Supplementary Methods

Background to the ScHARR bowel cancer screening model

The ScHARR bowel cancer screening model is a cohort state transition model built in Excel to appraise the options for colorectal (CRC) screening evaluating cost-effectiveness, cost-utility and resource impact (full report found elsewhere [1]). It models the life experience of a cohort of individuals aged 30 from the general population of England with normal epithelium, through to the development of adenomas, CRC and subsequent death. The cohort can undergo a vast variety of different CRC screening strategies, or no screening, according to pre-specified inputs. The model also includes post-polypectomy endoscopic surveillance, and symptomatic diagnosis of individuals with CRC. The model cycle is one year and its perspective is that of the English National Health Service (NHS) and Personal Social Services.

Underpinning the model is a set of 13 health states defined according to an individual's true underlying histological state (Supplementary Figure S1).CRC is divided into eight health states which describe the Dukes' stages A-D and whether or not the CRC has been clinically diagnosed (preclinical/clinical). Two adenoma health states are included: low-risk and intermediate/high-risk adenomas, as defined by the current British Society of Gastroenterology (BSG) guidelines for endoscopic surveillance following adenoma removal [2]. The "high risk adenomas" health state includes persons with at least 3 small adenomas or at least one adenoma of size >1cm. The "low-risk adenomas" health state includes persons with 1-2 small (<1cm) adenomas. These health states correspond to those used to determine an individual's surveillance strategy, so this approach eases the modelling of surveillance. Two further health states correspond to death either from CRC or from other causes.

The probability of transition from one health state to another cannot be directly measured in the population and therefore must be calibrated. Model calibration used the Metropolis Hastings algorithm in the methods described by Whyte et al., 2011 [3]. The set of calibrated

parameters include the annual transitions between health states as shown by black arrows in Supplementary Figure S1, and the annual probability that individuals in preclinical CRC states are diagnosed with cancer symptomatically (see Supplementary Table S4). The aim of the calibration was to obtain parameter sets whose predictions were close to observed data; in this case, the target data that was used included CRC incidence by age and stage in England prior to screening start[4] and adenoma prevalence data from autopsy and colonoscopy studies[5-11]. In older versions of the model, screening characteristics (sensitivity and specificity) were also estimated through calibration; however, in the current model version these were estimated using a different method (see below). Transitions from diagnosed CRC to CRC death were directly calculated using survival data by age and stage from 2004[12]. Transitions from any state to death from other causes were estimated using the Office for National Statistics (ONS) life tables [13], from which death from CRC (obtained from ONS death certificate data[14]) had been subtracted (Table S4).

The natural history and symptomatic diagnosis parts of the model are able to represent a scenario without screening. Screening is added through user specification of screening strategies that can vary by screening modality, age, screening interval, and number of screening episodes. Screening procedure is modelled to reflect the process within the NHS Bowel Cancer Screening Programme (BCSP). All eligible individuals are invited to screening. Screening non-responders are sent reminder invites; if they still do not respond they are returned to the screening pool for invitation at the next eligible date. Screening positives are sent for further investigation, either by colonoscopy (the majority) or computer tomography colonography (CTC).Published estimates of guaiac faecal occult blood test (gFOBT) and flexible sigmoidoscopy (FS) screening test characteristics (sensitivity and specificity) are available, but these estimates are imperfect as it is not possible to know with accuracy what the underlying prevalence of undiagnosed cancers and adenomas is and therefore how many false negatives

there are. Some small studies have used colonoscopy as a reference; however, colonoscopy itself does not have perfect sensitivity, particularly for low risk adenomas, and its sensitivity is highly variable depending upon colonoscopy quality. Other studies look at the number of interval cancers to estimate sensitivity to CRC, but this itself requires estimating sojourn time, and doesn't provide any estimates of sensitivity of screening to adenomas. Furthermore, the type of small scale randomised controlled trials that have done this often use highly unrepresentative populations that may have different underlying disease prevalence than the general population. Given that the aim of the model was to make decisions around the current BCSP, it was necessary that estimates of sensitivity and specificity were compatible with the detection rates found in that programme and in large scale trials such as the UK Flexible Sigmoidoscopy Screening Trial (UKFSST)[15], rather than using direct estimates from small trials.

