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Modelling cost-effective strategies for minimising socioeconomic inequalities in colorectal cancer screening outcomes in England

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ABSTRACT

Colorectal cancer (CRC) incidence and mortality is higher in socioeconomically deprived groups for a variety of reasons, but is exacerbated by poorer screening uptake. However, many strategies for improving screening participation exist. This analysis aimed to model the impact of screening on CRC inequalities in England and then compare different strategies for increasing participation, to determine the most cost-effective methods for reducing screening-induced inequalities. An existing health economic model, Microsimulation Model in Cancer of the Bowel was adapted. Screening-eligible individuals were simulated to investigate the impact of screening on CRC inequalities. Following this, four strategies for promoting screening participation were compared: 1) annual re-invitation of screening non-participants; 2) a national media advertising campaign; 3) text message reminders for non-participants; 4) health promotion in deprived populations. Cost-effectiveness, CRC outcomes, resource impacts and effects on CRC inequalities were assessed. Inequalities analysis was based on age-standardised CRC mortality by socioeconomic group. Screening was found to be highly cost-effective but CRC inequalities increased as screening effectiveness improved. Annual re-invitation of non-participants was most cost-effective for promoting particiption (incremental cost-effectiveness ratio = £4404 per quality-adjusted life-year), reducing CRC mortality (11,129 deaths averted), and reducing screening-induced inequality (slope of inequalities reduced from 20.80 to 19.38), although it required 42% more screening kits to be sent out. Other strategies were cost-effective compared with screening alone, and improved CRC outcomes, but had varying impacts on inequalities. Whilst bowel cancer screening increases socioeconomic inequalities in CRC mortality, effective and cost-effective strategies are available for mitigating screening-induced inequalities.

1. Introduction

Socioeconomic inequalities in colorectal cancer (CRC) incidence and mortality are common across high income countries including England, the United States, Germany, Sweden and Italy (Mihor et al., 2020; Singh and Jemal, 2017). In England from 2013 to 17, age-standardised CRC incidence rates ranged from 82 to 90 per 100,000, and mortality rates ranged from 19 to 24 per 100,000, in the least deprived and the most deprived males respectively. Smaller socioeconomic gradients were observed in females (Bowel Cancer Incidence by Deprivation, 2020). These gradients may partially be mediated through differences in CRC risk influenced by lifestyle factors including body mass index (BMI), alcohol consumption and diet (Brown et al., 2018). However; mortality gradients may also have other causes such as unequal response to treatments or presence of comorbidities, as they are persistent even when age, diagnostic stage and treatment type are taken into account (Fowler et al., 2017).

Screening for CRC is an effective way of reducing both incidence and mortality (IARC, 2019), and is also highly cost-effective (IARC, 2019; Lansdorp-Vogelaar et al., 2011; Lin et al., 2016; Murphy et al., 2017; Ran et al., 2019; Whyte et al., 2021). However, uptake of screening is lower in individuals with low socioeconomic status (SES) (de Klerk et al., 2018; Mosquera et al., 2020; van der Meulen et al., 2022). In England, the Bowel Cancer Screening Programme (BCSP) is available to adults aged between 60 and 74 who receive a biennial invitation to faecal immunochemical testing (FIT), although prior to the FIT roll-out, the BCSP used the less sensitive guaiac faecal occult blood test (gFOBT). Previous analysis has found socioeconomic gradients in uptake of gFOBT screening and colonoscopy follow-up in England (Morris et al., 2012; Solmi et al., 2015; von Wagner et al., 2011), indicating that screening has exacerbated pre-existing socioeconomic health inequalities (Asaria et al., 2015). The introduction of FIT screening in England in 2019 is

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Table 1
Baseline characteristics of a representatively sampled cohort of screening eligible individuals from the health survey for England 2014: age 50–74 (n = 10,000).

Characteristic	Mean	Standard deviation
Age (years)	60.93	7.15
BMI (kg/m^2)	28.37	4.73
Alcohol (units)	12.62	17.75
Physical activity (METS)	2839	5045
EQ-5D	0.822	0.244
Characteristic	Percentage	
Male	49.7%	
IMD Q1	18.7%	
IMD Q2	20.8%	
IMD Q3	22.3%	
IMD Q4	19.2%	
IMD Q5	19.0%	
White ethnicity	93.4%	
Current smokers	17.6%	
Past smokers	31.5%	
Family history of CRC	5.95%	
Health state normal epithelium*	73.6%	
Health state low risk adenoma*	20.7%	
Health state high risk adenoma*	4.62%	
Health state undiagnosed CRC*	0.47%	

*Calculated in the context of no past screening, will differ for scenarios that assume past screening. BMI Body Mass Index; METS Metabolic equivalents; EQ-5D EuroQol 5 Dimensions; IMD Q Index of Multiple Deprivation quintile; CRC Colorectal cancer.

expected to have reduced but not eliminated disparities in screening uptake (Moss et al., 2017). Strategies to rebalance socioeconomic differences in CRC health outcomes are therefore required.

Inequalities in CRC outcomes could be reduced if screening participation could be increased in lower SES populations. Many different mechanisms for improving screening participation have been evaluated, ranging from interventions that target non-participants with additional invitations and reminders, to interventions aimed at informing and educating the general population, prior to screening invitation (Duffy et al., 2017). However, the cost-effectiveness and inequalities impact of such interventions has not been investigated or compared so it is unclear which strategies might be best for improving equality in a cost-effective way.

