The cost-effectiveness of immunochemical faecal occult blood testing vs. guaiac faecal occult blood testing for colorectal cancer screening in the NHS Bowel Cancer Screening Programme

Report to the UK National Screening Committee

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1 Introduction

Objectives

This report presents the results of a cost-effectiveness analysis of faecal immunochemical testing (FIT) vs. guaiac faecal occult blood testing (gFOBT) for colorectal cancer screening for a UK population aged 60-75 years in the NHS Bowel Cancer Screening Programme (NHSBCSP).

A mathematical model was constructed in order to estimate the difference in costs and health outcomes of screening using FIT kits compared to current screening using gFOBT kits.

The model structure is based on a previous economic evaluation conducted in 2011, which evaluated various screening options for the NHSBCSP (Whyte et al., 2012).

The model has been populated with recent data including:

- updated unit costs for the cost year 2013/14
- updated colonoscopy complication figures from recently published data from the NHSBCSP (Rutter et al., 2014)
- screening test characteristics for a range of FIT cut-off values using detection rates from the NHSBCSP pilot of immunochemical testing for bowel screening (Moss, 2015) (referred to in this report as "the FIT pilot"), enabling the presentation of cost and effect outcomes across a range of FIT cut-off levels

The cost and quality of life outcomes of the model are presented for the base case assumption of a FIT cut-off of 180µg/g and also for a range of FIT cut-off values from 20 µg/g to 180 µg/g. A range of deterministic sensitivity analyses are presented which test the effect of uncertainty around key model parameters on the outcomes. Probabilistic sensitivity analyses are not presented in this report and will be incorporated in future work.

2 Model structure

Overview of model structure

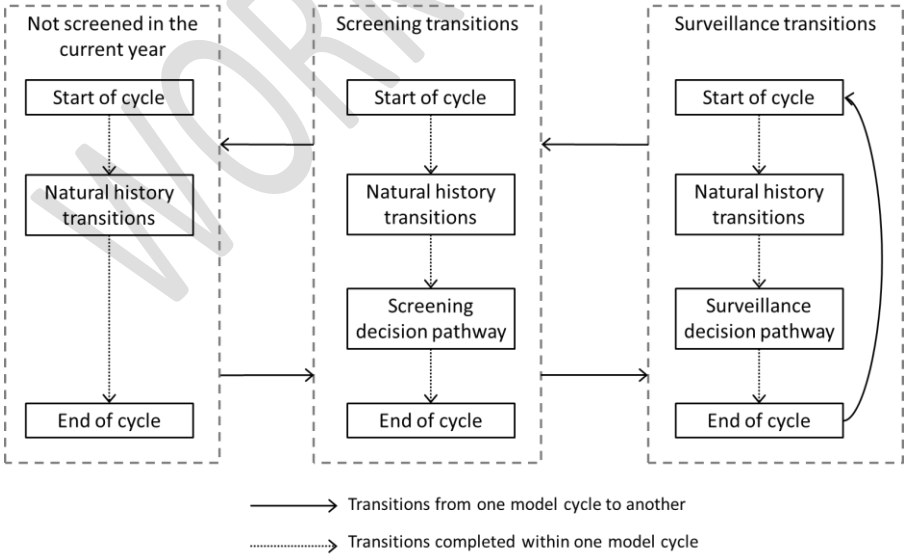
The model is composed of three parts as illustrated in Figure 1, each corresponding to the pathway subjects take in each model cycle: a non-screening year, a screening year, and surveillance transitions. All subjects begin in the non-screening part and can transition between each of the three model parts once per cycle of the model. The cycle length of the model is 1 year.

Within all three parts of the model subjects are grouped into health states corresponding to their underlying disease state: normal epithelium, presence of adenomas, undiagnosed and diagnosed colorectal cancer or death. Transitions between these health states occur once per cycle; see **Natural history transitions** for information on the transitions between underlying health states.

Each of the three model parts contains a set of decision rules that determine, given the underlying health state subjects are in at the start of the cycle, which health state subjects will move to by the end of the cycle, and therefore which part of the model they will move to in the next cycle. The transitions within the non-screening year correspond to the natural history transitions described in **Natural history transitions**. The transitions within the screening year consist of the natural history transitions followed by the screening decision pathway, as described in **Screening decision pathway**. The transitions for the surveillance cycles consist of the natural history transitions followed by the surveillance decision pathway, as described in **Surveillance decision pathway**.

In each arm of the model (FIT and gFOBT testing scenarios) all subjects begin the model at age 30 with normal epithelium (no adenomas or cancers). Once subjects reach the minimum screening age (60 years old) screening begins and all subjects move to the screening part of the model. At the end of each cycle in the non-screening part subjects always transition to the screening part. Similarly subjects can only spend one year undergoing screening transitions before moving to either a non-screening year or surveillance. This alternating pattern simulates bi-annual screening rounds. Subjects entering the surveillance part remain in that section of the model for several model cycles until they exit surveillance under the appropriate decision rules (see **Surveillance decision pathway** for information about transitions).

Figure 1: Diagram of overall model structure in three parts, each lasting for one model cycle (one year)



Natural history transitions

All subjects in the model are grouped according to their underlying health state. The possible health states are: normal epithelium, normal epithelium post-polypectomy, low risk adenoma (LR), high risk adenoma (HR), undiagnosed colorectal cancer (CRC) at each Duke's stage (A,B,C,D), diagnosed colorectal cancer at each Duke's stage (A,B,C,D), Death due to CRC, Death due to other causes (non-CRC mortality or perforation during colonoscopy). Transitions between health states occur once in each cycle. The health states and possible transitions are shown in Figure 2.