Sensitivity and specificity of gFOBT and FS was calculated by combining information about screening detection rates and false positives with model estimates of underlying disease prevalence (Table S4). Total disease prevalence (diagnosed plus undiagnosed CRC and adenomas) cannot be directly measured; however, following calibration of transition probabilities, the model could be used to estimate underlying disease prevalence in the absence of screening and it could be assumed that this modelled prevalence was comparable to the prevalence of disease in the English population prior to screening start. Data about detection rates for low risk adenoma, high risk adenoma and CRC at different ages following gFOBT or FS screening was obtained from the English BCSP[16]. Only prevalent (first screen) data was used. Sensitivity could then be calculated directly using the following formula:

$$\text{Sensitivity (screening type, disease)} = \frac{\text{Detection Rate (screening type, disease)}}{\text{Underlying Prevalence (disease)}}$$

Specificity was calculated in a similar way using information about false positives. Estimates of sensitivity and specificity of further investigations (colonoscopy and CTC) was obtained from published data (see supplementary Table S4).

Screening pathway parameters including those relating to screening participation, test completion and follow-up compliance were taken primarily from BCSP data[16], whilst potential harms from screening were also incorporated (Table S4). Follow-up surveillance by colonoscopy following removal of high risk adenomas was modelled according to current guidelines for surveillance from the British Society of Gastroenterology [17]. Intermediate risk is defined by the BSG as 3-4 small adenomas or one adenoma of at least 1cm in diameter, whereas high risk is defined as either five or more small adenomas, or three or more adenomas of which one is at least 1cm in diameter. Those at high risk are eligible for surveillance after one year, whilst those at intermediate risk are eligible for surveillance after three years. Whilst the model does not explicitly include an intermediate risk health state, the modelled cohort identified as high risk following screening is divided into intermediate and high risk in the proportions found in the BCSP, with each cohort following the relevant surveillance pathway.

A wide range of literature sources were used to populate the model with resource costs and utilities to enable cost-effectiveness analysis to be carried out. A detailed description of the calibration process, model structure, assumptions and full parameter list can be found elsewhere [1].

Using historical incidence and mortality data in the ScHARR bowel cancer screening model

CRC incidence:

CRC development is modelled through natural history transition probabilities that have been calibrated [3] against incidence data by age and stage from the cancer registry in England for the period 2004-2006[4]. Whilst this is relatively old data, it reflects the period prior to roll-out of

CRC screening in England and so enables parameters to be estimated for an unscreened population. However, there was a general trend for age standardised CRC incidence in the UK to increase slightly before 2005 (Supplementary Table S3); thought to reflect an increase in risk factors and improvements in diagnosis and recording according to CRUK[18]. This trend may have continued beyond 2005, but this is confounded by the effects of subsequent CRC screening. This alteration in CRC incidence over time means that the model could be inaccurately estimating absolute incidence in the absence of screening where a screening trial was carried out prior to 2005. If this is the case, then it may fail at estimating the relative benefits of screening.

Accurately altering the model to reflect either current incidence or historical incidence before 2005 would require recalibration of natural history parameters; a very time consuming process. To avoid having to do this for each validation, an extra parameter was added to the model which acted as a multiplier on the transition from normal epithelium to low risk adenomas to reflect the differences in age-standardised CRC incidence over time, available from CRUK for a time period from 1979 to 2013[18] (Supplementary Table S1). Multipliers were calculated by dividing the age-standardised incidence for each year by the age-standardised incidence for 2005. Note that this ignores any differences by age or cancer stage that may have occurred over time and therefore represents a simplification of the historical changes in CRC incidence. By choosing this particular transition for modification, this also assumes that there are proportional differences in the prevalence of LR and HR adenomas. Given that post 2005 incidence includes the impact of screening, multipliers were only calculated for historical analyses for pre 2005 and it was assumed that underlying incidence (minus the impact of screening) had not changed since that time.

CRC mortality:

The model estimates CRC mortality using detailed one and three year survival data by age and stage from 2012[12], combined with five year survival data by stage from 2002-2006 [19]. It is assumed in the model that individuals who survive for five years following diagnosis do not die of CRC. Recording of CRC survival following diagnosis has not been routinely performed in the UK and so data at the level of detail required for the model is not available historically. However, data on overall age adjusted CRC mortality is available from CRUK for a time period spanning 1971 to 2013[18]. This data indicates that CRC mortality has reduced considerably since the 1970s, thereby implying (given that incidence has increased) that there has been a significant increase in survival.

