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Modelling the impact of the coronavirus pandemic on bowel cancer screening outcomes in England: A decision analysis to prepare for future screening disruption

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ABSTRACT

The English Bowel Cancer Screening Programme invites people between the ages of 60 and 74 to take a Faecal Immunochemical Test every two years. This programme was interrupted during the coronavirus pandemic. The research aimed: (1) to estimate the impact of colorectal cancer (CRC) Faecal Immunochemical Test screening pauses of different lengths and the actual coronavirus-related screening pause in England, and (2) to analyse the most effective and cost-effective strategies to re-start CRC screening to prepare for future disruptions.

The analysis used the validated Microsimulation Model in Cancer of the Bowel built in the R programming language. The model simulated the life course of a representative English screening population from 2019, by age, sex, socio-economic deprivation, and prior screening history. The modelling scenarios were based on assumptions and data from screening centres in England.

Pausing bowel screening in England due to coronavirus pandemic is predicted to increase CRC deaths by 0.73% within 10 years and 0.13% over the population's lifetime, with excess deaths due to peak in 2023. More deaths are expected in men and people aged over 70. Pausing screening for longer would result in greater additional CRC cases and deaths.

Postponing screening for everyone would be the most cost-effective strategy to minimise the impact of screening disruption without any additional endoscopy capacity. If endoscopy capacity can be increased, temporarily raising the Faecal Immunochemical Test threshold to 190 µg/g may help to minimise CRC deaths, particularly if screening programmes start from age 50 in the future.

1. Introduction

The English Bowel Cancer Screening Programme (BCSP) has been very successful in detecting cancer early and so decreasing colorectal cancer (CRC) mortality in England (Richards, 2019; Moss et al., 2017; Logan et al., 2012). CRC screening via Guaiac Faecal Occult Blood Testing (gFOBT) for people aged 60 to 69 years began in England in 2006 (Richards, 2019). Currently, the BCSP invites people between the ages of 60 and 74 to take a Faecal Immunochemical Test (FIT) every two years. It is expected that the future screening programme will reduce the starting age to 50 years. (Richards, 2019)

The coronavirus disease 2019 (COVID-19) pandemic resulted in routine diagnostic delays and suspension of screening for CRC in England for around three months, similar to other countries (Maringe et al., 2020; de Jonge et al., 2021). A modelling study, analysing an 84%

decrease in referrals via the 2-week-wait urgent pathway, concluded that delays in symptomatic diagnosis in England could result in around 180 to 540 additional deaths over a three-month lockdown period (Sud et al., 2020a). Sud et al. (2020) estimated that a four-month diagnostic delay would result in more than 20% reduction in CRC Stage 3 survival over the year (Sud et al., 2020b). Other research assessed that diagnostic delays (screening plus symptomatic detection) in England could result in around 1500 additional deaths within five years (Maringe et al., 2020). While no study specifically analysed the impact of the CRC screening pause in England, a modelling analysis predicted around 320–440 additional deaths in the Netherlands, 1000 in Australia, and 800 in Canada in 30 years with a three-month screening disruption (de Jonge et al., 2021).

While a national-level interruption of cancer screening programmes occurred for the first time due to the pandemic, according to clinical

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experts short-term screening disruptions are not uncommon in individual screening centres in England. These screening disruptions put additional pressure on the endoscopy capacity required to address patient backlogs. Thus, policy makers should have a well thought-through and evidence-based strategy for managing routine public health programmes during short-term issues delaying screening and national emergencies, such as the COVID-19 outbreak.

Previous modelling studies demonstrated long-term benefits and cost-effectiveness of the CRC screening programme in England (Whyte et al., 2021; Whyte et al., 2017). This decision modelling study aimed to quantify the impact of screening pauses of different duration, and the actual COVID-19-related screening pause on future cancer outcomes in England. The research also analysed the most effective and cost-effective strategies to re-start CRC screening.

2. Methods

2.1. Model description

For this analysis, we used a validated model: Microsimulation Model in Cancer of the Bowel (MiMiC-Bowel), developed for previous research. (Mandrik et al., 2022; Thomas et al., 2021a; Thomas et al., 2021b) MiMiC-Bowel is an individual patient simulation model built in the R programming language. The model simulates the life course of patients representing the population of England. Each person in the model has a set of individual characteristics, which determines their cancer risk and response to screening and surveillance. The model has a lifetime horizon and takes an English National Health Service (NHS) perspective. The detailed description of the model, its calibration, and validation is reported online (Mandrik et al., 2021; Thomas et al., 2020).

Underpinning the model is a CRC natural history module with 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, and Other Cause Death. In the model, around 85% of CRC develops through adenomas and the rest through serrated pathways, reflected by the transition from normal epithelium directly to CRC. The model incorporates personalised relative CRC risk through the combination of individual risk factors (Thomas et al., 2020). Once an individual develops CRC, they have a probability of progressing to the next stage. At each stage, there is a probability that an individual will be diagnosed either through screening, surveillance or via symptomatic presentation. It was assumed that after diagnosis CRC stops progressing and individuals start following a disease pathway, which includes treatment costs, utility reductions and reduced survival compared to the general population. The model uses Office for National Statistics CRC survival data from 2013 to 2017 to estimate mortality from CRC by age, sex, cancer stage at diagnosis and time since diagnosis (Office for National Statistics, 2022).

The model incorporated historical screening through gFOBT and flexible sigmoidoscopy (FS) in order to accurately model the current health states of the population. The FIT uptake, sensitivity, and specificity were based on data from the English FIT pilot (Moss et al., 2017). A variety of sources were used to parameterise screening follow-up and surveillance (Thomas et al., 2020).

2.2. Simulated population

The model baseline population is composed of individuals eligible for screening, based on data about sex, age, and Indices of Multiple Deprivation quintile composition in England in 2019 (Table 1) (Office for National Statistics, 2018). The individual characteristics of the population were retrieved from the Health Survey for England (HSE) 2014 (Health Survey for England, 2014), an annual survey which is designed to provide a snapshot of the nation's health (see Supplementary detailed modelling methodology). We assessed the probability of being in each model health state at baseline for each person in the HSE through

Table 1

Population of screening age in England in 2019¹⁶.