The aim of this study was firstly to quantify the impact of FIT screening on socioeconomic inequalities in CRC mortality in England; and secondly to compare different evidence-based strategies for improving screening participation, using a health economic modelling approach to determine cost-effectiveness and equality impacts.

2. Methods

2.1. Model background

This analysis used a modification of a validated health economic model: Microsimulation Model in Cancer of the Bowel (MiMiC-Bowel) (Mandrik et al., 2021; Thomas et al., 2021a; Thomas et al., 2020; Thomas et al., 2021b). The model is an individual patient level microsimulation model, with annual cycles and lifetime horizon. It simulates the life course of individuals from Health Survey for England (HSE) 2014, representing the population of England (Health Survey for England 2014, 2014), who each have a set of characteristics that determine their cancer risk and screening response. In each year, individuals have a probability of moving through nine mutually exclusive health states: Normal Epithelium; Low Risk Adenoma; High Risk Adenoma; CRC Dukes Stage A; CRC Dukes Stage B; CRC Dukes Stage C; CRC Dukes Stage D; CRC Death; Other Cause Death (Supplementary Fig. 1). Individuals with CRC may be diagnosed via symptomatic/chance presentation or screening, whilst patients may have adenomas detected and removed through screening or surveillance. Screening, surveillance and CRC treatment incur costs and patients suffer utility decrements due to age, CRC diagnosis and screening harms. The model takes an English NHS perspective. A full set of model parameters is presented in Supplementary Table 1, and full details of the original model are available online (Thomas et al., 2020).

For this analysis, modifications were made to the model to enable it to simulate differences between individuals of different socioeconomic status, stratified in the model using index of multiple deprivation (IMD) quintiles, where quintile one represents the least deprived and quintile five the most deprived. A screening-aged population (specified as age 50–74) was sampled with replacement from HSE 2014 based on a set of weights pre-generated by iterative proportional fitting, taking into account the age, sex and IMD distribution of the most recently available (2019) English population (Populations by Index of Multiple Deprivation (IMD) Quintile, 2020). Baseline health state and screening history were assigned to each individual prior to model start, based on pre-generated individual health state probability tables that were calculated using the same model parameters as those used during the course of subsequent simulation (enabling a steady state screening scenario to be modelled). Summary statistics for the baseline population are in Table 1.

Health state transition probabilities were calibrated by age and sex (Mandrik et al., 2021). Personalised CRC risk was incorporated in the model through the inclusion of relative risks for individual risk factors including IMD quintile, ethnicity, smoking status, alcohol consumption, physical activity, body mass index (BMI), family history and polygenic risk (Brown et al., 2018; Huyghe et al., 2019; Lowery et al., 2016), combined to give each individual a personalised relative risk (Thomas et al., 2020). As correlations are observed between risk factors (e.g. between behavioural risk factors and IMD in HSE 2014; Supplementary Fig. 2), relative risks were calibrated to ensure that the correct ratio of CRC incidence was modelled in individuals with and without each risk factor (Supplementary Table 2). National Cancer Intelligence Network (NCIN) estimates of age-standardised CRC incidence by IMD quintile from 2001 to 2005 was used as a calibration target to ensure accurate representation of male and female socioeconomic gradients in CRC incidence prior to screening roll-out (Cancer by deprivation in England 1996–2011, 2014).

The model uses Office for National Statistics CRC survival data from 2013 to 2017 to estimate mortality from CRC by age, sex, cancer stage and time since diagnosis (Fowler et al., 2017). IMD mortality multipliers were incorporated in the model to enable observed differences in survival by IMD quintile to be included, assuming that multipliers would act proportionally across survival categories. The value of these multipliers was calibrated using age-standardised mortality data from NCIN from 2001 to 2005 as a target (Cancer by deprivation in England 1996–2011, 2014) (Supplementary Table 2). All-cause mortality data by IMD quintile was incorporated into the model to enable competing risks of death to be represented (*Life table by single year of age sex and deprivation deciles in England, between 2006 to 2008 and 2014 to* 2016, 2018).

Modelling of differential FIT screening uptake by age, sex, IMD quintile and screening history was based on data from multivariate analysis of uptake in the English FIT pilot (Moss et al., 2017), with modelling of differential uptake by ethnicity and in younger age groups being incorporated separately (Clark, 2019; Szczepura et al., 2008). Average FIT uptake ranges from 54% in the most deprived to 73% in the least deprived IMD quintile, whilst average uptake of colonoscopy is 85% (Moss et al., 2017). Screening sensitivity and specificity were calculated based on modelled prevalence and detection rates found in the FIT pilot (Moss et al., 2017). Calculated sensitivity and specificity values for different FIT thresholds is shown in Supplementary Table 3. No evidence was found to suggest differences in screening sensitivity or specificity by SES. Various sources were used to parameterise screening follow-up and surveillance (Supplementary Table 1). No other screening

parameters were assumed to differ by IMD quintile, due to lack of evidence.

Utility decrements due to CRC treatment and screening harms (bleeding, perforation and mortality) were incorporated as in the original model (Thomas et al., 2020). All individuals had a health-related quality of life measurement at model start from HSE 2014 (Health Survey for England 2014, 2014). Modelled costs included costs of CRC treatment, screening and surveillance and screening harms (Thomas et al., 2021b), and these were incorporated as in the original model (Thomas et al., 2020). These were inflated to 2019/2020 values using the NHS cost inflation pay and prices index (Janssen et al., 2020). Costs and quality-adjusted life-years (QALYs) were gathered according to NICE guidelines and discounted by 3.5% (*Guide to the Methods of Technology Appraisal*, 2013). A full parameter list is in Supplementary Table 1.