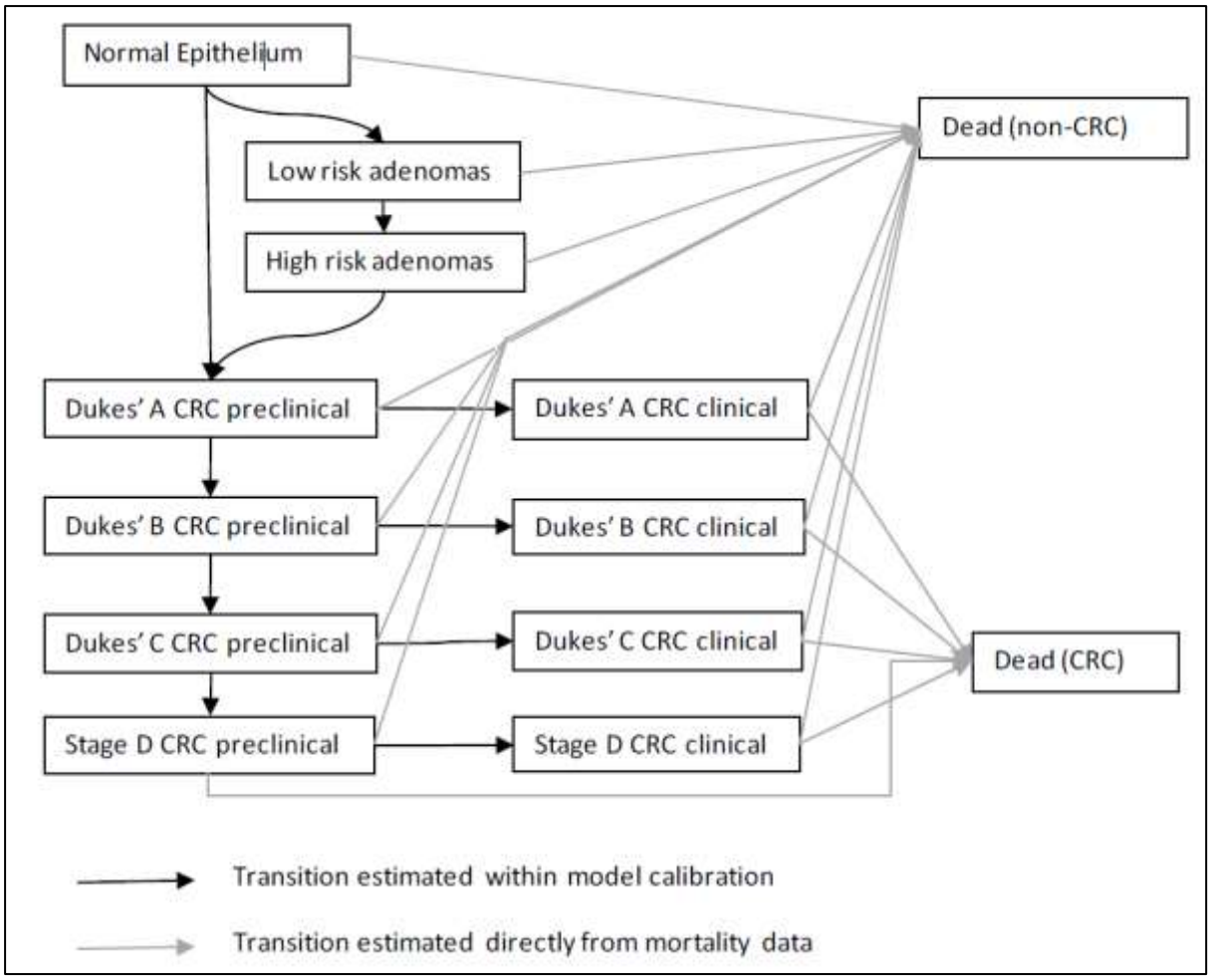
To enable historical CRC mortality to be modelled, an extra parameter was added to the model which acted as a multiplier on five year CRC survival to reflect the differences in age-standardised CRC mortality over time (Supplementary Table S1). Multipliers were calculated by dividing the age-standardised CRC mortality for each year by the age-standardised CRC mortality for 2004, given that it acts upon the 2002-2006 five-year survival data. Note that this ignores any differences by age or cancer stage that may have occurred over time and therefore represents a simplification of the historical changes in CRC mortality. The multiplier was adjusted to take account of concurrent incidence changes over time.