IMD quintile	Women, age groups			Men, age groups		
	60–64	65–69	70–74	60–64	65–69	70–74
1	264,777	218,802	187,467	268,472	223,728	201,988
2	288,032	248,443	230,290	298,732	262,993	251,038
3	319,310	285,289	283,863	332,229	306,335	308,111
4	328,502	300,309	310,694	343,801	324,864	337,894
5	326,617	299,957	317,836	341,363	326,020	350,145

Legend: IMD - Indices of Multiple Deprivation quintiles, where quintile 1 represents the most deprived and quintile 5 represents the least deprived.

simulation of 3.35 million individuals aged 30 years at baseline using the cohort model representing the screened population in England with the average FIT uptake of 65%. Then, we allocated a health state and a screening history (based on their projected age at last screen and other characteristics (Thomas et al., 2020)) to each person randomly within their defined probabilities.

2.3. Modelling parameters

Calibration of natural history disease parameters was against pre-screening data from 2005 (see supplementary Table 1) (Mandrik et al., 2021). The HSE 2014 population includes EQ-5D values for individuals that are used as baseline quality of life estimates in the modelling (Health Survey for England, 2014). The model includes utility decrements for CRC diagnosis, age, and screening-related harms. Costs used in the previously published model (Thomas et al., 2021a; Thomas et al., 2021b) were either inflated to 2019/20 values using the National Health Service cost inflation pay and prices index (costs for faecal tests and CRC treatment) (Thomas et al., 2020; Personal Social Services Research Unit, 2018) or updated using the most recent National Schedule of Reference Costs (2018/19) (NHS England, 2018). The model applied 3.5% discounting to both costs and effects.

The parameters of the original MiMiC-Bowel model were converted from annual to three-month cycle lengths to run the analysis (online supplementary detailed modelling methodology). All calibrated natural history disease parameters, CRC mortality, and other cause mortality were converted to rates and then to probabilities by time using logarithmic and exponential equations (Gidwani and Russell, 2020). The annual costs of CRC were converted from a one-year cycle to the three-month cycle duration linearly. The screening-related costs and harms were assigned to the cycle when the event occurred.

2.4. Model validity

MiMiC-Bowel was externally validated to sensitivity of FIT and FS screening tests in England and recent data on CRC incidence and mortality, and cross-validated to the US and German models (see Supplementary detailed modelling methodology) (Mandrik et al., 2021; Cancer Research UK, 2019).

2.5. Stakeholder involvement

We conducted two online panels with patients and other stakeholders (see the acknowledgement section). The first meeting informed the research questions, project plan, outcome choices, and analyses. At the end of the project, the stakeholders provided feedback on the modelling results and suggested research dissemination strategies. The contribution from the panels resulted in the choice of modelled duration for screening pauses and led us to include an additional scenario analysis with higher other cause mortality due to the possible increase in mortality from COVID-19 and other causes (Office for National Statistics, 2020).

2.6. Analysis plan

We analysed the outcomes using probabilistic sensitivity analysis on a population of 18 million people for model runs using three-month model cycles (modelling analysis 1) and nine million people for the analysis using annual cycles (modelling analysis 2). A lifetime horizon was used for all outcomes together with shorter (5, 10, and 20 years) horizons. We also calculated the resource use in the year of the screening restart.

Modelling analysis 1. Impact of colorectal cancer disruption on health outcomes.

We analysed screening disruptions of three, six, nine, and 12 months, plus an approximation of the real screening pause that occurred in 2020. For these scenarios we assumed that screening restart led to a continual postponement of screening for everyone, which is the closest to the actual re-start strategy after the 2020 screening pause. Based on data reporting an increase in other cause mortality during the pandemic (partly due to COVID-19 itself) (Office for National Statistics, 2020), we also conducted a scenario analysis considering a 1% increased mortality from other diseases during the ten-year period.

2.7. COVID-19 first wave scenario

The modelling of the actual screening pause that occurred in England in 2020 was based on aggregate data from individual anonymised screening centres in England ($N = 64$), provided by Public Health England Screening. These aggregate data included the number aged 60–74 years at each screening centre, the number of people who had been delayed in receiving their invitation as of 8th February 2021, and the average number of weeks behind screening due date as of 8th Feb 2021. The linear trend between the latter two parameters (Fig. 1) suggests that for the majority of the centres the delays in screening are ongoing. In most (55%) centres the delays were for roughly three months. To use the data in the state-transition model, we estimated the proportion of the population experiencing approximately zero (less than one-and-half months) delay, three (one-and-half to four-and-half) months delay, six (four-and-half to seven-and-half) months delay, and nine (seven-and-half to 10.5 months) delay from the total. We assumed that the centres experiencing three to nine months delay had an ongoing impact of the screening pause similar to the modelled hypothetical screening pauses of different lengths described above (i.e. would never catch up with the delayed screening). The centres experiencing less than one-and-half months delay (15.8% of the population) were considered to have caught up with screening within the three months after the screening pause. A weighted average population was used to calculate model outcomes based on three, six, and nine month pauses, and an additional

model run with a three-month pause assuming immediate catch up with screening.

Modelling analysis 2. Impact of screening restart scenarios on health outcomes and resource use.

Return-to-screening strategies after a 12-month screening pause were compared to uninterrupted screening. The compared scenarios assessed for the 60–74 year-old (current screened population) and 50–74 year-old (future screened population) are presented in Box 1.

3. Results

Impact of colorectal cancer screening disruption on health outcomes and resource use.

3.1. Impact of the screening pause on clinical outcomes

Pausing screening for three, six, nine, and 12 months increases total CRC cases, stage C & D CRC cases, and CRC deaths (Table 2).