2.2. Model analyses

Given that previous modelling around CRC screening inequalities has been set in a gFOBT screening context (Asaria et al., 2015), an initial analysis was carried out to assess the impact of FIT screening compared with no screening. Two different FIT screening scenarios were modelled: a) Screening with FIT at a cut-off of 120 μg/g, biennually from age 60–74 (current English BCSP); and b) screening with FIT at a cut-off of 80 μg/g, biennually from age 50–74 (representing a potential future English screening strategy but also current screening in other countries, many of whom start at age 50).

Four different interventions to improve screening uptake were modelled compared with no intervention, in both cases assuming screening with FIT at a cut-off of 120 μg/g, biennually from age 60–74. Interventions were chosen for modelling based on evidence from an updated systematic review of uptake interventions (Leaviss et al., n.d.), and an informal prioritisation workshop held with the Cancer Research UK (CRUK) early diagnosis team. Intervention effects for gFOBT screening were assumed to apply proportionally to FIT screening.

1. **Re-invitation**: A re-invitation strategy was modelled whereby those who didn't participate in their last screening invite were reinvited annually until they participated in screening or were above the upper age threshold for screening. It was assumed that uptake rate in those reinvited one year after screening non-participation was the same as that expected in the following screening round, based on FIT pilot data (Moss et al., 2017). It was assumed that the intervention would incur a one-off cost of £84,556 to modify the BCSP (inflated from (Raine et al., 2016)), in addition to the costs of sending extra FIT invitations and kits.
2. **Advertising**: A three-month national media advertising campaign based on the 2017 'Be Clear on Cancer' bowel screening campaign (regional pilot in the North-West of England), funded by CRUK with support from Public Health England, was modelled (*North West 'be Clear on Cancer' Bowel Cancer Screening Regional Pilot 2017: Final Evaluation Results: Cancer Research UK*, 2018). Screening uptake increasde by between 1.4% and 3.6% within the three months of the campaign depending upon prior screening history, sex and IMD quintile (Supplementary Table 4). The intervention was assumed to cost £3 million (maximum likely spend for such an intervention according to CRUK, personal communication).
3. **Text Reminders**: Data from a 2014 trial was used to model text message reminders for gFOBT screening non-participants (Hirst et al., 2017). The trial reported significantly increased uptake in first-time invitees (odds ratio of 1.29) with each text message costing £0.05. A one-off cost of £84,556 to modify the BCSP was included (Raine et al., 2016). The intervention was assumed to run continuously with individuals eligible for text reminders for each screening round that they did not participate in.

Table 2
Summary of incremental cost-effectiveness results, CRC outcomes, resource outcomes and inequalities measures for the modelled English population, comparing screening strategies FIT120, age 60–74 biennial and FIT 80, age 50–74 biennial against no screening over a lifetime horizon (95% credible intervals in brackets where available).

Outcome (incremental against no screening)		FIT120, age 60–74	FIT80, age 50–74
Total costs (per person, lifetime)		£37.99 (−£24.60; £107.34)	-£2.10 (−£66.86; £62.38)
CRC treatment costs (per person, lifetime)		-£25.56 (−£86.68; £43.04)	-£78.30 (−£144.86; −£12.85)
Screening costs (per person, lifetime)		£63.55 (£49.66; £79.59)	£76.20 (£60.19; £94.27)
QALYs (per person, lifetime)		0.0109 (−0.0059; 0.0261)	0.0154 (−0.0003; 0.0314)
INMB (£20,000/QALY threshold, per person, lifetime)		£181 (−£134; £470)	£310 (£6; £626)
INMB (£30,000/QALY threshold, per person, lifetime)		£290 (−£151; £676)	£463 (£58; £880)
ICER (against no screening)		£3472	Dominant
ICER (full incremental analysis)		Dominated	Dominant
Probability cost-effective (compared to no screening, £20,000/QALY threshold)		87.6%	97.9%
Probability cost-effective (compared to no screening, £30,000/QALY threshold)		88.3%	97.6%
Probability cost-effective (full incremental analysis, £20,000/QALY threshold)		18.4%	80.5%
Probability cost-effective (full incremental analysis, £30,000/QALY threshold)		22.1%	76.5%
Total CRC cases (English screening population, lifetime)		−120,461 (−303,849; 63,275)	−172,052 (−341,261; 1464)
Mean % reduction in CRC incidence (not age-standardised)		14.3%	20.4%
CRC stage C/D cases (English screening population, lifetime)		−156,039 (−250,334; −71,570)	−185,168 (−268,227; −104,102)
Mean % reduction in CRC stage C/D (not age-standardised)		25.1%	29.8%
Total CRC deaths (English screening population, lifetime)		−114,094 (−193,566; −39,201)	−136,285 (−214,711, −63,600)
Mean % reduction in CRC mortality (not age-standardised)		24.1%	28.8%
FIT invites (England, annual)		4,549,401	8,305,036
FIT responses (England, annual)		3,024,521	4,710,967
Mean FIT uptake (average across all episodes, England))		66.5%	56.7%
Screening colonoscopies performed (England, annual)		42,043	66,986
Inequalities outcome (for age-standardised CRC mortality, across IMD quintiles)	No screening	FIT120, age 60–74	FIT80, age 50–74
Slope index of inequalities	17.513	20.804	22.392
Relative concentration index	−0.03911	−0.06126	−0.07064

CRC Colorectal cancer; QALY Quality adjusted life year; INMB Incremental net monetary benefit; ICER Incremental cost-effectiveness ratio; FIT Faecal immunochemical test; IMD Index of Multiple Deprivation.