Other cause mortality:

Other cause mortality estimates are calculated in the model using Office of National Statistics (ONS) death certificate data by age, gender and cause to determine the proportion of deaths due to CRC in each age group[14], and then subtracting these from all-cause mortality data within ONS Life Tables[13], to produce other-cause mortality estimates. Historic Life Table data is available for all years from 1980-1982 onwards and therefore the most recent life table data (2014-2016) was replaced with the relevant year's data for historical analyses. Death certificate

data is only available online from 2008, with the most recent data available for 2016, so 2008 data was used for historical analyses for all years prior to 2008.

Supplementary Figure S1: Diagram of model natural history structure



Supplementary Table S1: Model adaptations made to validate against Nottingham guaiac faecal occult blood test (gFOBT) trial[20] long-term follow-up data.

STUDY CHARACTERISTICS	MODEL ADAPTATION
Population Characteristics	
Age distribution	The trial reports the number of individuals recruited in each five year age group between the ages of 45 and 74. To model this as closely as possible, six age cohorts were modelled with mean ages of 47; 52; 57; 62; 67 and 73 and results for each cohort normalised to the numbers reported in each age group.
Gender distribution	The structure of the model does not enable model gender distribution to be altered to that detailed in the trial protocol. However, gender distribution in the trial was fairly representative of that in the general population (on which data the model is based).
Socioeconomic deprivation	Deprivation is not incorporated in the model and was not detailed in the trial protocol.
Previous screening history	The trial was carried out prior to the initiation of screening in England so it was assumed in the model that no individuals had been screened prior to simulation of the trial.
Exclusion criteria	Individuals were excluded from the trial if they had serious illness including CRC; whilst the model only excludes those with a previous CRC diagnosis (other serious illnesses are not modelled). This may mean that modelled individuals are less healthy and more likely to die of other causes than trial individuals.
Screening Programme Details	
Invitation and test protocol	The model assumes a process similar to that used in the trial, with individuals being sent a reminder if they do not initially respond, and retesting of borderline results.
Type of screen (e.g. gFOBT)	gFOBT screening was used in the trial and in the model.
Test sensitivity and specificity	The values for gFOBT sensitivity and specificity currently used in the model are based upon recent data from the BCSP about detection rates of CRC and adenomas[16], combined with modelled estimates of underlying total prevalence of CRC and adenomas. Detection rates recorded in the Nottingham gFOBT trial did not differ substantially from those currently recorded in the BCSP, so test sensitivity and specificity were not altered for this validation.
Type and quality of further investigation in positive individuals	In the trial individuals were followed up by colonoscopy or barium enema. Because barium enema is no longer recommended, it was not incorporated in the model and instead it was assumed that individuals were followed up by colonoscopy or CTC (the latter in individuals who are unsuitable for colonoscopy). Note that colonoscopy quality may have improved since the trial ended.
Number of screening rounds	The trial averaged 3-6 rounds of screening per person. The model is a cohort model so cannot incorporate patient variability around number of screening rounds. It is also only able to simulate

	screening between the ages of 50 and 75. Therefore for most cohorts it was assumed that individuals received 4 rounds of screening, starting in the first year. For the cohort aged 47, screening was assumed to not start until age 50, and for the cohort aged 73, only 2 rounds of screening were modelled. Additional analyses were carried out in which individuals (apart from those in the age 73 cohort) received either 3 or 5 years of screening.
Screening interval	Both the trial and the model assume biennial screening.
Eligibility criteria (based on population characteristics or screening history)	Age criteria assumed to be the same in the model as in the trial. Initially, the trial did not re-invite individuals who had not accepted the first screening invite to further screening episodes, although this was altered in 1990, meaning some individuals had gaps of many years between screening invites. However, the model assumes that individuals are invited to all screening episodes for which they are eligible, irrespective of their previous screening acceptance, and that all screening episodes are equidistant.
Surveillance Programme Details	
Surveillance criteria	Both the trial and model include follow-up surveillance for individuals detected with adenomas or CRC, but it is unclear from the trial description whether this follow-up was equivalent to the current modelled surveillance programme, which follows BSG guidelines[17]. Assumed in the model that it is equivalent to the current programme.
Surveillance method	See above (surveillance criteria)
Surveillance sensitivity and specificity	See above (surveillance criteria)
Frequency of surveillance	See above (surveillance criteria)
Criteria for stopping surveillance	See above (surveillance criteria)
Uptake	
Uptake of screening	The trial reports that within the screening arm, 53.1% of people accepted the first offered screen, 59.6% of people completed at least one gFOBT screen, and 38.2% completed all offered screens. Uptake of gFOBT in the model was specified to reflect this.
Uptake of further investigations	This was not detailed in the trial protocol, so model default values based on BCSP data were assumed.
Uptake of surveillance	See above (surveillance criteria)
Study Follow-up	
Length of study follow-up	The trial has a median of 19.5 years follow-up per person, ranging from 0 to 28.4 years. In the model, a 20 year follow-up was assumed for everyone
Historical and Geographical Setting	
CRC incidence	The screening part of the trial took place between 1981 and 1995, whereas model inputs for CRC incidence, mortality and all-cause mortality reflect the most recent available data. The impact of using current versus historical data was tested by carrying out a series of analyses in which historical data from different years was