Figure 2: Diagram of underlying health states and natural history transitions

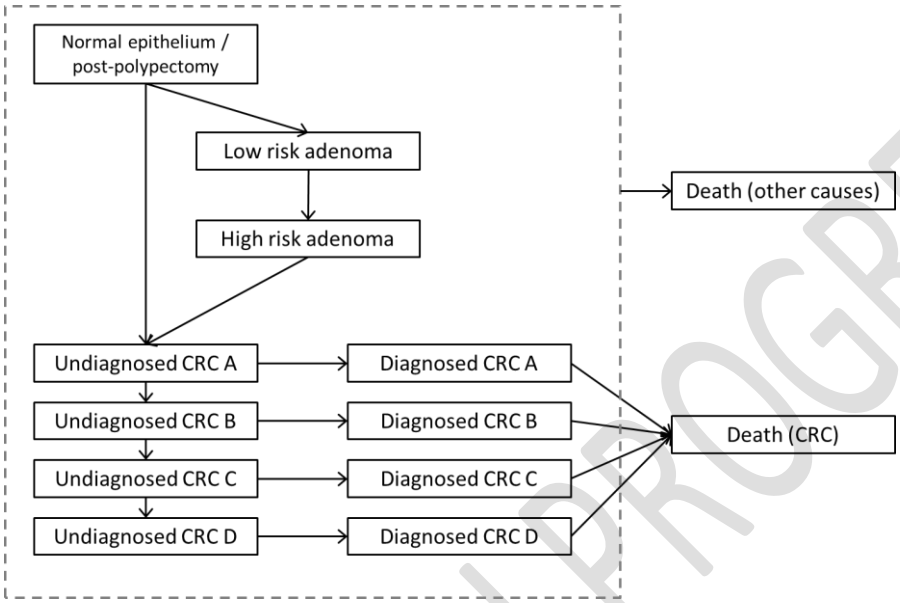


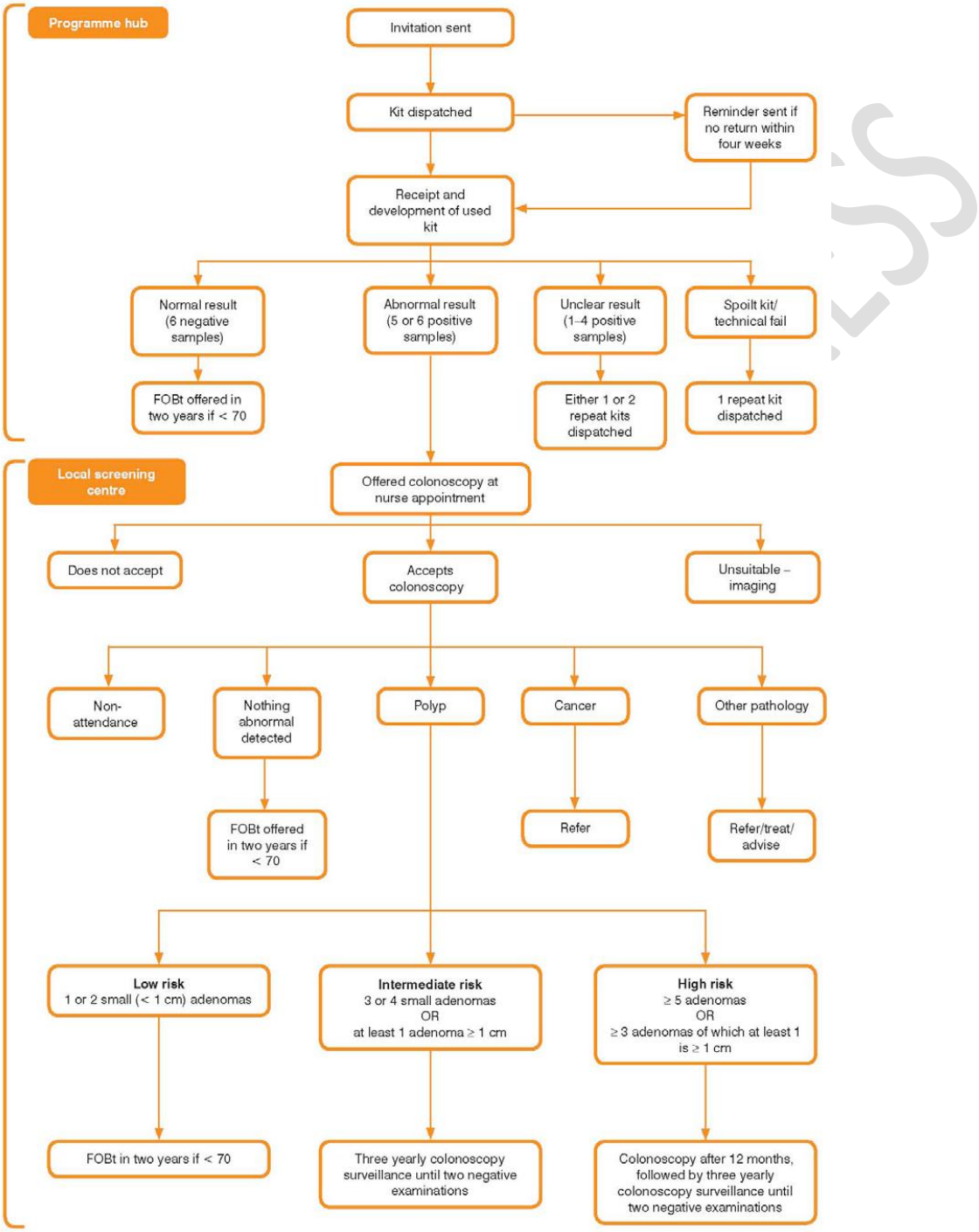
Figure note: Subjects can transitions from any health state within the dotted box to Death (other causes); CRC A: Duke's Stage A colorectal cancer

The transition probability parameters for the natural history part of the model are given in Section 3.

Screening decision pathway

The decision pathway used for the screening part of the model aligns with the current bowel cancer screening programme pathway, as shown in Figure 3. The pathway is the same for both arms, with either FIT or gFOBT as the kit used for screening.

Figure 3: Screening and surveillance pathway (source: NHS public health functions agreement 2015-16)



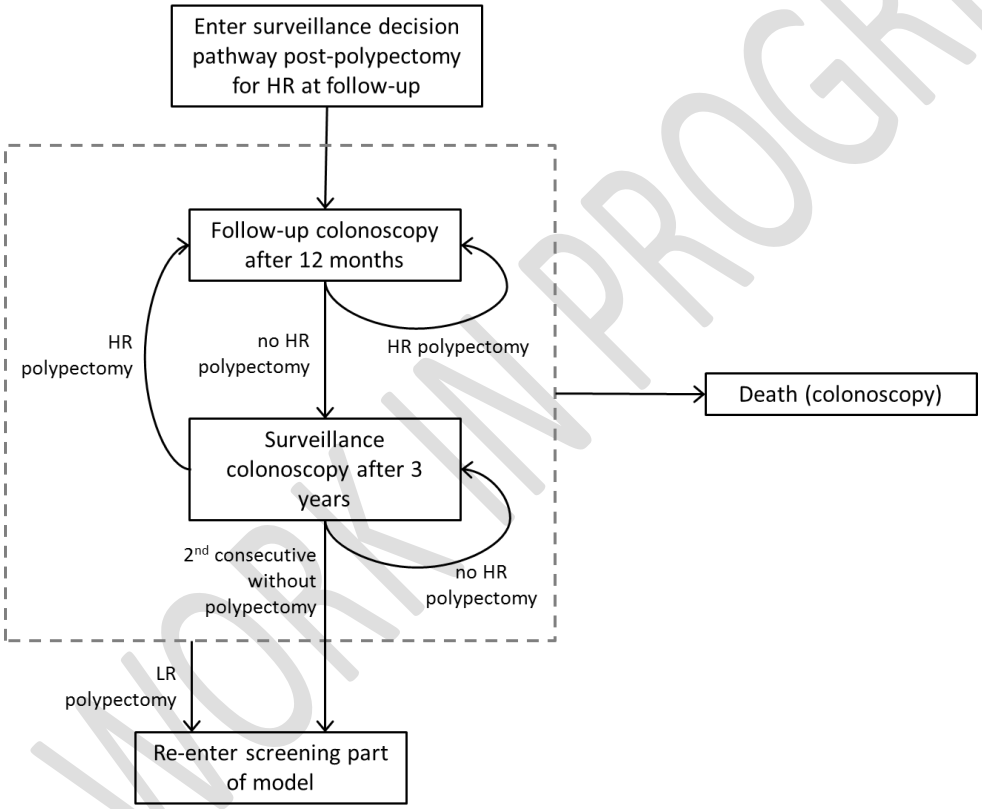
Surveillance decision pathway

As shown in Figure 3, following the screening pathway any subjects who have had polypectomy for high risk adenoma enter the surveillance part of the model in the next cycle. The surveillance transitions as described in this figure follow recommendations updated in 2010 (Cairns et al., 2010).

All subjects enter the surveillance part of the model after polypectomy for high risk adenoma, and subsequently undergo natural history transitions, followed by the surveillance decision pathway as shown in Figure 2. It is a structural assumption of the model that people exiting surveillance return to the screening part of the model (i.e. they receive a screening kit the next cycle after they discontinue surveillance).

The surveillance recommendations published in 2010 (Cairns et al., 2010) recommend that surveillance is stopped at age 75 years. However since people are still screened up to age 75 years the model assumes surveillance stops at age 80 years, so that those screened in the final screening year also have some years of surveillance after HR polypectomy.

Figure 4: Diagram of surveillance decision pathway



HR: high risk polyp; LR: low risk polyp

3 Model parameters

Population

The assumptions regarding population size and gender distribution are shown in Table 1. The model was run using a population size of 711,228 people at age 60 years, taken from ONS estimates (Office for National Statistics, 2014a) (latest available data). Screening pre-invites are assumed only to be sent to people without a diagnosis of CRC. This corresponds to a target screening population of 701,809 people at age 60 years, based on the estimated prevalence of CRC in the population at age 60 years using the natural history model.

Table 1: Population-based parameters

Parameter	Value	Source
Population size aged 60 years	711,228	(Office for National Statistics, 2014a)
Target screening population size aged 60 years (those without a diagnosis of colorectal cancer)	701,809	Model estimated using prevalence of CRC from natural history simulation
Percent male at age 60	49.2%	(Office for National Statistics, 2014a)

Natural history parameters

Parameters for natural history transitions were based on calibrated model parameters from the previous NHS BCSP model as reported in (Whyte et al., 2012). The parameters are summarised in Table 2.

Table 2: Natural history parameters

Parameter	Value	Source
Normal -> LR adenoma age 30	0.021	(Whyte et al., 2012)
Normal -> LR adenoma age 50	0.020	
Normal -> LR adenoma age 70	0.045	
Normal -> LR adenoma age 100	0.011	
LR adenoma -> HR adenoma age 30	0.009	
LR adenoma -> HR adenoma age 50	0.008	
LR adenoma -> HR adenoma age 70	0.008	
LR adenoma -> HR adenoma age 100	0.004	
HR adenoma -> pre-clinical Duke's A CRC age 30	0.029	
HR adenoma -> pre-clinical Duke's A CRC age 50	0.025	
HR adenoma -> pre-clinical Duke's A CRC age 70	0.054	
HR adenoma -> pre-clinical Duke's A CRC age 100	0.115	
Normal epithelium -> preclinical Duke's A CRC	0.000	
pre-clinical Duke's A CRC -> pre-clinical Duke's B CRC	0.508	
pre-clinical Duke's B CRC -> pre-clinical Duke's C CRC	0.692	
pre-clinical Duke's C CRC -> pre-clinical Duke's D CRC	0.708	
Symptomatic presentation with Duke's A CRC (pre-clinical -> clinical A)	0.044	
Symptomatic presentation with Duke's B CRC (pre-clinical -> clinical B)	0.176	
Symptomatic presentation with Duke's C CRC (pre-clinical -> clinical C)	0.369	
Symptomatic presentation with Duke's D CRC (pre-clinical -> clinical D)	0.735	
LR post-polypectomy to LR	0.100	
LR post-polypectomy to HR	0.040	
HR post-polypectomy to LR	0.188	
HR post-polypectomy to HR	0.568	

("->" denotes transition probability); LR: low risk; HR: high risk; CRC: colorectal cancer; all variables presented by age were converted to piecewise linear distributions for use in the model

All-cause mortality

All-cause mortality estimates were taken from ONS national life tables for 2011-13 (Office for National Statistics, 2014b) (latest available data). All-cause mortality was weighted by the proportion of male/females in the population from Table 1. For people in clinical CRC states non-cancer mortality rates were obtained by removing cancer-specific mortality from the all-cause mortality rates.

