas and practice. This could perhaps be formalised and meetings could either be longer or more frequent.
	Is there anything on data, resources/staffing/equipment or anything else that we should also be commenting on?	It is essential that all laboratories engaging in FIT testing undergo robust external quality assessment. It is also, we believe, essential that all the Hubs and preferably all the UK Nations use the same analyser and the same criteria for triggering colonoscopy. A coordinated UK Quantitative FIT

		Screening Programme will generate large amounts of unique data over a short period of time and we believe that an ongoing process of monitoring and evaluation should be complemented by a research based approach to optimising the screening programme. By way of example it would be extremely useful to compare existing processes with risk adjusted screening using age and gender. In addition, there may be merit in decreasing the cut off and increasing the screening interval and there may also be mileage in varying the screening interval according to the observed faecal haemoglobin concentration. We also believe that it is very important to stress to people having a flexible sigmoidoscopy that subsequent participation in the FIT programme is a crucial component of the screening programme, as flexible sigmoidoscopy does not offer protection against right sided cancer, and the duration of the effect of a single sigmoidoscopy at the age of 55 is unknown.