	used where available, to represent either current data, data from 1981 (the start of the trial), from 1995 (end of the screening period), or from 2005 (half-way between the end of the screening period and follow-up).
CRC mortality	See above (CRC incidence)
Other-cause mortality	See above (CRC incidence)
Outcomes for Comparison	
Relative outcomes	Rate ratios used to compare relative incidence and mortality in screening versus no screening arms
Absolute outcomes	Absolute rates per 100,000 person years for incidence and mortality.
CRC = colorectal cancer; BCSP = Bowel Cancer Screening Programme; gFOBT = guaiac faecal occult blood test; FS = flexible sigmoidoscopy; BSG = British Society of Gastroenterology; LR = low risk; HR = high risk.	

Supplementary Table S2: Model adaptations made to validate against UK Flexible Sigmoidoscopy Screening Trial (UKFSST) [15,21] long-term follow-up data.

STUDY CHARACTERISTICS	MODEL ADAPTATION
Population Characteristics	
Age distribution	The trial enrolled individuals aged between 55 and 65 and the exact number of individuals of each age was available from the study authors (personal communication from W. Atkin). The model simulated the correct number of individuals in each age-year cohort and added results together to produce a total.
Gender distribution	The structure of the model does not enable model gender distribution to be altered to that detailed in the trial protocol. However, gender distribution in the trial was fairly representative of that in the general population (on which data the model is based).
Socioeconomic deprivation	Deprivation is not incorporated in the model and was not detailed in the trial protocol.
Previous screening history	The trial was carried out prior to the initiation of gFOBT screening in England so it was assumed in the model that no individuals had been screened prior to simulation of the trial.
Exclusion criteria	Individuals were excluded from the trial if they had a history of CRC, adenomas or inflammatory bowel disease; if they had severe or terminal disease; if they had a life expectancy of less than five years; if they were unable to provide informed consent or if they had had a sigmoidoscopy or colonoscopy within the past three years. Furthermore, individuals with a strong family history of CRC or symptoms of CRC were managed outside the trial because randomisation would not have been in their interest. However in the model only those with a previous CRC diagnosis or adenomas are excluded from screening (other serious illnesses or personal characteristics are not modelled).
Screening Programme Details	
Invitation and test protocol	The model assumes a process similar to that used in the trial.
Type of screen (e.g. gFOBT)	FS screening was used in the trial and in the model.
Test sensitivity and specificity	Values for FS sensitivity currently used in the model are based upon recent data from the BCSP about detection rates of CRC and adenomas[16]. Detection rates in the BCSP are lower than those recorded by the UKFSS trial, suggesting that test sensitivity may have been higher in the trial than has been found following roll-out of screening; this is plausible given that the examination quality could have been higher in trial conditions than in practice. To model the trial accurately, FS sensitivities were increased proportionately relative to the observed detection rates in the trial compared to the BCSP (FS sensitivity for LR adenomas = 0.241; FS sensitivity for HR adenomas = 0.781; FS sensitivity for CRC