In general, with longer screening pauses, greater impacts on CRC incidence and mortality are observed. When the screening is paused, CRC incidence initially decreases because of diagnostic delays (Fig. 2a, b). When screening restarts, the model predicts a rapid increase in the number of additional CRC cases peaking in 2022 (Supplementary Fig. 1); although cumulative incidence does not catch up with the non-interrupted screening scenario until after 2025 (Table 2, Fig. 2a,b). This additional CRC incidence will gradually decrease until 2034, after which, cumulative CRC incidence decreases (Fig. 2a,b) and the surplus in CRC cases (Supplementary Fig. 1) becomes negative.

Additional CRC mortality resulting from disrupted screening is expected to peak in the years 2023–2024 (Supplementary Fig. 1). The difference in cumulative number of CRC deaths increases up to the years 2032 (Fig. 2c) and reduces afterwards since for some patients screening would only postpone CRC death rather than prevent it. When other cause mortality is assumed to be 1% higher incremental CRC mortality due to the screening pause are smaller than in the base-case scenario (see online supplementary Fig. 2).

Modelling of the actual screening pause based on screening centre data gave results that were slightly larger than the three-months pause screening scenario. The analysis predicted that the screening pause in England will result in more than 270 additional CRC cases (0.13% increase), 880 CRC stage C,D cases (0.58% increase), and 700 additional CRC deaths (0.73% increase) within the next 10 years (Table 2). Within a 40-year horizon the model predicted a 0.034% increase in CRC incidence, 0.16% increase in CRC stage C,D incidence, and 0.13% increase in CRC deaths.

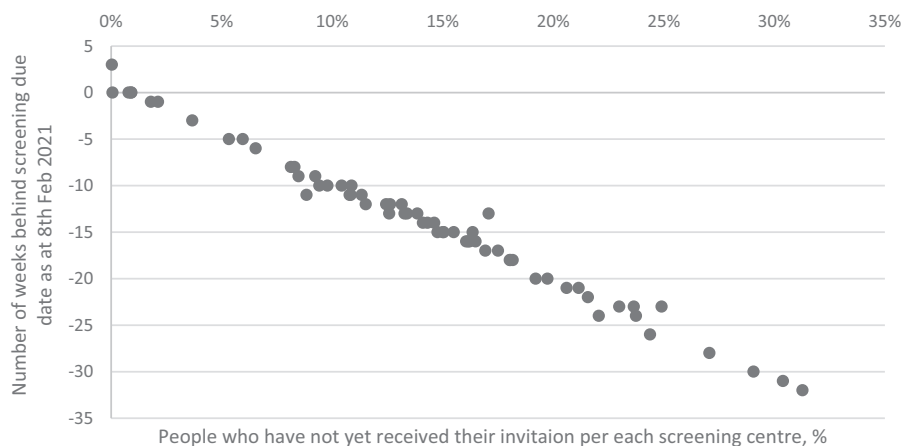


Fig. 1. Number of average weeks behind screening by the size of population who have not received their screening invitation in each screening centre.

Box 1

Return-to-screening strategies for colorectal cancer screening programme.

Scenario 1. Postponing screening for everyone (including the older age group) resulting in later screening initiation. This scenario assumed that each cohort that missed their screening during the pause will be prioritised for screening over the next cohorts due to be screened.

Scenario 2. Omitting screening invitations that were due during the pause entirely and not inviting this population until their next scheduled screening invite. For the oldest age groups two options are considered:

- 2.1. The oldest group will miss their last screening episode;
- 2.2. The oldest group will get their last screening delayed to the age of 76 years.

Scenario 3. Catching up screening in all who missed it over the next year with:

- 3.1. Assumed unlimited healthcare capacity (all people who missed screening are invited within the next cycle, i.e. within the next year);
- 3.2. Inviting everyone who missed screening within the next cycle, but temporarily increasing the FIT threshold to 190 µg/g during this cycle, which will reduce the positivity compared to the current threshold of 120 µg/g. This will reduce the numbers that will be referred to colonoscopy compared with scenario 3.1, although will still require some additional colonoscopy capacity compared with uninterrupted screening.

Table 2

Change in colorectal cancer incidence and mortality among individuals of screening age (60–74 years old) relative to uninterrupted FIT screening in England.

Outcomes by years*	Undisrupted FIT screening	Impact of screening pause: increment in number of events in comparison with undisrupted FIT screening, number (%)				Covid-19 first wave **
		3 months	6 months	9 months	12 months	
CRC incidence						
2020–2025	133,849	–232 (–0.2%)	–277 (–0.2%)	–510 (–0.4%)	–781 (–0.6%)	–232 (–0.2%)
2020–2030	222,400	177 (0.1%)	570 (0.3%)	1124 (0.5%)	1949 (0.9%)	279 (0.1%)
2020–2040	372,665	304 (0.1%)	632 (0.2%)	1186 (0.3%)	2263 (0.6%)	438 (0.1%)
2020–2060	448,702	49 (0.0%)	365 (0.1%)	760 (0.2%)	1611 (0.4%)	153 (0.0%)
CRC Duke 3,4 incidence						
2020–2025	94,117	481 (0.5%)	852 (0.9%)	1257 (1.3%)	1320 (1.4%)	556 (0.6%)
2020–2030	151,594	830 (0.5%)	1252 (0.8%)	1882 (1.2%)	2306 (1.5%)	882 (0.6%)
2020–2040	262,103	689 (0.3%)	866 (0.3%)	1190 (0.5%)	1491 (0.6%)	736 (0.3%)
2020–2060	357,281	493 (0.1%)	668 (0.2%)	837 (0.2%)	875 (0.2%)	509 (0.1%)
CRC mortality						
2020–2025	51,140	315 (0.6%)	559 (1.1%)	783 (1.5%)	638 (1.2%)	370 (0.7%)
2020–2030	96,647	661 (0.7%)	961 (1.0%)	1403 (1.5%)	1817 (1.9%)	703 (0.7%)
2020–2040	185,105	494 (0.3%)	730 (0.4%)	964 (0.5%)	1861 (1.0%)	506 (0.3%)
2020–2060	268,963	326 (0.1%)	559 (0.2%)	651 (0.2%)	1344 (0.5%)	318 (0.1%)

Legend to Table 3: CRC - colorectal cancer; FIT - Faecal Immunochemical Test.