Cancer-related mortality

Cancer-related mortality was estimated from 5-year survival statistics presented by colorectal cancer stage at diagnosis (Aravani, 2009). A Weibull model was used to extrapolate the 5-year statistics to the maximum time horizon of the model. Figure 5 illustrates the model fit to the data and the extrapolated colorectal cancer survival rates over time, by Duke's stage at diagnosis.

Figure 5: Weibull extrapolation of 5-year CRC survival data (shown up to 35 years from diagnosis)

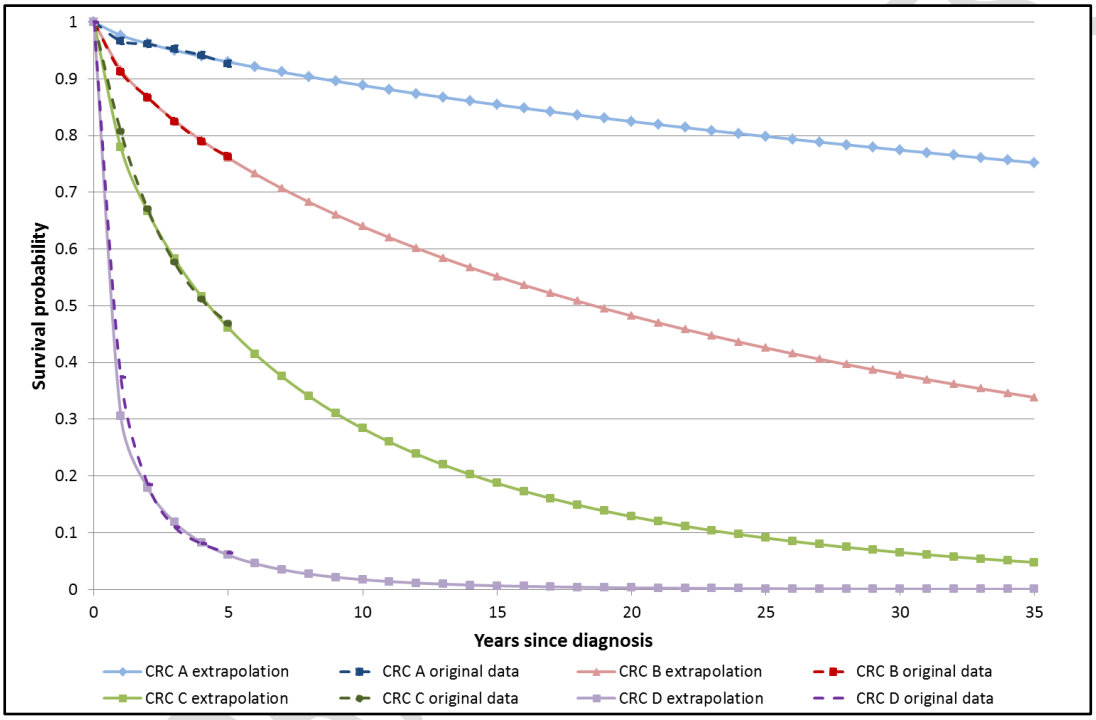


Figure note: CRC A original data: 5-years survival estimates from (Aravani, 2009); CRC A extrapolation: Weibull fit to 5-year estimates extrapolated to a greater number of years since diagnosis than original data

Screening parameters

The screening test parameters used in the model are summarised in Table 5.

Screening test characteristics

There were two potential sources of sensitivity estimates for FIT and gOBT: estimated screening test characteristics using the detection rates from the FIT pilot, or estimates from the published literature.

A meta-analysis published in 2014 (Launois et al., 2014) compared the detection rates and test characteristics of FIT (OC test series, Magstream) and gFOBT (Hemoccult) in studies that used colonoscopy to confirm screening test kit accuracy. The OC test series consists of OC-Sensor, OC-Hemodia, OC-Micro and OC-Sensor kits. The authors of the study state that these kits can be considered equivalent according to conventions in other recent systematic reviews, therefore the results presented for "OC-Sensor" were calculated using combined detection rates from any of these test kits. The stated inclusion criteria stipulate that the study populations should be aged 40 years or over, however due to limited numbers of studies on which to base the meta-analysis the authors include four studies with a up to 27.2% of the population aged between 20 and 40 years. Therefore the populations from the included studies do not match the UK screening age range.

The FIT pilot was based on a population from two UK BCSP screening hubs, therefore it was assumed that the demographics of the study subjects (particularly the age range of the screened population) more closely match the UK population than the populations included in the meta-analysis. Both FIT and gFOBT were used in the same population concurrently meaning the prevalence of underlying disease can be assumed to be equal for each group of subjects enabling direct comparison of the detection rates. Therefore the results from the FIT pilot were used to estimate screening test characteristics for the base case.

Sensitivity was calculated using the detection rates for each type of neoplasia from the FIT pilot, and the estimated prevalence of neoplasia in the population from the natural history model at the start of screening (age 60 years). The use of prevalence estimates from a single year of the model introduces uncertainty around the estimates, and as such the test characteristics are varied in the model sensitivity analyses (see Section 6).

The test characteristics were estimated separately for each cut-off value for the FIT test based on the results from the FIT pilot. CRC detection in the FIT pilot results was not separated by disease stage at diagnosis, therefore sensitivity and specificity were estimated for CRC as a whole. The test characteristics for detection of high risk adenoma were estimated by combining the detection rates for intermediate risk adenoma and high risk adenoma from the FIT pilot in order to match the definition of the high risk health state in the model.

Table 3 summarises the results of the FIT pilot as used to estimate the test characteristics of gFOBT and FIT. Table 4 summarises the assumed prevalence rates from the natural history model, and the estimates for the test characteristics used in the base case for each FIT cut-off.

Table 3: FIT pilot results used in the estimation of sensitivity of screening kits

	gFOBT	FIT 20 µg/g	FIT 40 µg/g	FIT 100 µg/g	FIT 150 µg/g	FIT 180 µg/g
Returned kit	667,945	27,167	27,167	27,167	27,167	27,167
Screened positive	11,575	2,127	1,415	656	483	412
Attended colonoscopy	9,835	1,824	1,202	546	400	339
Tested +ve for LR	1,913	471	298	124	81	63
Tested +ve for HR/IR	2,364	471	351	183	133	116
Tested +ve for Cancer	818	73	65	44	40	36
ALL	5,095	1,015	714	351	254	215
Normal	4,740	809	488	195	146	124

Table 4: Assumptions regarding the sensitivity of screening kits

Underlying disease	Prevalence*	gFOBT	FIT 20 µg/g	FIT 40 µg/g	FIT 100 µg/g	FIT 150 µg/g	FIT 180 µg/g
Low risk adenomas	43.83%	1.0%	6.0%	3.8%	1.6%	1.1%	0.8%
High risk adenomas**	4.29%	9.9%	48.1%	36.2%	19.3%	14.1%	12.4%
Colorectal cancer (any stage)	0.56%	26.4%	57.5%	51.6%	35.7%	32.6%	29.5%
Specificity - all neoplasia (LR, HR, CRC)	48.68%	98.4%	93.2%	95.9%	98.3%	98.7%	98.9%

* Prevalence of disease estimated using natural history model – calculated by dividing the number of people with the underlying disease by the total number in the screened population (i.e. those without a diagnosis of CRC) . The prevalence of low risk and high risk adenomas, and CRC at age 60 were used along with the detection rates from the FIT pilot to estimate sensitivity and specificity for each screening test and cut-off; ** Definition of high risk in the model incorporates both high and intermediate risk neoplasia as defined in FIT pilot to align with the health states used in the model

At the lowest cut-off of 20 µg/g the sensitivity of the FIT test is assumed to be 6.0% for low risk adenomas, 48.1% for high risk adenomas and 57.5% for colorectal cancer. This is consistent with the sensitivity estimates used for the same cut-off in previous economic evaluations (Whyte et al., 2012, Lejeune et al., 2014, Sharp et al., 2012) but may be considered low when compared to some of the values reported elsewhere in the literature (Launois et al., 2014, Kovarova et al., 2012, Hernandez et al., 2014, Imperiale et al., 2014). Therefore a sensitivity analysis was carried out to assess the impact on the model results of increasing the sensitivity of the FIT kit (see Section 6).

Screening uptake

Estimates for screening uptake were taken from the FIT pilot results. Uptake rates correspond to the number of people returning a kit with a definitive result of the number sent a pre-invite letter. Uptake rates are summarised in Table 5. Uptake is split by 5-year age bands in the model.

A summary of all model parameters relating to screening test kits and colonoscopies is given in Table 5.