	= 0.679). Note that this assumes that underlying age-specific rates of CRC and adenomas are similar between current day BCSP participants and historical UKFSS trial participants, which may not be the case.
Type and quality of further investigation in positive individuals	Further investigation was carried out using colonoscopy in both the trial and the model. Note that colonoscopy quality may have improved since the trial ended.
Number of screening rounds	The UKFSST is a trial of once-only FS screening, so a single screening round was modelled.
Screening interval	Not relevant as one-off screen
Eligibility criteria (based on population characteristics or screening history)	Age criteria assumed to be the same in the model as in the trial.
Surveillance Programme Details	
Surveillance criteria	Both the trial and model include follow-up surveillance for individuals detected with adenomas or CRC, but it is unclear from the trial description whether this follow-up was equivalent to the current modelled surveillance programme, which follows BSG guidelines[17]. Assumed in the model that it is equivalent to the current programme.
Surveillance method	See above (surveillance criteria)
Surveillance sensitivity and specificity	See above (surveillance criteria)
Frequency of surveillance	See above (surveillance criteria)
Criteria for stopping surveillance	See above (surveillance criteria)
Uptake	
Uptake of screening	Uptake for FS screening was changed from 44% as currently used in the model based upon data from the BCSP, to 71% to reflect the trial.
Uptake of further investigations	This was not detailed in the trial protocol, so model default values based on BCSP data were assumed.
Uptake of surveillance	See above (surveillance criteria)
Study Follow-up	
Length of study follow-up	Follow-up data from the trial is available for two time-points: 11.2 years and 17.1 years. The model was set to simulate life-time follow-up, with the data for the 11 year and 17 year time points extracted for comparison against trial data.
Historical and Geographical Setting	
CRC incidence	The trial was carried out between 1996 and 1999 with follow-up data published in 2010 and 2017, whereas model inputs for CRC incidence, mortality and all-cause mortality reflect the most recent available data. The impact of using current versus historical data was tested by carrying out a series of analyses in which historical data from different years was used where available, to represent either current data, data from 1996 (the start of the trial); from

	2003 (halfway between the trial start and first follow-up), or from 2010 (first follow-up date).
CRC mortality	See above (CRC incidence)
Other-cause mortality	See above (CRC incidence)
Outcomes for Comparison	
Relative outcomes	Rate ratios used to compare relative incidence and mortality in screening versus no screening arms
Absolute outcomes	Absolute rates per 100,000 person years for incidence and mortality.
CRC = colorectal cancer; BCSP = Bowel Cancer Screening Programme; gFOBT = guaiac faecal occult blood test; FS = flexible sigmoidoscopy; BSG = British Society of Gastroenterology; LR = low risk; HR = high risk.	

Supplementary Table S3: Age standardised colorectal cancer (CRC) incidence and mortality from Cancer Research UK data[18], and multipliers to modify the transition from normal epithelium to low risk adenoma in the model. Note that values in bold are replaced by 1 in the model as CRC incidence estimates post 2005 include changes in incidence due to screening that should not be represented in the model no screening arm.

Year	Age Standardised CRC Incidence (per 100,000)	Incidence Multiplier (compared to 2005 data)	Age Standardised CRC Mortality (per 100,000)	Mortality Multiplier (compared to 2004 data)
1980	63.7	0.89	45.4	1.58
1981	64.5	0.90	44.6	1.51
1982	66.4	0.93	43.2	1.48
1983	65.7	0.92	44.1	1.48
1984	67.0	0.94	45.7	1.55
1985	66.3	0.93	45.3	1.49
1986	68.2	0.95	43.8	1.47
1987	66.9	0.93	43.9	1.46
1988	67.5	0.94	43.7	1.44
1989	68.1	0.95	43.7	1.42
1990	69.1	0.97	42.8	1.40
1991	69.0	0.96	42.3	1.39
1992	68.6	0.96	42.5	1.33
1993	72.0	1.01	39.7	1.28
1994	70.0	0.98	38.7	1.25
1995	69.9	0.98	37.9	1.23
1996	69.1	0.97	37.2	1.16
1997	72.0	1.01	36.2	1.13
1998	71.9	1.00	35.4	1.10
1999	72.6	1.01	34.4	1.06
2000	73.3	1.02	33.2	1.03
2001	72.6	1.01	32.7	1.05
2002	70.2	0.98	32.5	1.05
2003	69.3	0.97	32.0	1.03
2004	69.6	0.97	31.7	1.00
2005	71.3	1.00	31.2	0.98
2006	71.6	**1.00**	30.7	0.95
2007	72.4	**1.01**	30.3	0.93
2008	73.3	**1.02**	30.3	0.91
2009	74.7	**1.04**	29.1	0.87
2010	75.4	**1.05**	28.8	0.86
2011	75.1	**1.05**	28.3	0.84
2012	75.6	**1.06**	28.6	0.86
2013	74.9	**1.05**	27.7	0.88

Supplementary Table S4: Summary of model parameters used in the validation analyses, their data sources and changes made to parameters as part of validation. Other model parameters relating to costs, utilities and other screening modalities that were not used in this validation exercise are not shown here but can be found elsewhere[1].