* Outcomes in 5, 10, 20, and 40 years, starting from the time of the screening pause in April 2020.

** Scenario based on data from screening centres.

3.2. Other outcomes of the screening pause

Screening disruption leads to fewer life-years (LY) saved (–0.0006 to –0.0017) and fewer quality-adjusted life-years (QALYs) (–0.0003 to –0.0012). Similar to other outcomes, the reduction in LYs and QALYs increases with duration of screening pause (online supplementary Table 2). Modelling of the actual screening pause based on data from screening centres (COVID-19 first wave scenario) suggests that 6960 LYs and 3500 QALYs could be lost during the lifetime of the screening population.

Disrupting screening also results in lower resource use since some people are dying from other causes before getting their delayed screening invitation (online supplementary Table 2). For the English population, this would mean 164,000 fewer invitations (96,000 fewer performed FITs) with a three-month screening pause and 681,000 fewer invitations (373,000 fewer performed FITs) with a 12-month screening pause over the lifetime. In the scenario based on data from screening centres, the pause is expected to result in 200,000 fewer invitations and 112,000 fewer FITs performed over the lifetime of the screening cohort.

3.3. Impact of screening restart scenarios on CRC outcomes, resource use, and cost-effectiveness

From multiple return-to-screening strategies (Box 1), Scenario 3.1 (catching up screening in all who missed it over the next year with assumed unlimited healthcare capacity) resulted in by far the smallest increase in CRC cases and deaths (Fig. 3).

From scenarios taking endoscopy capacity constraints into account, Scenario 1 (postponing screening for everyone resulting in later screening invitation) and Scenario 3.2 (increasing the FIT threshold to 190 mg/ml during the first year) minimise the impact on CRC incidence and CRC mortality caused by the screening pause. Scenario 3.2 also minimised the impact on LYs and QALYs compared to undisrupted screening (online supplementary Fig. 3). The difference in the impact of different screening re-start scenarios on CRC mortality is smaller with longer follow-up (Fig. 4). This is because for some patients screening postpones but does not prevent CRC mortality.

From the scenarios with the least negative impact on patient outcomes, Scenario 1 did not require any additional FIT screens or colonoscopy capacity to follow-up FIT positive results in the year of screening restart (modelled year 2) (Table 3). Both Scenarios 3.1 and

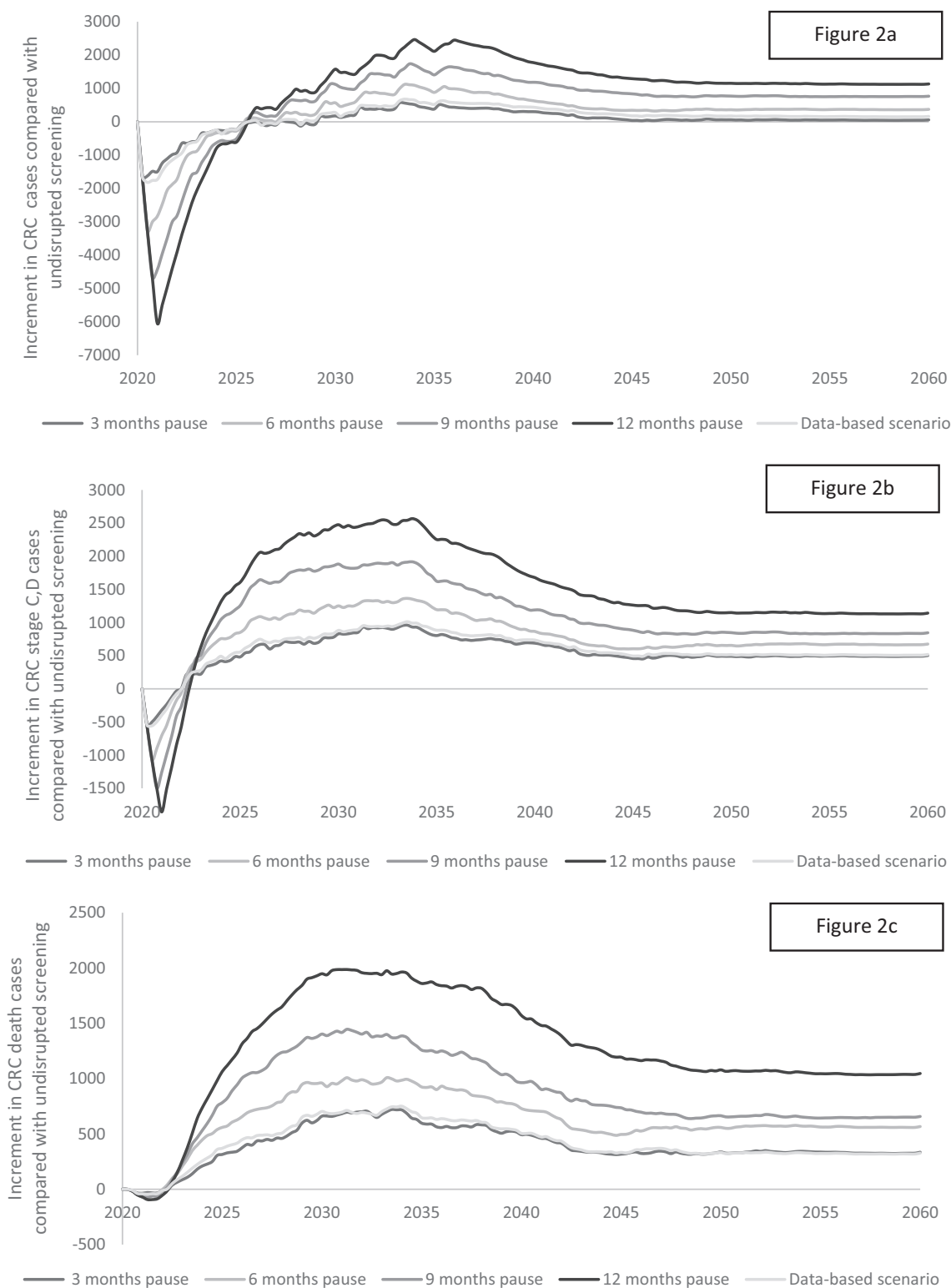


Fig. 2. Projected incremental changes in cumulative colorectal cancer incidence and mortality over time among individuals of screening age (60–74 years old) compared with uninterrupted FIT screening in England.