Table 5: Summary of diagnostic test characteristics

Parameter	Value	Source
gFOBT – uptake of those sent a pre-invite	60-64: 54.50% 65-69: 63.64% 70-74: 61.62% (Overall: 59.32%)	(Moss, 2015)
gFOBT – proportion declining after pre-invitation	2.17%	(Moss, 2015)
gFOBT – average number of kits required	1.07	(Moss, 2015)
gFOBT – sensitivity	see Table 4	estimated using natural history transitions and (Moss, 2015)
gFOBT - specificity age 50	see Table 4	estimated using natural history transitions and (Moss, 2015)
gFOBT - specificity age 70	see Table 4	estimated using natural history transitions and (Moss, 2015)
iFOBT – uptake after pre-invite letter	60-64: 63.71% 65-69: 68.88% 70-74: 67.57% (Overall: 66.37%)	(Moss, 2015)
iFOBT – proportion declining after pre-invitation	2.15%	(Moss, 2015)
iFOBT – average number of kits required	1.02	(Moss, 2015)
iFOBT - sensitivity	see Table 4	estimated using natural history transitions and (Moss, 2015)
iFOBT - specificity age 50	see Table 4	estimated using natural history transitions and (Moss, 2015)
iFOBT - specificity age 70	see Table 4	estimated using natural history transitions and (Moss, 2015)
Colonoscopy uptake – follow-up	0.791	(Whyte et al., 2012)
Colonoscopy uptake – surveillance	0.824	(Whyte et al., 2012)
Sensitivity for LR adenomas	0.77	(van Rijn et al., 2006)
Sensitivity for HR adenomas	0.98	(van Rijn et al., 2006)
Sensitivity for CRC	0.98	(van Rijn et al., 2006)
Colonoscopy perforation rate (without polypectomy)	0.031%	(Rutter et al., 2014)
Colonoscopy perforation rate (with polypectomy)	0.091%	(Rutter et al., 2014)
Average number of polyps resected if polypectomy	2.3	(Rutter et al., 2014)
Proportion of colonoscopies resulting in hospitalisation for bleeding (transfusion)	0.04%	(Rutter et al., 2014)
Proportion of perforations resulting in death	5.2%	(Gatto et al., 2003)

Quality of life

In order to capture quality of life, utility weights are applied to the health states in the model.

The utility weights used in the model were taken from an analysis that pooled the data from four Health Surveys for England in order to compare self-reported health status and quality of life responses for subjects with or without a specified list of health conditions. The mean EQ-5D score for respondents with cancer was 0.697, while for those without cancer the mean EQ-5D was 0.798. The mean age for respondents for this health state was 60.9 years, which corresponds well to the age at which screening is started in the BCSP. These utility values were also used in the previous economic evaluation to compare screening options for the NHSBCSP (Whyte et al., 2012).

The estimation of utility weights by Duke's stage CRC is a key area of research that would decrease the levels of uncertainty surrounding the quality of life outcomes of the model. The limitations in quality of life data should be taken into account when interpreting model results which incorporate quality of life outcomes. To capture the uncertainty around the utility estimates, these parameters were varied in a sensitivity analysis (see Section 6).

Discounting

In line with recommendations published by the National Institute for Health and Care Excellence (NICE, 2013), discounting is applied within the model at a rate of 3.5% per year for both costs and effects. The "current year" of the model is assumed to be the age at which screening begins, i.e. 60 years of age.

Unit costs

The units costs used in the model are summarised in Table 6. The cost year is 2013/14 and any unit cost estimates that were from previous years were inflated to 2013/14 prices using the hospital and community health services inflation index for prices.

A further breakdown of the unit cost of screening kits is given in Table 7.

Table 6: Cost parameters

Parameter	Value (£, cost year 2013/14)	Source
gFOBT		
Cost of gFOBT screen (non-compliers)	0.82	(Reed, 2014), inflated from 2012/13 to 2013/14
Cost of gFOBT screen (returned kit)	2.01	(Reed, 2014), inflated from 2012/13 to 2013/14
FIT		
Cost of iFOBT screen (non-compliers)	1.65	(Reed, 2014), inflated from 2012/13 to 2013/14
Cost of iFOBT screen (returned kit)	5.09	(Reed, 2014), inflated from 2012/13 to 2013/14
Hospital services		
Appointment with Specialist Screening Practitioner	10.50	(Curtis, 2014) Mean salary band 6, 15 minute appointment duration assumed
Non-attendance rate after SSP appointment	0.5%	Personal communication, Stephen Halloran
Colonoscopy without polypectomy	507.82	(Department of Health, 2014), Day Case (diagnostic)
Colonoscopy with polypectomy	583.11	(Department of Health, 2014), Day Case (therapeutic)
Cost of admittance for bleeding (overnight stay on medical ward)	460.98	(Department of Health, 2014) Weighted average of all Non-elective inpatient, short stay gastrointestinal bleed groups (FZ38G,H,J,K,L,M,N,P)
Cost of perforation (major surgery)	2545.96	(Department of Health, 2014) Weighted average of all Non-elective inpatient, long stay Major Therapeutic Endoscopic, Upper or Lower Gastrointestinal Tract Procedures, 19 years and over, with CC Score 3+
Pathology cost for adenoma	10	(Department of Health, 2014)
Pathology cost for cancer	10	(Department of Health, 2014)
CRC		
Lifetime cost - screen-detected Dukes' stage A	13469	(Pilgrim, 2009) inflated to 2013/14
Lifetime cost - screen-detected Dukes' stage B	18532	(Pilgrim, 2009) inflated to 2013/14
Lifetime cost - screen-detected Dukes' stage C	25416	(Pilgrim, 2009) inflated to 2013/14
Lifetime cost - screen-detected Dukes' stage D	27796	(Pilgrim, 2009) inflated to 2013/14

Table 7: Breakdown of cost per screening kit (Reed, 2014), inflated from 2012/13 to 2013/14 prices

Cost item	gFOBT(£, 2013/14)	FIT(£, 2013/14)
Equipment (Post room)		
gFOBT test kit printer	0.02	0.00
Equipment (Laboratory)		
Analyser and Device cost (manufacturer's quoted price per kit)	0.43	2.72
Guillotine	0.00	N/A
Equipment maintenance cost	0.01	0.01
Test tube racks	-	0.00
Refrigerator for FIT kits and reagents	-	0.00
Postage and Packaging		
Initial kits price per pack (Outsource mail company)	0.08	0.10
Outgoing Postage costs	0.27	0.63
Return kits postage costs (1st class)	0.44	0.50
Outgoing postage from additional kits required (gFOBT 11% FIT 2%)	0.37	0.63
Additional printing costs (pre-printed headed paper/Labels)	0.01	0.28
Instruction leaflets	0.01	-
Pre-printed envelopes (Outsourced Mail)	0.02	-
Pre-printed envelopes (Internal Mail)	0.03	-
Staff Cost (Post room)	0.01	0.01
Staff Cost (Lab)	0.31	0.19
Waste Disposal	0.00	0.00
TOTAL COST PER KIT	**2.01**	**5.09**

4 Results – base case

Base case results are presented for a population size of 701,809 people aged 60 years sent pre-invites (see Section 3). The base case assumes the highest FIT cut-off used in the FIT pilot (180 µg/g) to give outcomes for the scenario where the additional resource demand on the screening and colonoscopy services due resulting from the introduction of FIT testing is minimised. Results are presented at different FIT cut-off values in Section 5, and also in the sensitivity analyses in Section 6.

Resource use and costs associated with screening kits

The costs associated with screening kits are first presented for the first year of screening only (population age 60 years) in Table 8, followed by the total costs for all screening years in Table 9.

In the first year of the model (people aged 60 years) the total number of kits returned was 402,351 for gFOBT and 450,166 for FIT, with a positivity rate of 1.86% for gFOBT and 1.65% for FIT at the 180 µg/g cut-off. Although unreturned kits represent a smaller proportion of the number of pre-invites for the FIT arm, the unit cost of an unreturned kit is greater for FIT (£1.65) than for gFOBT (£0.82), meaning the total cost of unreturned kits is greater for FIT even though uptake is higher.

The total cost of screening in the first year of the model is £1,107,578 for gFOBT and £2,761,024 for FIT, which is a cost per person sent a pre-invite of £1.58 for gFOBT and £3.93 for FIT. The total cost of screening is higher for FIT than for gFOBT due to a higher uptake and higher screening kit costs.

Were FIT to be implemented nationally the unit cost of FIT kits may be lower than is assumed in the base case, therefore a sensitivity analysis was performed to assess the impact of lowering the cost of FIT kits (see Section 6).

Table 8: Resource use and costs associated with screening kits in the first year of screening (age 60 years), FIT 180 µg/g

	Resource use			Cost		
	gFOBT	**FIT 180 µg/g**	**Inc.**	**gFOBT**	**FIT 180 µg/g**	**Inc.**
Total number of pre-invites sent in first year (excluding repeat kits)	701,809	701,809	-	-	-	-
Number of people returning kit in first year (normal result)	375,329	439,745	64,416	-	-	-
Number of people returning kit in first year (positive result)	7,133	7,366	233	-	-	-
Positivity rate	1.86%	1.65%	-0.22%	-	-	-
Number of people not returning kit in first year	319,347	254,698	-64,649	-	-	-
Total number of kits returned (normal result)*	402,351	450,166	47,815	£810,183	£2,291,569	£1,481,386
Total number of kits returned (positive result)*	7,646	7,540	-106	£15,397	£38,383	£22,986
Total number of kits sent but not returned*	342,339	260,734	-81,605	£281,998	£431,072	£149,075
TOTAL COSTS ASSOCIATED WITH SCREENING KITS	-	-	-	£1,107,578	£2,761,024	£1,653,446
TOTAL COSTS per person in screening population at age 60 years	-	-	-	£1.58	£3.93	£2.36

* Includes duplicate kits

Table 9 shows the total resource use and costs associated with screening for all screening years (i.e. aged 60-75 years).