Parameter	Default Value	Data Source	Validation: Nottingham gFOBT Trial	Validation: UKFSST
Natural History: Normal epithelium to LR adenomas - age 30	0.021	Calibration*	Incidence multiplier applied to model historical incidence see Table S3	Incidence multiplier applied to model historical incidence see Table S3
Natural History: Normal epithelium to LR adenomas - age 50	0.020	Calibration*	Incidence multiplier applied to model historical incidence see Table S3	Incidence multiplier applied to model historical incidence see Table S3
Natural History: Normal epithelium to LR adenomas - age 70	0.045	Calibration*	Incidence multiplier applied to model historical incidence see Table S3	Incidence multiplier applied to model historical incidence see Table S3
Natural History: Normal epithelium to LR adenomas - age 100	0.011	Calibration*	Incidence multiplier applied to model historical incidence see Table S3	Incidence multiplier applied to model historical incidence see Table S3
Natural History: LR adenomas to high risk adenomas - age 30	0.009	Calibration*	Unchanged	Unchanged
Natural History: LR adenomas to high risk adenomas - age 50	0.008	Calibration*	Unchanged	Unchanged
Natural History: LR adenomas to high risk adenomas - age 70	0.008	Calibration*	Unchanged	Unchanged
Natural History: LR adenomas to high risk adenomas - age 100	0.004	Calibration*	Unchanged	Unchanged
Natural History: HR adenomas to Dukes A CRC - age 30	0.029	Calibration*	Unchanged	Unchanged
Natural History: HR adenomas to Dukes A CRC - age 50	0.025	Calibration*	Unchanged	Unchanged
Natural History: HR adenomas to Dukes A CRC - age 70	0.054	Calibration*	Unchanged	Unchanged
Natural History: HR adenomas to Dukes A CRC - age 100	0.115	Calibration*	Unchanged	Unchanged
Natural History: Normal epithelium to CRC Dukes A	0.000	Calibration*	Unchanged	Unchanged
Natural History: Preclinical CRC: Dukes Stage A to B	0.508	Calibration*	Unchanged	Unchanged
Natural History: Preclinical CRC: Dukes Stage B to C	0.692	Calibration*	Unchanged	Unchanged
Natural History: Preclinical CRC: Dukes Stage C to D	0.708	Calibration*	Unchanged	Unchanged
Natural History: Any health state to other cause death	Varies by age	ONS Life Table Data 2014-16[13]; ONS Death Certificate Data 2016[14].	If available, ONS data from selected years used instead to model historical mortality	If available, ONS data from selected years used instead to model historical mortality
Natural History: CRC health states to CRC mortality	Varies by age and stage	Rachet, 2012 CRC Survival data (from 2004)[12]	Mortality multiplier applied to model historical mortality see Table S3	Mortality multiplier applied to model historical mortality see Table S3