Scenario 3.2. required additional FIT invites (4 million for both) and colonoscopy capacity: 24,000 for 3.1 and 13,000 for 3.2 in the year of screening restart.

The decrement in resource use and delay in diagnosis for some of the patients who have slowly progressing cancer resulted in generally lower discounted costs (online supplementary Fig. 4). However, since biennial FIT screening is cost-effective (Whyte et al., 2017; Thomas et al., 2021b),

all return-to-screening strategies had negative net monetary benefit for the screened population in England compared with uninterrupted screening. The return-to-screening scenarios with smallest negative clinical impact (Scenarios 3) were the most cost-effective (Fig. 5).

Disrupting the screening has a bigger impact on men than women in all screening restart scenarios because of the higher CRC risk in this subgroup. For instance, disrupting the screening for 12 months is predicted

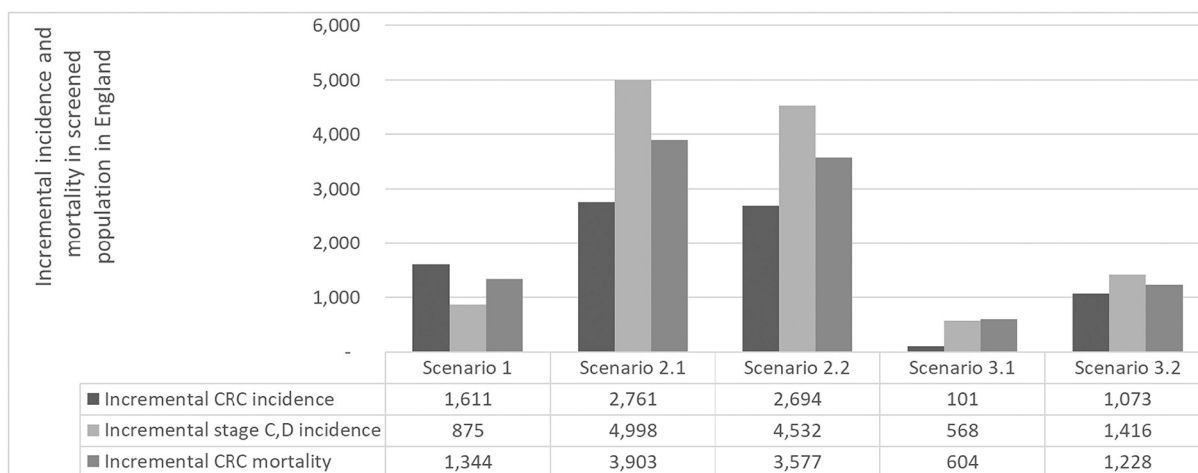


Fig. 3. Incremental cumulative CRC incidence and mortality over population lifetime after a 12-month screening pause with different return-to-screening scenarios compared with undisrupted screening: 60–74 year-old population.

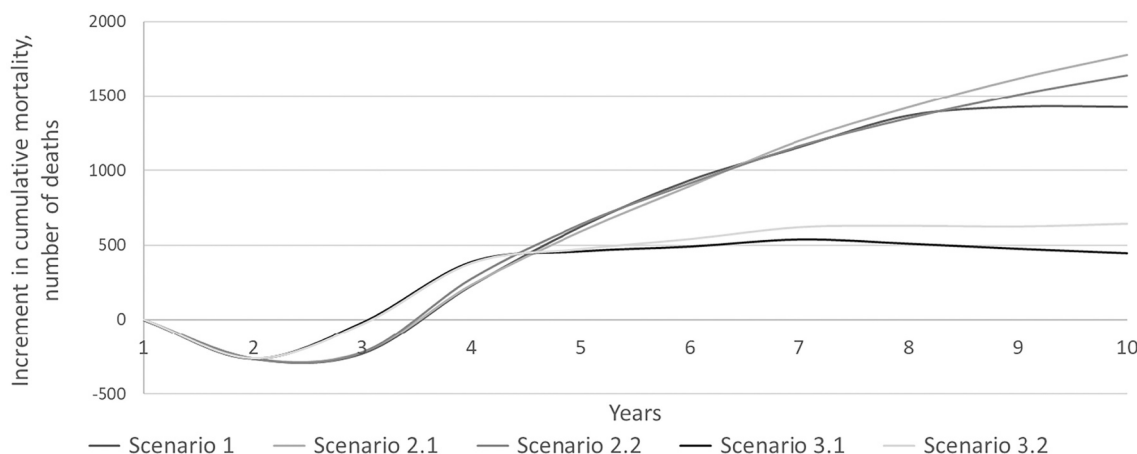


Fig. 4. Incremental cumulative CRC mortality over 10 years after a 12-month screening pause with different return-to-screening scenarios, compared with undisrupted screening.

Table 3

Incremental FIT screening and colonoscopy follow-up in the year following the screening re-start after a 12 month screening pause with different return-to-screening scenarios compared with undisrupted screening: 60–74 year-old population.

	Scenario 1	Scenario 2.1	Scenario 2.2	Scenario 3.1	Scenario 3.2
FIT invitations, 2021	-97,709	0	0	4,165,188	4,165,188
FIT performed, 2021	-117,760	0	0	1,688,100	1,688,100
Screening colonoscopies performed, 2021	-591	0	0	23,709	13,325

to lead to around 900 additional CRC deaths in men and 530 in women in 10 years in screening re-start Scenario 1 and 400 additional deaths in men and 230 in women in Scenario 3.2 (Fig. 6). Disrupting screening has a larger negative impact on mortality over 10 years in the older population (Fig. 6).