The total number of screening kits returned over the 15 years of screening was 3,180,573 for gFOBT and 3,404,140 for FIT. The total cost of screening was £9,793,539 higher for FIT than for gFOBT, an incremental cost of £13.95 per person sent a pre-invite.

The cost of screening is higher overall for FIT because of increased uptake and also because the cost of the FIT kits is higher than the cost of gFOBT. Sensitivity analyses were performed for both of these parameters, as presented in Section 6.

Table 9: Resource use and costs associated with screening kits, all screening years, FIT 180 µg/g

	Resource use			Cost		
	gFOBT	FIT 180 µg/g	Incremental	gFOBT	FIT 180 µg/g	Incremental
Total number of pre-invites sent over time (excluding repeat kits)	5,106,756	5,103,068	-3,688	-	-	-
Number of people returning kit (normal result)	2,966,967	3,325,341	358,374	-	-	-
Number of people returning kit (positive result)	59,085	60,099	1,014	-	-	-
Positivity rate	1.95%	1.78%	-0.18%	-	-	-
Number of people not returning kit	2,080,705	1,717,628	-363,076	-	-	-
Total number of kits returned (normal result)*	3,180,573	3,404,140	223,567	£5,114,886	£13,898,631	£8,783,745
Total number of kits returned (positive result)*	63,338	61,523	-1,815	£101,352	£249,131	£147,779
Total number of kits sent but not returned*	2,230,505	1,758,330	-472,175	£1,496,613	£2,358,629	£862,016
Total screening costs	-	-	-	£6,712,851	£16,506,390	£9,793,539
Total cost per person sent a pre-invite	-	-	-	£9.57	£23.52	£13.95

* Includes duplicate kits

Resource use and costs associated with colonoscopy and polypectomy

Table 10 shows the resource use and costs associated with colonoscopies and polypectomy at follow-up after screening and during surveillance.

The number of follow-up colonoscopies was 46,736 for gFOBT and 47,538 for FIT. Polypectomy for low risk adenoma was performed in 10,010 follow-up colonoscopies for gFOBT and 9,357 follow-up colonoscopies for FIT.

Polypectomy for high risk adenoma was performed 12,409 times at follow-up for gFOBT and 16,800 times for FIT. There were fewer colonoscopies without polypectomy for FIT during follow-up (21,370) than for gFOBT (24,315), meaning complications such as perforation occurred slightly less often in the FIT arm (28 perforations) than in the gFOBT arm (29 perforations).

Over all screening years more people in the FIT arm entered surveillance (16,000 for FIT compared to 12,409 for gFOBT) because of the higher number of high risk adenomas detected in the FIT arm. The number of people entering surveillance following screening is shown in Figure 6. The total number of people in surveillance in each year of the model is shown in Figure 7.

The total number of colonoscopies during surveillance was 39,451 for FIT and 29,090 for gFOBT. People entering surveillance have the same disease progression whether in the gFOBT or FIT arm since all subjects start in the same disease state (post-polypectomy for high risk adenoma) and the transitions are not dependent on the test kit characteristics. Therefore the proportion of people entering surveillance that subsequently have polypectomy is the same for both arms.

Of surveillance colonoscopies the number including polypectomy for low risk adenomas was 6,700 for FIT and 4,941 for gFOBT (17% of all surveillance colonoscopies for both arms). The number of polypectomies for high risk adenomas was 16,055 for gFOBT and 21,768 for FIT (55% of all surveillance colonoscopies for both arms). The high detection rate for high risk adenoma is reflective of the assumption that people who have had a polypectomy for high risk adenoma (i.e. those entering surveillance) subsequently have a higher risk than people in the general population of developing further high risk adenomas.

The total cost associated with follow-up and surveillance colonoscopies was £5,088,836 higher for FIT (£7.25 higher for FIT per person sent a pre-invite), driven by the greater number of high risk adenomas detected during population screening and therefore the higher costs of surveillance colonoscopies in the FIT arm. The results show than an increase in demand on colonoscopy services would be expected even at the high FIT cut-off assumed in the base case.

Table 10: Resource use and costs associated with colonoscopy and polypectomy, all screening years , FIT 180 µg/g

	Resource use			Cost		
	gFOBT	FIT 180 µg/g	Incremental	gFOBT	FIT 180 µg/g	Incremental
Follow-up colonoscopies without polypectomy	24,315	21,379	-2,935	£10,119,674	£8,891,749	-£1,227,925
Follow-up colonoscopies with polypectomy for HR adenomas	12,409	16,800	4,391	£6,028,722	£8,210,214	£2,181,491
Follow-up colonoscopies with polypectomy for LR adenomas	10,010	9,357	-653	£4,858,834	£4,559,274	-£299,560
Total number of follow-up colonoscopies	46,736	47,538	802	-	-	-
Major bleeds requiring hospitalisation (follow-up)	19	19	0	£6,848	£6,973	£125
Perforation (follow-up)	29	28	-2	£59,150	£56,029	-£3,121
Deaths due to perforation	1	1	0	£670	£633	-£36
Total costs (follow-up colonoscopy)	-	-	-	£21,073,898	£21,724,872	£650,974
Number of people entering surveillance after polypectomy for HR	12,409	16,800	4391	-	-	-
Surveillance colonoscopies without polypectomy	8,094	10,982	2,889	£2,978,891	£4,065,106	£1,086,215
Surveillance colonoscopies with polypectomy for LR adenomas	4,941	6,700	1,759	£7,035,787	£9,593,583	£2,557,796
Surveillance colonoscopies with polypectomy for HR adenomas	16,055	21,768	5,713	£2,153,004	£2,936,063	£783,058
Total number of surveillance colonoscopies	29,090	39,451	10,361	-	-	-
Major bleeds requiring hospitalisation (surveillance)	12	16	4	£3,871	£5,279	£1,408
Perforation (surveillance)	14	19	5	£25,470	£34,744	£9,275
Deaths due to perforation	1	1	0	£303	£414	£110
Total costs (surveillance colonoscopies)	-	-	-	£12,197,327	£16,635,189	£4,437,862
TOTAL (all colonoscopies)	75,826	86,990	5	£33,271,225	£38,360,061	£5,088,836
Total per person sent a pre-invite	0.11	0.12	0.00	£47.41	£54.66	£7.25

Figure 6: Number of people entering surveillance from screening in each year

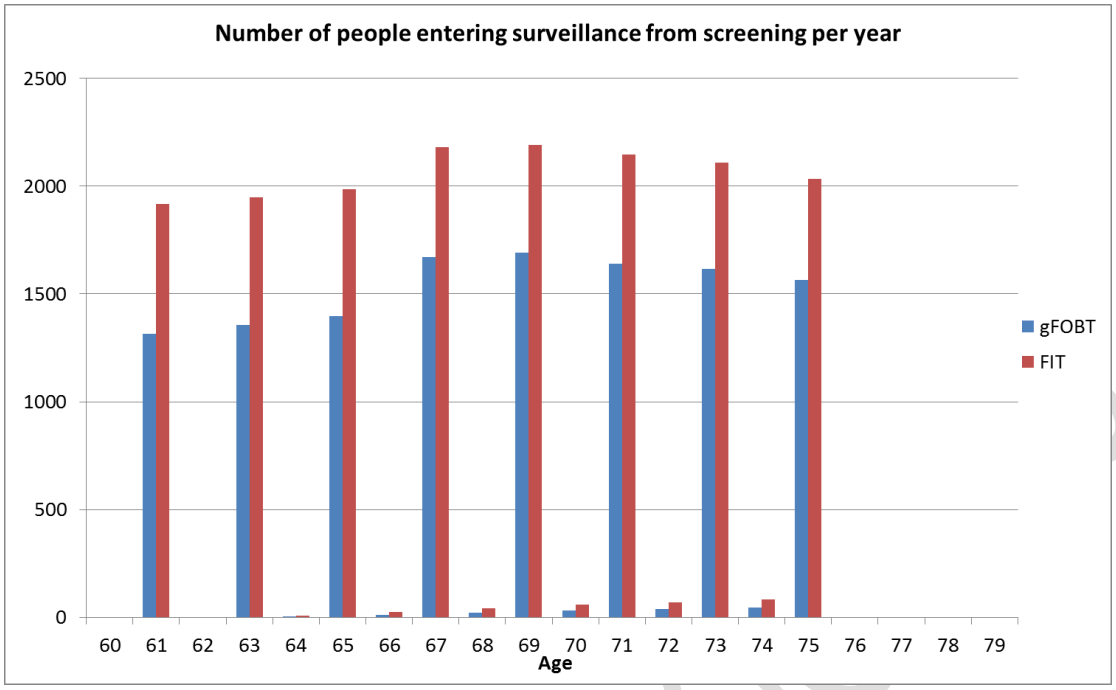
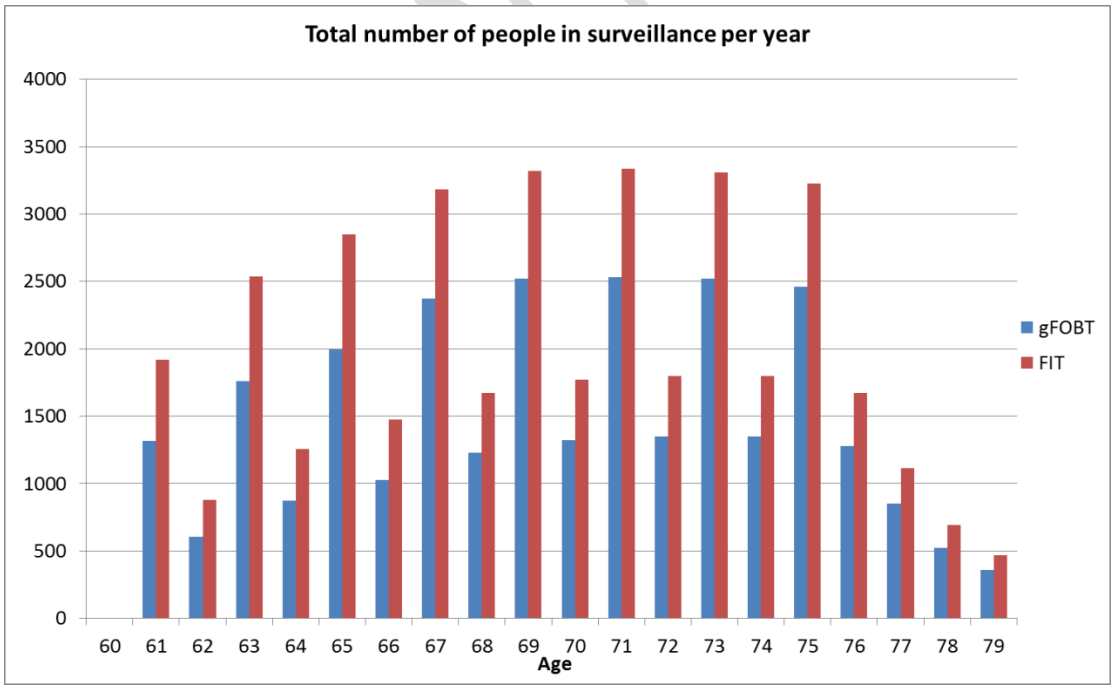