4. **Health Promotion**: A telephone-based health promotion intervention aimed at deprived populations was modelled based on a service evaluation from 2012 (Shankleman et al., 2014). The study reported that gFOBT uptake was increased in first-time invitees (odds ratio of 1.75 for women and 1.61 for men). The intervention was assumed to cost £6.64 per person based on inflated suggestions for roll-out costs in practice given in the paper. Health promotion was given only to first-time participants from the most deprived populations (IMD4 and IMD5), in order to reflect the targeting of the original intervention.

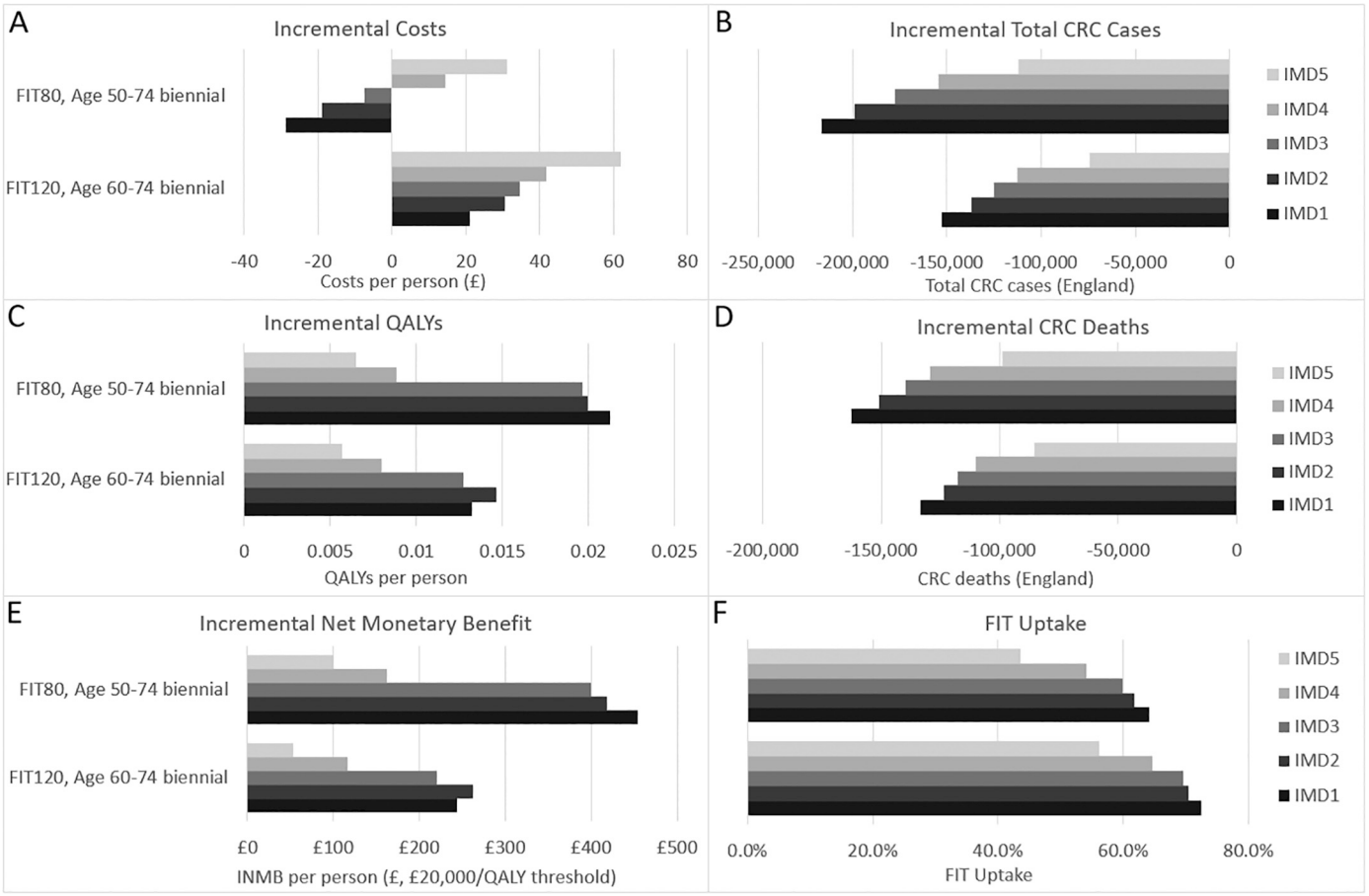

Fig. 1. Incremental outcomes for each IMD quintile for the modelled English population, comparing screening strategies against no screening over a lifetime horizon. IMD1 represents the least deprived quintile and IMD5 the most deprived. A) Total costs; B) CRC Cases; C) QALYs; D) CRC Deaths; E) Net monetary benefit; F) Average FIT uptake over multiple screening episodes.

Additional sensitivity analyses were performed for the re-invitation and text reminder interventions, in which they were given only to the most deprived people (assumed to be those in IMD4 and IMD5). A further set of sensitivity analyses was carried out assuming screening with FIT at a cut-off of 80 μg/g, biennually from age 50–74.