3.4. Re-start of the future screening programme in England for 50–74 years old population

The results of the modelling analysis for a screening population aged 50–74 years were comparable with the screening population aged 60 to 74 years (online supplementary Figs. 5–8). However, the incremental benefit of Scenario 1 on CRC incidence and mortality over scenario 2.1 and 2.2 was negligible in this population group (Fig. 7).

4. Discussion

We estimate that the pause in CRC screening that occurred in England due to the COVID-19 outbreak, will lead to around 270 additional CRC cases and 700 additional CRC deaths over the next 10 years, resulting in 6960 LYs and 3500 QALYs lost during the lifetime of the screening population. Longer CRC screening pauses would be expected to have greater impacts. Our predictions indicate that the peak in additional CRC deaths is expected in the year 2023 (i.e. three years after the screening pause), although deaths will continue to accumulate at a lower rate for another 10 years beyond this. Additional CRC cases and deaths are likely to disproportionately affect males and people aged 70 years or more at the time of the pause. Because in general FIT screening is cost-effective, return-to-screening scenarios with the smallest negative clinical impact, are likely to be the most cost-effective.

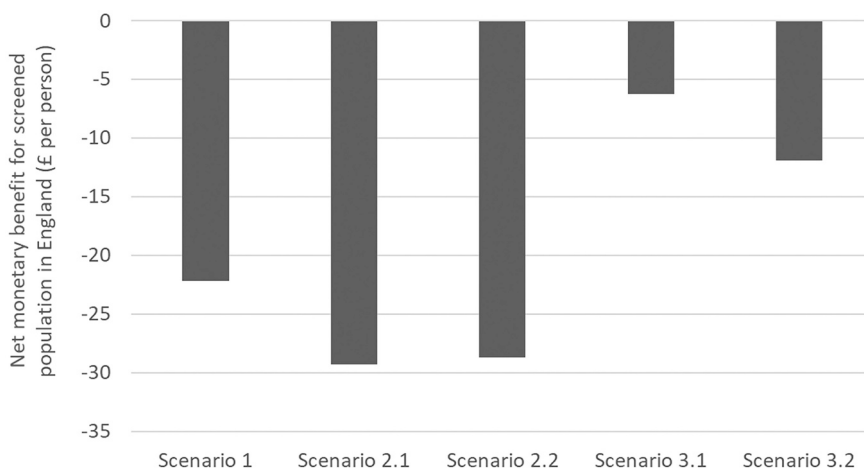


Fig. 5. Incremental net monetary benefit with different return-to-screening scenarios after a 12-month screening pause compared with uninterrupted screening: 60–74 year-old population.

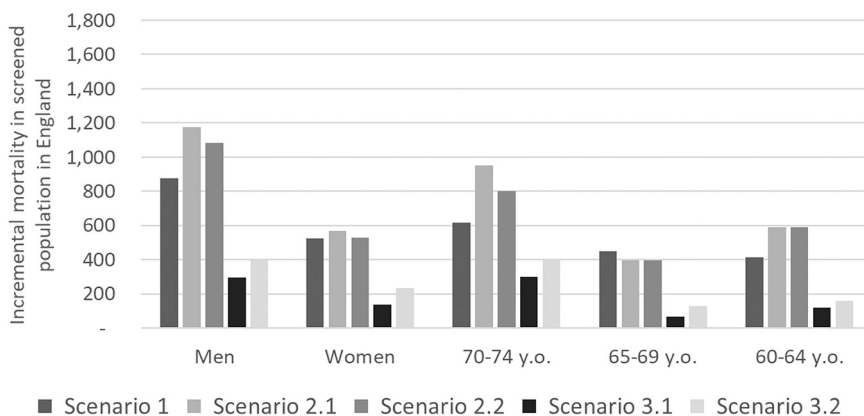


Fig. 6. Incremental cumulative CRC mortality over 10 years after a 12-month screening disruption with different return-to-screening scenarios: sub-group analysis.

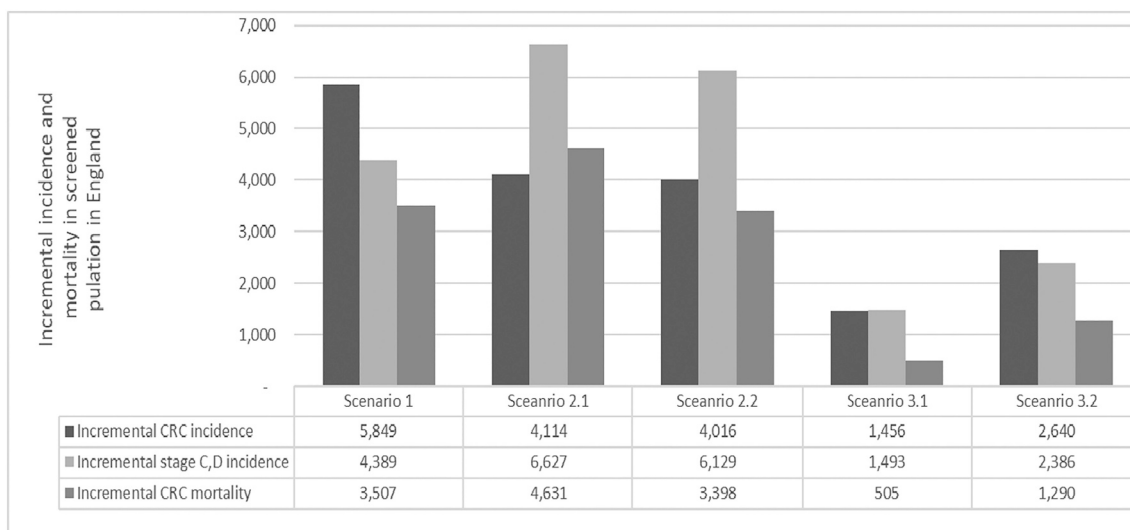


Fig. 7. Incremental cumulative CRC incidence and mortality over population lifetime after a 12-month screening disruption with different return-to-screening scenarios compared with uninterrupted screening: 50–74 year-old population.