Symptomatic presentation with CRC Dukes A	0.044	Calibration*	Unchanged	Unchanged
Symptomatic presentation with CRC Dukes B	0.176	Calibration*	Unchanged	Unchanged
Symptomatic presentation with CRC Dukes C	0.369	Calibration*	Unchanged	Unchanged
Symptomatic presentation with CRC Dukes D	0.735	Calibration*	Unchanged	Unchanged
Screening Tests: gFOBT Sensitivity for LR adenomas	0.006	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Unchanged	Not relevant
Screening Tests: gFOBT Sensitivity for HR adenomas	0.097	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Unchanged	Not relevant
Screening Tests: gFOBT Sensitivity for CRC	0.168	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Unchanged	Not relevant
Screening Tests: gFOBT Specificity	0.989	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Unchanged	Not relevant
Screening Tests: FS Sensitivity for LR adenomas	0.241	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Not relevant	Unchanged (no information about LR adenomas in UKFSST)[15]
Screening Tests: FS Sensitivity for HR adenomas	0.677	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Not relevant	Changed to 0.781 to reflect proportional increase in detection rates in UKFSST[15]
Screening Tests: FS Sensitivity for CRC	0.437	Calculated from NHS BCSP 2014/15 data[16], and model prevalence	Not relevant	Changed to 0.679 to reflect proportional increase in detection rates in UKFSST[15]
Screening Tests: FS Specificity	1.000	Assumption	Not relevant	Unchanged
Diagnostic Tests: Colonoscopy Sensitivity for LR adenomas	0.765	Van Rijn et al, 2006[22]	Unchanged	Unchanged
Diagnostic Tests: Colonoscopy Sensitivity for HR adenomas	0.980	Bressler et al, 2007[23]	Unchanged	Unchanged
Diagnostic Tests: Colonoscopy Sensitivity for CRC	0.980	Bressler et al, 2007[23]	Unchanged	Unchanged
Diagnostic Tests: Colonoscopy Specificity	1.000	Assumption	Unchanged	Unchanged
Diagnostic Tests: CTC Sensitivity for LR adenomas	0.627	Atkin et al, 2013[24]	Unchanged	Unchanged
Diagnostic Tests: CTC Sensitivity for HR adenomas	0.804	Atkin et al, 2013[24]	Unchanged	Unchanged
Diagnostic Tests: CTC Sensitivity for CRC	0.960	Atkin et al, 2013[24]	Unchanged	Unchanged
Diagnostic Tests: CTC Specificity	0.881	Lin et al., 2015[25]	Unchanged	Unchanged
Diagnostic Tests: Proportion CTC of all referrals	Varies by age	NHS BCSP 2014/15[16]	Unchanged	Unchanged
Harm: Colonoscopy (without polypectomy) perforation rate	0.0003	Rutter et al, 2014[26]	Unchanged	Unchanged
Harm: Colonoscopy (with polypectomy) perforation rate	0.0009	Rutter et al, 2014[26]	Unchanged	Unchanged

Harm: Colonoscopy Probability of death following perforation	0.0519	Gatto et al, 2003[27]	Unchanged	Unchanged
Harm: Colonoscopy probability of hospitalisation for bleeding	0	Rutter et al, 2014[26]	Unchanged	Unchanged
Harm: FS (without polypectomy) perforation rate	0.0001	UKFSST[15]	Unchanged	Unchanged
Harm: FS (with polypectomy) perforation rate	0.0645	UKFSST[15]	Unchanged	Unchanged
Harm: FS Probability of death following perforation	0.0003	Gatto et al, 2003[27]	Unchanged	Unchanged
Harm: FS probability of hospitalisation for bleeding	0.0004	UKFSST[15]	Unchanged	Unchanged
Harm: CTC perforation rate	0.0002	Bellini et al, 2014[28]	Unchanged	Unchanged
Harm: CTC Probability of death following perforation	0	Bellini et al, 2014[28]	Unchanged	Unchanged
Participation: Mean gFOBT uptake over all screening rounds	0.582	NHS BCSP 2014/15[16]	Changed to 0.531 to reflect Nottingham gFOBT trial data[29]	Not relevant
Participation: Proportion completing at least one gFOBT screening round	0.682	NHS BCSP 2014/15[16]	Changed to 0.596 to reflect Nottingham gFOBT trial data[29]	Not relevant
Participation: gFOBT participation for a round for those who comply with at least one gFOBT test	0.854	NHS BCSP 2014/15[16]	Changed to 0.891 to reflect Nottingham gFOBT trial data[29]	Not relevant
Participation: Follow-up compliance FOBT screening	0.872	NHS BCSP 2014/15[16]	Unchanged	Not relevant
Participation: Follow-up compliance FS screening	0.963	UKFSST[15]	Not relevant	Unchanged
Participation: Colonoscopy surveillance compliance	0.825	NHS BCSP 2014/15[16]	Unchanged	Unchanged
Participation: FS screening compliance	0.444	NHS BCSP 2014/15[16]	Not relevant	Changed to 0.710 to reflect UKFSST value[15]
Participation: CTC follow-up compliance	0.992	Plumb et al, 2013[30]	Unchanged	Unchanged
*Calibration targets include CRC Incidence by Age and Stage, 2004-2006, Oxford, NY and Eastern Incidence Data[4]; Autopsy and colonoscopy data[5-11] CRC = colorectal cancer; LR = low risk; HR = high risk; UKFSST = UK Flexible Sigmoidoscopy Screening Trial; gFOBT = guaiac faecal occult blood test; FS = flexible sigmoidoscopy; NHS BCSP = National Health Service Bowel Cancer Screening Programme; CTC = computed tomography colonography; ONS = Office for National Statistics				

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