2.3. Model outcomes

Modelled outcomes included lifetime per person costs, QALYs and cost-effectiveness (Incremental cost-effectiveness ratios [ICERs] and incremental net monetary benefit [INMB] (*Guide to the Methods of Technology Appraisal*, 2013)), total and late stage CRC cases, CRC deaths, and annual resource use for England including number of FIT invites, FIT responses and colonoscopy utilisation. Two measures of health inequalities were calculated across IMD quintiles; an absolute measure (slope index of inequalities), and a relative measure (relative concentration index) (Atkin et al., 2017; Regidor, 2004a; Regidor, 2004b). Age-standardised CRC mortality was chosen as the outcome of interest for inequalities analysis given that; a) FIT screening has been demonstrated to reduce mortality whereas the impact on incidence is less clear (Chiu et al., 2015; Scholefield et al., 2012); b) the data suggests high levels of inequality in CRC mortality across IMD quintiles but does not report inequalities in other measures known to be affected by screening such as stage distribution (Cancer by deprivation in England 1996–2011, 2014); c) the inequality impacts on mortality are larger than those on incidence (Supplementary Table 2) enabling clearer assessment of differences between the interventions analysed here.

Lifetime results were obtained using probabilistic sensitivity analysis (PSA), based on modelling of 10 million individuals for the screening and sensitivity analyses (10,000 individuals × 1000 PSA samples) and 100 million individuals for the intervention analyses (100,000 individuals × 1000 PSA samples). Deterministic results from 10 million individuals were used for estimates of annual resource requirements (from the first year after intervention implementation), and calculations of age-standardised mortality for inequalities analysis.

This study was based on publicly available anonymised databases and is thus exempt from ethical compliance.

3. Results

Comparison of FIT screening against no screening indicates that screening is highly effective and cost-effective (e.g. INMB = £181 for FIT120 screening at £20,000/QALY threshold, Table 2 & Supplementary Fig. 3), but that benefits of screening are unequally distributed by IMD quintile (Fig. 1), and socioeconomic inequalities in age-standardised CRC mortality are increased (e.g. slope of inequalities of 17.51 for no screening increases to 20.80 for FIT120 screening, Fig. 2). The model predicts that inequalities are likely to increase further as more effective and efficient screening strategies based on lower FIT thresholds and wider age group eligibility are implemented.

The most cost-effective strategy for increasing screening uptake was found to be annual re-invitation of all screening non-participants (Table 3, Fig. 3 & Supplementary Fig. 4), with an ICER of £5404 in full incremental analysis with other interventions, and a 97.6% probability of being the most cost-effective intervention at the £20,000 per QALY threshold. It is also the most clinically beneficial with 11,129 CRC