COVID-19 created a disruption in healthcare services in England. As our data-based scenario demonstrates, the impact of the FIT screening disruption on CRC outcomes was due to the backlog of patients which

continued to exist even nine months after screening restarted. Such disruptions of CRC screening due to the COVID-19 pandemic have been observed globally, not just in England. Other countries reported CRC

screening pauses and a reduction in CRC screening uptake (Kortlever et al., 2021; Patel et al., 2021), with a systematic review by Mazidimoradi et al. (2021) suggesting that participation in CRC screening programmes decreased by 28–100% at different points in the pandemic, while emergency colonoscopy has been reported to have increased by 2–9% (Mazidimoradi et al., 2021).

Endoscopy services have been operating with reduced capacity since CRC screening re-started in England. (The Lancet Gastroenterology, 2020) Scarce endoscopy resources necessitate a trade-off in screening restart strategies to ensure impacts on the population's health are minimised. Our results show that the best strategy using current endoscopy capacity would involve postponing screening for everyone to reduce delays for each cohort equally. Other international research concluded that screening restart strategies considering screening catch-up could minimise the negative impact of screening disruptions compared with no catch-up strategies (de Jonge et al., 2021). Similar results were observed in our modelling also suggesting that temporarily increasing the FIT threshold could be considered if some additional endoscopy capacity is available. In the US, where the FIT screening is mainly opportunistic, a modelling study concluded that a strategy of increasing FIT uptake from 15% to 22% could be an effective approach to improve clinical outcomes (Issaka et al., 2021).

Our study is the first modelling study assessing the impact of COVID-19 specifically on CRC screening, based on actual data, and including multiple CRC outcomes. Maringe et al. (2020) estimated that delays in CRC screening and diagnosis in England could result in 1445 to 1563 additional deaths over the next five years (Maringe et al., 2020). Loveday et al. (2021) concluded that if the recommended two-week diagnosis for symptomatic CRC patients is extended to two months, this will result in 653 additional deaths (Loveday et al., 2021). Our model predicts that within five years 370 CRC deaths could be attributed to the screening pause alone, going up to 700 additional deaths within ten years. The results are generally comparable with those reported for other countries (0.1–0.3% increase over 30–40 years of follow-up without screening catch-up) (de Jonge et al., 2021).

The study had several limitations. The aim of the project was specifically to assess the screening-related impact of COVID-19, so any impact of delay to treatment or symptomatic diagnosis was not incorporated into the model. The subgroup analysis was based on the assumption that screening pauses affected all of the subgroups proportionately, given a lack of data to suggest otherwise, but this may not have been the case. To decrease the computational burden and heterogeneity in predictions of small effects, we modelled the return-to-screening scenarios based upon the 12-month screening pause only, although we do not expect conclusions to differ with shorter pauses.

5. Conclusion

The CRC screening pause that occurred due to COVID-19 is predicted to result in a small increase in CRC cases and CRC deaths in the next 10 years, with deaths expected to peak in 2023. Longer CRC screening pauses would be expected to result in greater additional CRC incidence and mortality. Selection of the optimal strategy for screening restart depends on available endoscopy capacity. If no additional capacity is available, postponing screening for everyone is likely to be the optimal strategy for minimising deaths and maximising cost-effectiveness.

Disclosure of funding and conflicts of interest

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CRedit authorship contribution statement

Olena Mandrik: Conceptualization, Methodology, Software, Investigation, Data curation, Funding acquisition, Writing – original draft. **James Chilcott:** Conceptualization, Methodology, Writing – review & editing. **Chloe Thomas:** Conceptualization, Methodology, Data curation, Validation, Funding acquisition, Writing – review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpmed.2022.107076>.

References

- Adult Cancer Survival Tables, 2022. One and Five Year Net Survival for Adults Diagnosed between 2013 and 2017. Office for National Statistics, England. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsd> iagnosed. accessed 20th October 2019.
- Bowel Cancer Incidence Statistics, 2022. Cancer Research UK. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer/incidence#heading-One>. accessed 20th June 2019.
- Changes in all-Cause and COVID-19 Mortality over Time, 2020. England and Wales: Deaths Occurring between 28 December 2019 and 4 September 2020, 18 December 2020 ed. Office for National Statistics.
- Gidwani, R., Russell, L.B., 2020. Estimating transition probabilities from published evidence: a tutorial for decision modelers. *Pharmacoeconomics* 38 (11), 1153–1164. <https://doi.org/10.1007/s40273-020-00937-z>.
- Health Survey for England, 2014. NHS Digital; 2014. Available from: https://data.gov.uk/dataset/health_survey_for_england.
- Issaka, R.B., Taylor, P., Baxi, A., et al., 2021. Model-based estimation of colorectal cancer screening and outcomes during the COVID-19 pandemic. *JAMA Netw. Open* 4 (4), e216454. <https://doi.org/10.1001/jamanetworkopen.2021.6454> [published Online First: 2021/04/13].
- de Jonge, L., Worthington, J., van Wifferen, F., et al., 2021. Impact of the COVID-19 pandemic on faecal immunochemical test-based colorectal cancer screening programmes in Australia, Canada, and the Netherlands: a comparative modelling study. *Lancet Gastroenterol. Hepatol.* 6 (4), 304–314. [https://doi.org/10.1016/S2468-1253\(21\)00003-0](https://doi.org/10.1016/S2468-1253(21)00003-0) [published Online First: 2021/02/07].
- Kortlever, T.L., de Jonge, L., Wisse, P.H.A., et al., 2021. The national FIT-based colorectal cancer screening program in the Netherlands during the COVID-19 pandemic. *Prev. Med.* 151, 106643 <https://doi.org/10.1016/j.jpmed.2021.106643> [published Online First: 2021/07/05].
- Logan, R.F., Patnick, J., Nickerson, C., et al., 2012. Outcomes of the bowel cancer screening Programme (BCSP) in England after the first 1 million tests. *Gut* 61 (10), 1439–1446. <https://doi.org/10.1136/gutjnl-2011-300843> [published Online First: 2011/12/14].
- Loveday, C., Sud, A., Jones, M.E., et al., 2021. Prioritisation by FIT to mitigate the impact of delays in the 2-week wait colorectal cancer referral pathway during the COVID-19 pandemic: a UK modelling study. *Gut* 70 (6), 1053–1060. <https://doi.org/10.1136/gutjnl-2020-321650> [published Online First: 2020/08/29].
- Mandrik, O., Thomas, C., Strong, M., Whyte, S., 2021. Calibration and Validation of the Microsimulation Model in Cancer of the Bowel (MiMiC-Bowel), an Individual Patient Simulation Model for Investigation of the Cost-Effectiveness of Personalised Screening and Surveillance Strategies. SCHARR HEDS Discussion Papers. School of Health and Related Research, University of Sheffield, Sheffield.
- Mandrik, O., Thomas, C., Whyte, S., Chilcott, J., 2022. Calibrating natural history of Cancer models in the presence of data incompatibility: problems and solutions. *Pharmacoeconomics* 40 (4), 359–366. <https://doi.org/10.1007/s40273-021-01125-3>.