Figure note: People enter surveillance following population-level screening in the year after polypectomy for high risk adenoma. For people who are entering surveillance for the first time this occurs in odd years (since screening and follow-up colonoscopy occurs in even years), however if a person exits surveillance (due to two negative surveillance colonoscopies or a non-attendance) they are screened bi-annually from the year after they exit surveillance and can therefore subsequently re-enter surveillance in either odd or even years.

Figure 7:Total number of people entering or remaining in surveillance in each year until age 80 years



Resource use and costs associated with management of colorectal cancer

Table 11 shows the total number of people diagnosed with colorectal cancer (which includes those detected through screening and also those presenting to health services outside of the screening programme) over all screening years.

The proportion of cancer incidence for each stage of cancer was very similar for both arms. Cancer incidence was reduced by 5.1% and cancer mortality by 5.4% for FIT compared to gFOBT using a FIT cut-off of 180 µg/g. Cancer incidence and mortality are shown by FIT cut-off level in Section 5.

Table 11: Resource use and costs associated with colorectal cancer, all screening years, FIT 180 µg/g

	Resource use			Cost		
	gFOBT	FIT 180 µg/g	Inc.	gFOBT	FIT 180 µg/g	Incremental
Number diagnosed (CRC stage A)	4,201 (9%)	4,057 (10%)	-144	£32,489,068	£31,266,310	-£1,222,758
Number diagnosed (CRC stage B)	9,021 (20%)	8,613 (20%)	-408	£94,482,397	£89,739,024	-£4,743,373
Number diagnosed (CRC stage C)	11,402 (26%)	10,823 (26%)	-578	£161,900,625	£152,749,775	-£9,150,849
Number diagnosed (CRC stage D)	19,881 (45%)	18,722 (44%)	-1,159	£304,007,238	£284,263,782	-£19,743,457
CRC incidence (any CRC)	44,504	42,215	-2,289 (-5.1%)	£592,879,328	£558,018,891	-£34,860,437
CRC mortality (any CRC)*	37,730	35,694	-2,036 (-5.4%)	-	-	-

* The cost of death due to CRC is included in the CRC management costs

Total costs

Table 12 shows the total costs in the base case setting for screening, colonoscopy, CRC management and overall, for all screening years.

The costs associated with screening and colonoscopies are higher for FIT than for gFOBT as described above. However the overall cost of FIT for the screened population was £612,885,342 compared to £632,863,404 for gFOBT, meaning the use of FIT screening results in an overall reduction in costs of £19,978,062 or £28 per person sent a pre-invite.

Table 12: Total costs for all screening years, FIT 180 µg/g

	Cost		
	gFOBT	FIT 180 µg/g	Incremental
Screening	£6,712,851	£16,506,390	£9,793,539
Follow-up colonoscopy	£21,073,898	£21,724,872	£650,974
Surveillance colonoscopies	£12,197,327	£16,635,189	£4,437,862
CRC management	£592,879,328	£558,018,891	-£34,860,437
Total costs	£632,863,404	£612,885,342	-£19,978,062
Total cost per person sent a pre-invite	£902	£873	-£28

Life years, quality of life and incremental cost-effectiveness ratios

Table 13 shows the total life years for the population, and per person sent a pre-invite. The total incremental costs are also shown, along with the resulting incremental cost-effectiveness ratio (incremental cost per life year gained). Table 14 shows the equivalent results for quality-adjusted life years (QALYs).

FIT is associated with an increase of 0.019 life years, and 0.014 QALYs per person sent a pre-invite. The incremental cost per QALY gained was -£2,047 (the negative value results from a cost saving combined with a QALY gain).

Table 13: Total life years and incremental cost-effectiveness ratio, all screening years, FIT 180 µg/g

	Life years			Incremental cost	ICER (LY)
	gFOBT	FIT 180µg/g	Inc.		
Total	11,263,240	11,276,575	13,335	-£19,978,062	-
Total per person in target screening population	16.05	16.07	0.019	-£28	-£1,498*

* Cost saving, LY gain;

Table 14: Total quality of life, and incremental cost-effectiveness ratios, all screening years, FIT 180 µg/g

	Quality adjusted life years			Incremental cost	ICER (QALY)
	gFOBT	FIT 180µg/g	Inc.		
Total	8,962,563	8,972,325	9,762	-£19,978,062	-
Total per person in target screening population	12.77	12.78	0.014	-£28	-£2,047*

* Cost saving, QALY gain

5 Summary of results at different FIT cut-offs

The FIT cut-off value used in the base case was 180 µg/g, in order to present outcomes for the scenario where the impact on screening and colonoscopy services is minimised. This report section presents equivalent results at varying FIT cut-off levels, to assess the expected cost and effect outcomes should a different cut-off value be adopted in the screening programme.

Assumptions regarding sensitivity and specificity of screening kits

Altering the FIT cut-off value changes the sensitivity and specificity of the screening test for detecting adenomas and colorectal cancer. Table 15 summarises the test characteristics at each cut-off level, as calculated using the FIT pilot results and the prevalence of adenomas and colorectal cancer in the population as predicted by the model.

Table 15: Assumptions regarding the sensitivity of screening kits at a range of FIT cut-off values

Underlying disease	Prevalence (estimated)*	gFOBT	FIT 20 µg/g	FIT 40 µg/g	FIT 100 µg/g	FIT 150 µg/g	FIT 180 µg/g
Low risk adenomas	43.83%	1.0%	6.0%	3.8%	1.6%	1.1%	0.8%
High risk adenomas**	4.29%	9.9%	48.1%	36.2%	19.3%	14.1%	12.4%
Colorectal cancer (any stage)	0.56%	26.4%	57.5%	51.6%	35.7%	32.6%	29.5%
Specificity - all neoplasia (LR, HR, CRC)	48.68%	98.4%	93.2%	95.9%	98.3%	98.7%	98.9%

* Prevalence of disease estimated using natural history model – calculated by dividing the number of people with the underlying disease by the total number in the screened population (i.e. those without a diagnosis of CRC) . The prevalence of LR, HR and CRC at age 60 were used along with the detection rates from the FIT pilot to estimate sensitivity and specificity for each screening test and cut-off; ** Definition of high risk in the model incorporates both high and intermediate risk neoplasia as defined in FIT pilot

Cancer incidence at a range of FIT cut-off values

Table 16: Cancer incidence and mortality at a range of FIT cut-off values

Base case	CRC Duke's stage A diagnoses	CRC Duke's stage B diagnoses	CRC Duke's stage C diagnoses	CRC Duke's stage B diagnoses	Overall CRC incidence (% reduction from gFOBT)	Overall CRC mortality (% reduction from gFOBT)
gFOBT	4,201	9,021	11,402	19,881	44,504 (-)	37,730 (-)
20 µg/g	3,500	6,945	8,516	14,267	33,228 (25.3%)	27,460 (27.2%)
40 µg/g	3,596	7,255	8,935	15,048	34,835 (21.7%)	28,996 (23.1%)
100 µg/g	3,899	8,155	10,185	17,474	39,713 (10.8%)	33,449 (11.3%)
150 µg/g	4,006	8,455	10,593	18,247	41,301 (7.2%)	34,844 (7.6%)
180 µg/g	4,057	8,613	10,823	18,722	42,215 (5.1%)	35,694 (5.4%)

Total costs associated with cancer management are summarised in Table 17.