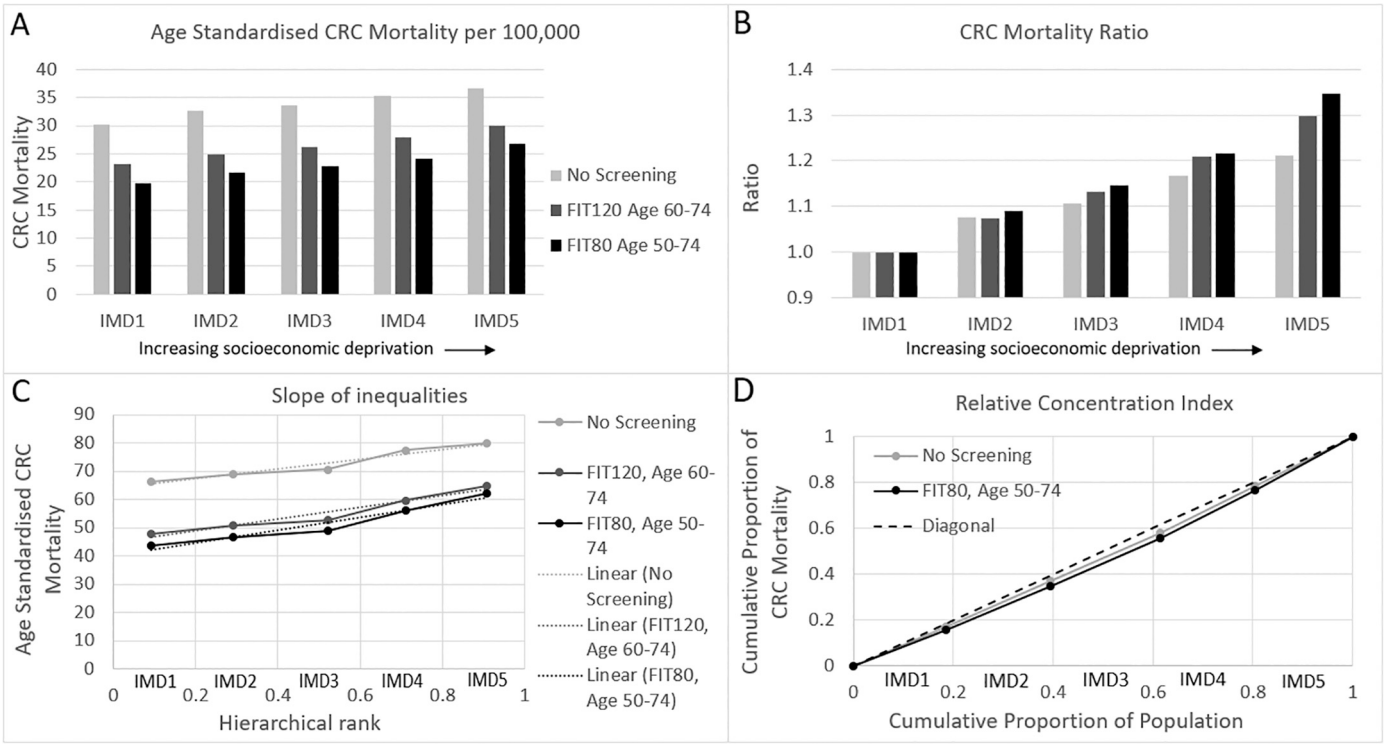

Fig. 2. Graphical representation of inequalities metrics for age-standardised CRC mortality across IMD quintiles, with and without screening. A) Age-standardised CRC mortality per 100,000 for each IMD quintile; B) CRC mortality ratios for each IMD quintile compared with IMD1; C) Slope of inequalities (represented by linear projection, greater slope = greater inequality); D) Relative concentration index (represented by area between curve and diagonal, greater area = greater inequality). Relative concentration index for FIT120, Age 60–74 not shown as very close to curve for FIT80, Age 50–74.

deaths estimated to be prevented over the lifetime of the English population currently aged 50–74. More deaths were prevented in the most deprived subgroups (Supplementary Fig. 5), resulting in the greatest reduction in CRC mortality inequalities of any intervention (e.g. slope of inequalities reduced from 20.80 to 19.38). *Re*-invitation requires a significant investment in additional FIT screening kits (42% increase), most of which do not get used (uptake of additional invitations is only 22%), and also requires more additional colonoscopy resource than any other scenario tested (up to 14% more annually).

The text reminder intervention produced very few QALYs (0.00022 per person) or clinical benefits (e.g. 1002 CRC deaths prevented), but per person intervention costs were extremely low (£0.01), which made this intervention highly cost-effective (e.g. ICER = £467). Whilst the probability text message reminders is the most cost-effective intervention is only 1.2% at the £20,000/QALY threshold, it rapidly increases as the cost-effectiveness threshold is reduced, being the most cost-effective intervention if the willingness to pay threshold is under £5000/QALY (Fig. 3). Additional resource use was also extremely low (e.g. only 2% increase in colonoscopy use), suggesting that it could be a good option if screening resources or intervention costs are scarce. However, little impact on inequalities was seen.

The advertising campaign was the least cost-effective strategy and was dominated in full incremental analysis. Even compared against no intervention, cost-effectiveness was uncertain, with only 53.7% probability of being cost-effective at the £20,000/QALY threshold. The CRC impacts estimated were small (99 deaths prevented), but resource impacts were also low (e.g. only 1.8% more screening colonoscopies required), and no reduction in inequalities was estimated despite the intervention resulting in slightly higher proportional uptake increases in deprived populations.

The health promotion intervention was dominated by the re-invitation intervention in full incremental analysis, although was highly cost-effective against no intervention (with 95.9% probability at the £20,000/QALY threshold), and against the other interventions. Despite its lower effectiveness and cost-effectiveness, this intervention was equally able to reduce inequalities in age-standardised CRC mortality as the re-invitation intervention, due to its targeting specifically to deprived SES groups. Similarly, targeting the re-invitation or text reminder interventions just to the deprived SES groups, significantly improved the ability of these interventions to reduce inequalities. In the case of the re-invitation intervention, this targeting reduced the slope of inequalities down to the level expected with no screening (from 20.80 to 17.14). However, targeting interventions solely to deprived groups reduced the overall clinical and net monetary benefits compared with targeting interventions to all (e.g. only 4857 CRC deaths prevented with re-invitation rather than 11,129 when targeted to all, Supplementary Table 5).

Similar results were obtained in the context of FIT80 screening from age 50–74 (Supplementary Table 6). The text reminder and health promotion interventions are less impactful in terms of costs incurred, benefits gained and inequalities reduced. This is because these interventions affect only first-time invitees, of which there is only a single year within the modelled age 50–74 population who benefit. However, if the intervention was to be continued beyond one year total benefits and impacts on inequalities would be scaled up accordingly.

4. Discussion

This analysis has confirmed that FIT screening, whilst highly cost-effective (as found previously (IARC, 2019; Lansdorp-Vogelaar et al., 2011; Lin et al., 2016; Murphy et al., 2017; Ran et al., 2019; Whyte et al., 2021)), and effective at reducing CRC mortality across the socioeconomic spectrum, is nonetheless likely to increase observed inequalities in age-standardised CRC mortality due to the lower uptake of screening in low SES groups. These findings are in line with previous studies examining the impacts of gFOBT screening on health inequalities (Asaria

Table 3
Full set of incremental cost-effectiveness results, CRC outcomes, resource outcomes and inequalities measures for the modelled English population comparing different uptake interventions against no uptake intervention in the context of FIT120, age 60–74 biennial screening (95% credible intervals in brackets where available).