- Maringe, C., Spicer, J., Morris, M., et al., 2020. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol.* 21 (8), 1023–1034. [https://doi.org/10.1016/s1470-2045\(20\)30388-0](https://doi.org/10.1016/s1470-2045(20)30388-0) [published Online First: 2020/07/24].
- Mazidimoradi, A., Tiznobaik, A., Salehiniya, H., 2021. Impact of the COVID-19 pandemic on colorectal cancer screening: a systematic review. *J. Gastrointest. Cancer* 1–15. <https://doi.org/10.1007/s12029-021-00679-x> [published Online First: 2021/08/19].
- Moss, S., Mathews, C., Day, T.J., et al., 2017. Increased uptake and improved outcomes of bowel cancer screening with a faecal immunochemical test: results from a pilot study within the national screening programme in England. *Gut* 66 (9), 1631–1644. <https://doi.org/10.1136/gutjnl-2015-310691> [published Online First: 2016/06/09].
- National Schedule of Reference Costs 2017/18, 2018. NHS Improvement. Available from: <https://improvement.nhs.uk/resources/reference-costs/>. accessed 20th March 2019.
- Patel, S., Issaka, R.B., Chen, E., et al., 2021. Colorectal cancer screening and COVID-19. *Am. J. Gastroenterol.* 116 (2), 433–434. <https://doi.org/10.14309/ajg.0000000000000970> [published Online First: 2020/10/11].
- Populations by Sex, Age Group And Index of Multiple Deprivation (IMD) Quintile, England, 2001 to 2017, <https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/adhocs/009283populationsbysexagegroupandimdquintileengland2001to2017>, 2018. Office for National Statistics.
- Richards, M., 2019. Report of the independent review of adult screening programmes in England. In: Appendix D: NHS Bowel Cancer Screening Programme. NHS England. Available from: <https://www.england.nhs.uk/wp-content/uploads/2019/02/report-of-the-independent-review-of-adult-screening-programme-in-england.pdf>. accessed 6th January 2020.
- Sud, A., Torr, B., Jones, M.E., et al., 2020a. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. *Lancet Oncol.* 21 (8), 1035–1044. [https://doi.org/10.1016/S1470-2045\(20\)30392-2](https://doi.org/10.1016/S1470-2045(20)30392-2).
- Sud, A., Jones, M., Broggio, J., et al., 2020b. Quantifying and Mitigating the Impact of the COVID-19 Pandemic on Outcomes in Colorectal Cancer. *The Lancet Gastroenterology*, 2020. H. Resuming bowel cancer screening post-COVID-19. *Lancet Gastroenterol. Hepatol.* 5 (8), 711. [https://doi.org/10.1016/s2468-1253\(20\)30200-4](https://doi.org/10.1016/s2468-1253(20)30200-4) [published Online First: 2020/07/01].
- Thomas, C., Mandrik, O., Whyte, S., 2020. Development of the Microsimulation Model in Cancer of the Bowel (MIMIC-Bowel), an Individual Patient Simulation Model for Investigation of the Cost-effectiveness of Personalised Screening and Surveillance Strategies.
- Thomas, C., Mandrik, O., Saunders, C.L., et al., 2021a. The costs and benefits of risk stratification for colorectal cancer screening based on phenotypic and genetic risk: a health economic analysis. *Cancer Prev. Res. (Phila.)* 14 (8), 811–822. <https://doi.org/10.1158/1940-6207.Capr-20-0620> [published Online First: 2021/05/28].
- Thomas, C., Mandrik, O., Whyte, S., et al., 2021b. Should colorectal cancer screening start at different ages for men and women? Cost-effectiveness analysis for a resource-constrained service. *Cancer Rep. (Hoboken)*, e1344. <https://doi.org/10.1002/cnr2.1344> [published Online First: 2021/02/04].
- Unit Costs of Health and Social Care 2018, 2018. Personal Social Services Research Unit [Available from: <https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/>. accessed 20th March 2019.
- Whyte, S., Thomas, C., Kearns, B., et al., 2017. Optimising Bowel Cancer Screening Phase 1: Optimising the Cost Effectiveness of Repeated FIT Screening and Screening Strategies Combining Bowel Scope and FIT Screening: SchARR. University of Sheffield. Available from: https://www.sheffield.ac.uk/scharr/sections/heds/discussion-papers/18_04-1.782806.
- Whyte, S., Thomas, C., Chilcott, J., et al., 2021. Optimizing the design of a repeated fecal immunochemical test bowel cancer screening programme with a limited endoscopy capacity from a health economic perspective. *Value Health.* <https://doi.org/10.1016/j.jval.2021.10.002>.