Overall cost and quality of life outcomes

Table 17 and Table 18 summarise the total cost, quality of life, and ICER outcomes for all subjects in the model (Table 17) and per person sent a pre-invite (Table 18) across a range of FIT cut-off values.

Under base case model assumptions FIT is cost-saving and results in QALY gains for all FIT cut-off values. The greatest number of QALYs gained (45,621 incremental QALYs) is achieved at the lowest cut-off value of 20 µg/g, while this cut-off value also represents the greatest cost saving due to large savings on cancer management costs. However this cut-off value is also associated with a large cost impact relating to colonoscopy costs, meaning that although costs are saved overall with FIT the impact on colonoscopy services at low cut-offs may be prohibitively large.

Table 17: Total incremental costs and QALYs for the whole population, and incremental cost-effectiveness ratios for a range of FIT cut-off values, all screening years

Base case	Inc. screening cost	Inc. col cost	Inc. CRC cost	Inc. costs	Inc. QALYs	ICER
20 µg/g	£9,705,698	£125,195,905	-£177,648,229	-£42,746,626	45621	-£937*
40 µg/g	£9,730,979	£80,608,338	-£150,513,913	-£60,174,596	39684	-£1,516*
100 µg/g	£9,773,759	£26,153,106	-£73,364,084	-£37,437,220	19611	-£1,909*
150 µg/g	£9,787,814	£10,956,063	-£49,507,120	-£28,763,243	14258	-£2,017*
180 µg/g	£9,793,539	£5,088,836	-£34,860,437	-£19,978,062	9762	-£2,047*

* Cost saving, QALY gain

Table 18: Total incremental costs and QALYs per person sent a pre-invite, and incremental cost-effectiveness ratios for a range of FIT cut-off values, all screening years

Base case	Inc. screening cost	Inc. col cost	Inc. CRC cost	Inc. costs	Inc. QALYs	ICER
20 µg/g	£14	£178	-£253	-£61	0.065	-£937*
40 µg/g	£14	£115	-£214	-£86	0.057	-£1,516*
100 µg/g	£14	£37	-£105	-£53	0.028	-£1,909*
150 µg/g	£14	£16	-£71	-£41	0.020	-£2,017*
180 µg/g	£14	£7	-£50	-£28	0.014	-£2,047*

* Cost saving, QALY gain

6 Sensitivity analyses

Sensitivity analysis 1: Cost of screening kits

Table 19 shows the total and incremental costs and effects for the base case FIT cut-off (180 µg/g), assuming the unit cost of gFOBT and FIT kits are equal. The total cost of screening is higher for FIT because of higher uptake.

Table 19: Screening costs assuming the unit cost of the FIT kits is equal to gFOBT, all screening years, FIT 180 µg/g

	Resource use			Cost		
	gFOBT	FIT	Incremental	gFOBT	FIT	Incremental
Total number of invites sent over time (excluding repeat kits)	5,106,756	5,103,068	-3,688	-	-	-
Number of people returning kit (normal result)	2,966,967	3,325,341	358,374	-	-	-
Number of people returning kit (positive result)	59,085	60,099	1,014	-	-	-
Positivity rate	1.95%	1.78%	-0.18%	-	-	-
Number of people not returning kit	2,080,705	1,717,628	-363,076	-	-	-
Total number of kits returned (normal result)*	3,180,573	3,404,140	223,567	£5,114,886	£5,497,816	£382,930
Total number of kits returned (positive result)*	63,338	61,523	-1,815	£101,352	£98,548	-£2,804
Total number of kits sent but not returned*	2,230,505	1,758,330	-472,175	£1,496,613	£1,175,158	-£321,455
TOTAL COSTS associated with screening	-	-	-	£6,712,851	£6,771,522	£58,671
TOTAL COSTS per person in screening population at age 60 years	-	-	-	£9.57	£9.65	£0.08

Table 21 shows the incremental costs and effects for different FIT cut-offs assuming the unit cost of gFOBT and FIT kits are equal. Table 21 shows the total costs per person sent a pre-invite.

Table 20: Total costs for different FIT cut-off values assuming the unit cost of the FIT kits is equal to gFOBT, all screening years, FIT 180 µg/g

	Inc. screening cost	Inc. col cost	Inc. CRC cost	Inc. costs	Inc. QALYs	ICER
20 µg/g	£22,645	£125,195,905	-£177,648,229	-£52,429,678	£45,621	-£1,149
40 µg/g	£33,016	£80,608,338	-£150,513,913	-£69,872,560	£39,684	-£1,761
100 µg/g	£50,560	£26,153,106	-£73,364,084	-£47,160,418	£19,611	-£2,405
150 µg/g	£56,323	£10,956,063	-£49,507,120	-£38,494,733	£14,258	-£2,700
180 µg/g	£58,671	£5,088,836	-£34,860,437	-£29,712,930	£9,762	-£3,044

Table 21: Total costs per person sent a pre-invite for different FIT cut-off values assuming the unit cost of the FIT kits is equal to gFOBT, all screening years, FIT 180 µg/g

	Inc. screening cost	Inc. col cost	Inc. CRC cost	Inc. costs	Inc. QALYs	ICER
20 µg/g	£0	£178	-£253	-£75	0.065	-£1,149
40 µg/g	£0	£115	-£214	-£100	0.057	-£1,761
100 µg/g	£0	£37	-£105	-£67	0.028	-£2,405
150 µg/g	£0	£16	-£71	-£55	0.020	-£2,700
180 µg/g	£0	£7	-£50	-£42	0.014	-£3,044

Sensitivity analysis 2: FIT test characteristics

At the lowest cut-off of 20 µg/g the sensitivity of the FIT test is assumed to be 6.0% for low risk adenomas, 48.1% for high risk adenomas and 57.5% for colorectal cancer. This is consistent with the estimates used for the same cut-off in previous economic evaluations (Whyte et al., 2012, Lejeune et al., 2014, Sharp et al., 2012) but may be considered low when compared to some of the values reported elsewhere in the literature (Launois et al., 2014, Kovarova et al., 2012, Hernandez et al., 2014, Imperiale et al., 2014). Therefore a sensitivity analysis was carried out to assess the impact on the model results of increasing the sensitivity of the FIT kit. The results are presented in Table 22. It should be noted that some of the sensitivity values are not intended to be plausible values (for example setting the sensitivity equal to 1), but are used to investigate the effect of varying the sensitivity estimates to high values.

As the sensitivity of FIT increases, the incremental costs of FIT compared to gFOBT increase, mainly due to the increased cost of colonoscopy. FIT ceases to be cost-saving as the sensitivity is increased beyond 10%, despite having consistently lower cancer management costs even at the highest sensitivity values.

As the sensitivity of FIT increases, the incremental life years per person increase slightly, but the incremental QALYs per person decrease slightly, which reflects the fact that as test sensitivity increases the diagnosis rate of colorectal cancer (which carries a lower utility in the model than undiagnosed cancer) increases.

The incremental cost per QALY gained ceases to be negative once the total costs for FIT are greater than those for gFOBT (i.e. after an increase in FIT sensitivity of 10%). The ICER increases as the sensitivity increases, however it remains low compared to the recommended NICE threshold of £20,000-£30,000 per QALY gained, even at very high sensitivity estimates.

Table 22: Sensitivity analysis – increasing the sensitivity of FIT

Scenario (absolute increase in FIT sensitivities)	FIT 20 µg/g	+ 10%	+ 20%	+ 30%	+ 40%	Max
FIT sensitivity for LR adenoma	0.060	0.160	0.260	0.360	0.460	1.000
FIT sensitivity for HR adenoma	0.481	0.581	0.681	0.781	0.881	1.000
FIT sensitivity for CRC	0.575	0.675	0.775	0.875	0.975	1.000
Inc. screening costs	£13.83	£13.78	£13.72	£13.67	£13.62	£13.47
Inc. follow-up colonoscopy costs	£117.45	£217.05	£306.21	£386.25	£458.34	£720.39
Inc. surveillance colonoscopies costs	£60.79	£80.86	£101.14	£121.35	£141.27	£194.91
Inc. CRC management costs	-£253.13	-£234.98	-£227.07	-£226.35	-£230.43	-£127.35
Inc. total costs for all screening years	-£60.91	£76.91	£194.24	£295.21	£383.13	£801.89
Inc. life years per person	0.085	0.098	0.110	0.122	0.131	0.134
Inc. QALYs per person	0.767	0.743	0.729	0.721	0.717	0.682
ICER (incremental cost per QALY gained)	-937	1057	2415	3367	4064	8757

Sensitivity analysis 3: Cancer management costs

In the base case FIT was found to be cost-saving due to lower cancer treatment costs despite having higher screening and colonoscopy-related costs. Therefore FIT would no longer be cost-saving if the cancer management costs were low enough so that they did not outweigh the cost of screening and colonoscopy, as in the base case results.