Outcome (incremental against no intervention)		Re-invitation	Advertising	Text reminders	Health promotion
Total costs (per person, lifetime)		£10.03 (£2.77; £17.78)	£0.24 (−£0.03; £0.55)	£0.10 (−£1.14; £1.41)	£1.37 (−£0.63; £3.32)
Intervention costs (per person, lifetime)		£0.01 (£0.00; £0.01)	£0.18 (£0.15; £0.22)	£0.01 (£0.01; £0.01)	£0.95 (£0.01; £1.23)
CRC treatment costs (per person, lifetime)		-£0.84 (−£8.28; £6.81)	£0.01 (−£0.27; £0.31)	-£0.34 (−£1.89; £0.93)	-£0.35 (−£2.19; £1.44)
Screening costs (per person, lifetime)		£10.87 (£8.30; £13.84)	£0.05 (£0.01; £0.10)	£0.43 (£0.05; £0.94)	£0.77 (£0.24; £1.39)
QALYs (per person, lifetime)		0.00206 (0.00075; 0.00346)	0.00002 (−0.00002; 0.00008)	0.00022 (−0.00001; 0.00060)	0.00034 (0.00003; 0.00075)
INMB (£20,000/QALY, per person, lifetime)		£31.15 (£6.27; £58.04)	£0.16 (−£0.44; £1.31)	£4.34 (£-0.35; £11.66)	£5.40 (£-0.52; £12.94)
INMB (£30,000/QALY, per person, lifetime)		£51.73 (£19.64; £85.98)	£0.36 (−£0.67; £1.97)	£6.56 (£0.75; £16.52)	£8.79 (£1.40; £19.03)
ICER (against FIT120, age 60–74)		£4871	£11,976	£467	£4035
ICER (full incremental analysis)		£5404	Dominated	£467	Dominated
Probability cost-effective (compared to no intervention, £20,000/QALY threshold)		99.6%	53.7%	95.0%	95.9%
Probability cost-effective (compared to no intervention, £30,000/QALY threshold)		99.9%	59.7%	94.9%	97.3%
Probability cost-effective (full incremental analysis, £20,000/QALY threshold)		97.6%	0.0%	1.2%	1.5%
Probability cost-effective (full incremental analysis, £30,000/QALY threshold)		98.9%	0.0%	0.6%	0.7%
Total CRC cases (England, lifetime)		−11,870	−92	−1290	−2093
CRC stage C/D cases (England, lifetime)		−15,016	−136	−1366	−2376
Total CRC deaths (England, lifetime)		−11,129	−99	−1002	−1794
Additional FIT invites (% increase England y1)		42.1%	0	0	0
Additional FIT responses (% increase England y1)		13.6%	1.8%	2.1%	3.9%
FIT uptake (for additional invites, England)		21.5%	N/A	N/A	N/A
FIT uptake (average across all episodes, England)		64.3%	66.6%	67.6%	68.4%
Additional colonoscopies (% increase England y1)		14.0%	1.8%	2.0%	3.5%
Inequalities outcome (for age-standardised CRC mortality, across IMD quintiles)	FIT120, age 60–74 biennial	Re-invitation	Advertising	Text reminders	Health promotion
Slope index of inequalities	20.804	19.384	20.823	20.803	19.674
Relative concentration index	−0.06126	−0.05924	−0.06134	−0.06142	−0.05822

CRC Colorectal cancer; QALY Quality adjusted life year; INMB Incremental net monetary benefit; ICER Incremental cost-effectiveness ratio; FIT Faecal immunochemical test; IMD Index of Multiple Deprivation; y1 year one.

et al., 2015). Furthermore, we estimate that proposed improvements to the English BCSP, whereby screening will be at higher sensitivity and start at a younger age (similar to other European countries) (IARC, 2019), are likely to increase inequalities further unless specific steps are taken to mitigate this.

Four different strategies for increasing screening participation have been investigated in this analysis. The interventions have been found to be effective in improving long-term CRC outcomes, are cost-effective (compared to no intervention) and are expected to reduce, or at least not increase inequalities. These interventions are not mutually exclusive, so implementation of multiple interventions simultaneously might accumulate benefits and reduce inequalities further. Whilst the impact on inequalities is in some scenarios fairly large, particularly if interventions are targeted specifically to deprived SES groups, even the most beneficial strategy can only mitigate the negative impacts of screening on inequalities, and does not go beyond that to reduce the inequalities observed prior to screening programme implementation (Cancer by deprivation in England 1996–2011, 2014). Recent evidence suggests that if take-up by low SES populations could be improved this could even reverse inequalities in CRC mortality, due to higher detection rates in these groups (van der Meulen et al., 2022); however, none of the strategies analysed here has sufficient impact on uptake to be able to do this. Other strategies, perhaps targeting inequalities in cancer risk factors or access to treatment will therefore be needed if inequalities in CRC risk and stage-dependent mortality are also to be reduced.

Whilst restricting interventions to deprived populations tends to improve equality, we find it is less effective and cost-effective than giving the intervention to everyone, with such interventions dominated in cost-effectiveness analysis compared with similar interventions with wider eligibility criteria. This leads to a policy dilemma in which the maximum effectiveness and cost-effectiveness can be achieved by giving the intervention to everyone, but the maximum equality benefits are achieved by targeting the intervention only to the most deprived people. In practise limiting interventions to the most deprived populations only may be a way of enabling total intervention costs and scarce resources to be reduced. However, as IMD is an area-based measure of deprivation, it may not be the most appropriate for targeting of individual-level interventions.

The re-invitation strategies were the most effective, cost-effective, and most likely to reduce inequalities of the interventions tested here. However, these interventions have not yet been trialled and the analysis depends upon data around uptake in previous non-participants for biennial (rather than annual) re-invitation (Moss et al., 2017). Future piloting of this intervention would be recommended to observe whether assumptions hold and enable re-estimation of cost-effectiveness results prior to full implementation.

Whilst the cost-effectiveness of a small number of other CRC screening participation interventions has been modelled previously (Asaria et al., 2015; Ladabaum et al., 2015; Whyte and Harnan, 2014), the strength of this analysis is its assessment of multiple different interventions within the same modelling framework. This has led to challenges in comparing one-off interventions that impact the whole screening population at a single point in time with interventions targeted to first-time invitees, continuously year after year. Here w modelled a mixed screening age cohort of individuals (age 50–74); however there have been limitations with this, particularly when assessing interventions within the future screening context, in which screening starts at age 50. In this case there is only one year of first-time

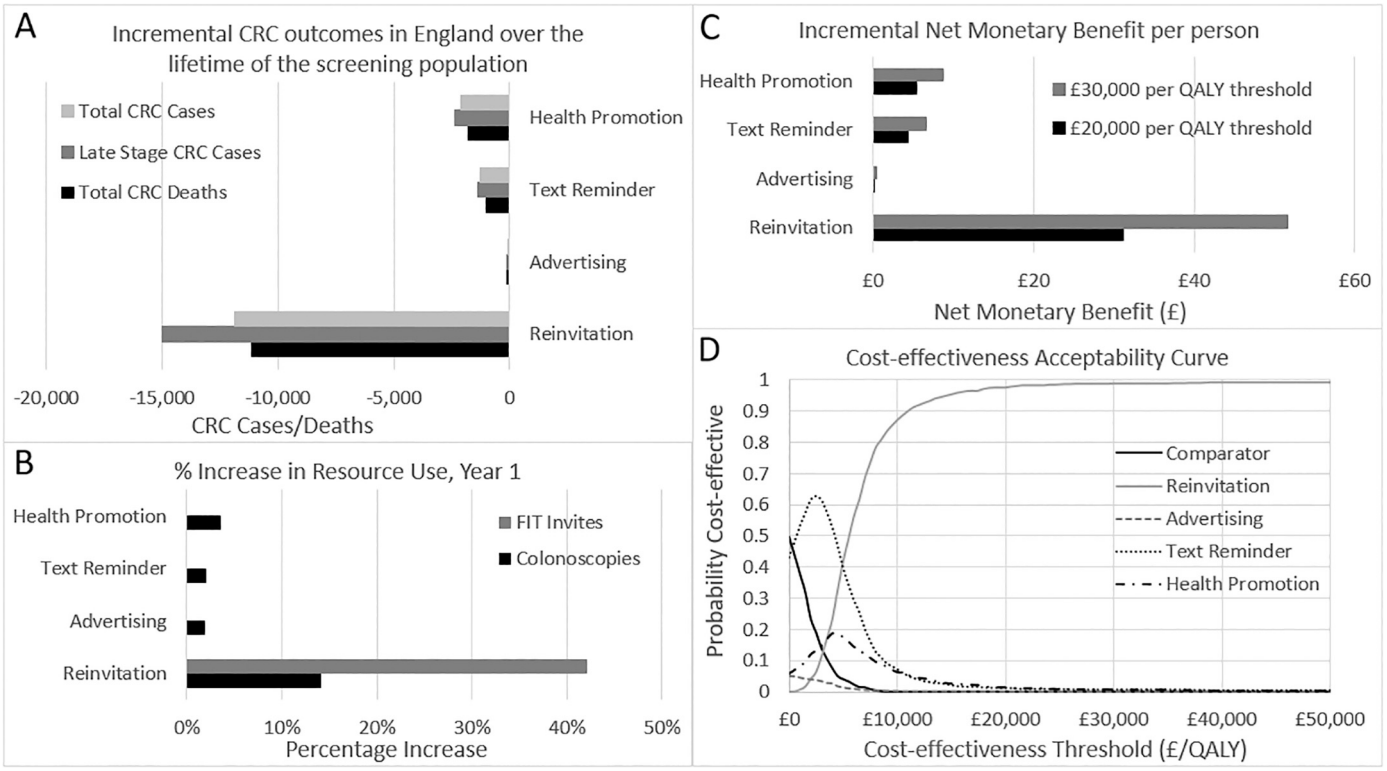

Fig. 3. Comparison of key outcomes for uptake interventions in the context of screening at FIT120, age 60–74: A) Incremental CRC outcomes; B) Percentage increase in resource use; C) Incremental net monetary benefit; D) Cost-effectiveness acceptability curve comparing all four uptake interventions against no intervention comparator.

invitees within the model, which reduces the scale of the benefits that can be obtained by the intervention.

All interventions assessed here aim to increase overall gFOBT/FIT screening participation and none were targeted at improving participation in follow-up investigations such as colonoscopy in those who test positive for FIT. However, this is likely to be particularly highly cost-effective given that such individuals are at much higher risk for CRC than the general population. It could also improve socioeconomic inequalities if low SES groups (who are also likely to have lower follow-up (Morris et al., 2012)) were targeted. As yet, only a few interventions have been designed aimed specifically at follow-up, so further research in this area would be welcome (Wu et al., 2019; Zorzi et al., 2014).

In conclusion, CRC screening is highly cost-effective and effective at reducing CRC mortality in all SES groups but is likely to increase socioeconomic inequalities. This study shows that there are cost-effective interventions available that can help mitigate screening-induced inequalities. Future research should investigate the feasibility and real-world effectiveness of the most promising interventions, together with identifying interventions that can help mitigate other sources of inequalities in bowel cancer outcomes.

Data availability

All data generated by this study is either included as part of this publication or is available from the authors on request.

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Credit author statement

Chloe Thomas: Conceptualisation, Funding acquisition, Methodology, Formal analysis, Writing – original draft. **Olena Mandrik:** Formal analysis, Validation, Writing – review & editing. **Sophie Whyte:** Conceptualisation, Funding acquisition, Writing – review & editing.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2022.107131.

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