The costs of cancer management were altered, first for the base case IT cut-off of 180 µg/g and also for the lowest FIT cut-off of 20 µg/g. The results are shown in Table 23.

CRC remained cost-saving for a both cut-offs up to a 50% decrease in cancer management costs.

Table 23: Effect of reducing cancer management costs on overall costs and ICER

Scenario (absolute increase in FIT sensitivities)	FIT 180 µg/g	Cancer costs -10%	Cancer costs -30%	Cancer costs -50%	FIT 20 µg/g	FIT 20, CRC costs -10%	FIT 20, CRC costs -30%	FIT 20, CRC costs -50%
Inc. CRC management costs	-£49.67	-£44.71	-£39.74	-£34.78	-£253.13	-£227.83	-£202.52	-£177.22
Inc. total costs	-£28.47	-£23.50	-£18.54	-£13.57	-£60.91	-£35.61	-£10.30	£15.00
Inc. life years per person	0.019	0.019	0.019	0.019	0.085	0.085	0.085	0.085
Inc. QALYs per person	0.732	0.732	0.732	0.732	0.767	0.767	0.767	0.767
ICER (incremental cost per QALY gained)	-2047	-1690	-1333	-976	-937	-548	-159	231

Sensitivity analysis 4: Deterministic sensitivity analyses

A range of deterministic sensitivity analyses were carried out to assess the impact of variation in key parameters in the model. Screening test uptake, colonoscopy compliance and sensitivity, and utility values for cancer-free and CRC diagnosed health states were varied independently by ±10% of their base case values. The results are given in Table 24 and Table 25.

For all scenarios FIT remained cost-saving, and the ICER varied from –£2,182 to -£1,939, with reduced costs and QALY gains in all cases.

Table 24: Deterministic sensitivity analyses, FIT 180 µg/g

	Base case	gFOBT uptake		FIT uptake		Colonoscopy compliance	
		-10%	+10%	-10%	+10%	-10%	+10%
Screening costs	£13.95	£14.39	£13.52	£12.60	£15.31	£13.97	£13.94
Follow-up colonoscopy costs	£0.93	£3.85	-£1.98	-£2.03	£3.85	£0.96	£0.83
Surveillance colonoscopies costs	£6.31	£7.96	£4.67	£4.10	£8.48	£4.53	£8.72
CRC management costs	-£49.67	-£66.09	-£33.66	-£29.57	-£69.12	-£44.28	-£55.56
Total costs	-£28.47	-£39.86	-£17.45	-£14.89	-£41.46	-£24.81	-£32.05
Life years per person	0.019	0.027	0.012	0.010	0.028	0.018	0.020
QALYs per person	0.732	0.724	0.749	0.750	0.726	0.726	0.740
ICER (incremental cost per QALY gained)	-£2,047	-£2,071	-£2,002	-£1,957	-£2,074	-£1,939	-£2,140

Table 25: Deterministic sensitivity analyses, FIT 180 µg/g (continued)

	Base case	Colonoscopy sensitivity		Utility for cancer free health states		Utility for CRC health states	
		-10%	+10%	-10%	+10%	-10%	+10%
Screening costs	£13.95	£13.95	£13.96	£13.95	£13.95	£13.95	£13.95
Follow-up colonoscopy costs	£0.93	£1.25	£0.90	£0.93	£0.93	£0.93	£0.93
Surveillance colonoscopies costs	£6.31	£6.34	£6.25	£6.31	£6.31	£6.31	£6.31
CRC management costs	-£49.67	-£49.00	-£49.75	-£49.67	-£49.67	-£49.67	-£49.67
Total costs	-£28.47	-£27.44	-£28.63	-£28.47	-£28.47	-£28.47	-£28.47
Life years per person	0.019	0.019	0.019	0.019	0.019	0.019	0.019
QALYs per person	0.732	0.730	0.732	0.704	0.760	0.687	0.778
ICER (incremental cost per QALY gained)	-£2,047	-£1,983	-£2,057	-£2,127	-£1,972	-£2,182	-£1,927

7 Conclusions

Discussion of results

The base case results used high a FIT cut-off of 180 µg/g to show outcomes for the scenario where the impact of introducing FIT on screening and colonoscopy eservices would be minimised.

The results demonstrate that even at the high base case FIT cut-off an increased demand on colonscopy services would be expected (£7.25 more per person sent a pre-invite for FIT), as well as increased demand on screening (£13.95 more per person sent a pre-invite for FIT) due to higher uptake in the FIT arm and higher unit costs for FIT kits than gFOBT kits in the base case. It could be argued that in the interests of minimising this increased demand on colonoscopy services a high cut-off should be used, however it is important to also consider the long term consequences of the difference in detection rates between FIT and gFOBT in terms of cancer incidence and cancer management costs.

In the base case, for a FIT cut-off of 180 µg/g the total cancer incidence is reduced by 5.1% with FIT compared to gFOBT. This results in a reduction in CRC management costs for FIT of £50 per person sent a pre-invite. When the lowest FIT cut-off of 20 µg/g is considered, the reduction in CRC management costs for FIT is £253 per person sent a pre-invite. The largest health gain (in terms of both life years and quality adjusted life years) is achieved at the lowest FIT cut-offs.

The model results by cut-off value suggest FIT is cost-saving compared to gFOBT, and also results in QALY gains for all cut-offs (incremental cost per QALY gained ranging from -£2,047 for 180 µg/g to -£937 for 20 µg/g). The results of the deterministic sensitivty analyses (varying key model parameters by a 10% range, and adjusting the sensitiivity of FIT and cost of CRC management) show that the results are robust to uncertainty in assumptions about the model parameters. More specifically, FIT remained cost-saving or cost-effective (well below the £20,000 to £30,000 threshold recommended by NICE) in all sensitivity analyses, including those performed using the lowest FIT cut-off of 20 µg/g.

Conclusions

In conclusion, the results presented above suggest that FIT is cost-effective under base case assumptions and across various sensitivity analyses at a range of FIT cut-off values. The results also suggest that FIT is cost-saving compared to gFOBT for all FIT cut-off values using base case model assumptions.

Using a high FIT cut-off reduces the impact on screening and colnoscopy services over the screening period (60-75 years), however the model results suggest that high cut-offs do not minimise overall costs to the NHS. Rather the results suggest that taking into account the reduction in colorectal cancer incidence, higher overall cost savings along with increased health gains would be acheived with lower FIT cut-off values. However there may be a point at which the impact on colonoscopy services resulting from initially adopting a low cut-off may be prohibitively large.

Comparison to other evaluations

The previous economic evaluation of FIT for the NHSBCSP (Whyte et al., 2012) found that FIT screening from age 60-75 years at a cut-off of 20 µg/g was cost saving compared to gFOBT in the same screening age range. FIT was found to be associated with an increase in QALYs of 0.016 compared to gFOBT, and a reduction in costs per person of £63. CRC incidence and mortality were both reduced, as was the case in the results of this analysis, and although the number of colonoscopies increased with FIT screening, the resulting increase in costs was similarly offset by a cost saving on cancer management costs.

The results also broadly align with the conclusions of several other previous economic evaluations, for example (Lejeune et al., 2014, van Rossum, 2011, Berchi et al., 2010, Heitman et al., 2010) although due to differing country settings and parameterisations the numerical results are not directly comparable.

Strengths and limitations

The model used data from the recent FIT pilot study in order to inform the screening test characteristics of gFOBT and FIT screening kits. The use of the FIT pilot outcomes is a key strength of the analysis, and improves upon the current evidence base for the impact of FIT in the UK setting by providing UK-specific data on both gFOBT and FIT, and enabling the presentation of results by FIT cut-off. This had not been possible in previous studies due to lack of appropriate data (Whyte et al., 2012, Sharp et al., 2012).

As noted previously, the estimates of quality of life used in the model were not disaggregated by colorectal cancer disease stage due to a lack of estimates available in the literature. Therefore the quality of life results from the model are subject to considerable uncertainty, due to the broad definitions of "CRC free" and "any stage CRC". The estimation of utility weights by Duke's stage CRC is a key area of research that would decrease the levels of uncertainty surrounding the quality of life outcomes of the model.

The prevalence of disease in the population was estimated using the model calibration parameters presented in the previous economic analysis for the NHSBCSP (Whyte et al., 2012). The model calibration was based on prevalence, incidence data and screening test detection rates sourced from the literature before the study was published in 2011. Future work could include updating the parameters for the natural history model and test characteristics using more recent data from the literature and incorporating the FIT pilot results in the model calibration.

Results from the FIT pilot suggested that the test characteristics and uptake of screening varied by screening round (first, incident, prevalent rounds). However the design of the model does not track the history of subjects' transitions (specifically whether or not they had responded to previous screening rounds) in order to apply different probabilities depending on patient history. Future work could include methods for disaggregating subjects in the model by screening round, and applying the appropriate rates from the FIT pilot results to each group.

Additional work will include probabilistic sensitivity analyses to capture uncertainty around multiple model parameters simultaneously, and the incorporation of uncertainty around the natural history parameters as this has not been included in this report.

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