Impact of screening participation on modelled mortality benefits of a multi-cancer early detection test by socioeconomic group in England

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ABSTRACT

Background Cancer burden is higher and cancer screening participation is lower among individuals living in more socioeconomically deprived areas of England, contributing to worse health outcomes and shorter life expectancy. Owing to higher multi-cancer early detection (MCED) test sensitivity for poor-prognosis cancers and greater cancer burden in groups experiencing greater deprivation, MCED screening programmes may have greater relative benefits in these groups. We modelled potential differential benefits of MCED screening between deprivation groups in England at different levels of screening participation.

Methods We applied the interception multi-cancer screening model to cancer incidence and survival data made available by the National Cancer Registration and Analysis Service in England to estimate reductions in late-stage diagnoses and cancer mortality from an MCED screening programme by deprivation group across 24 cancer types. We assessed the impact of varying the proportion of people who participated in annual screening in each deprivation group on these estimates.

Results The modelled benefits of an MCED screening programme were substantial: reductions in late-stage diagnoses were 160 and 274 per 100 000 persons in the least and most deprived groups, respectively. Reductions in cancer mortality were 60 and 99 per 100 000 persons in the least and most deprived groups, respectively. Benefits were greatest in the most deprived group at every participation level and were attenuated with lower screening participation.

Conclusions For the greatest possible population benefit and to decrease health inequalities, an MCED implementation strategy should focus on enhancing equitable, informed participation, enabling equal participation across all socioeconomic deprivation groups.

Trial registration number NCT05611632.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Multi-cancer early detection (MCED)-based screening has the potential to substantially reduce late-stage cancer diagnosis and mortality if it is introduced at a population level; however, little is known about the potential impact of socioeconomic group and participation levels on these benefits.

WHAT THIS STUDY ADDS

⇒ By applying an interception model to estimate the benefits of multi-cancer screening in terms of reductions in late-stage diagnoses and cancer mortality, we found that more deprived groups stand to benefit the most from MCED-based screening: with 100% participation, there were 160 and 274 fewer late-stage cancer diagnoses per 100 000 persons in the least and most deprived groups, respectively, with reductions in cancer mortality of 60 and 99 per 100 000 persons in the least and most deprived groups, respectively.

⇒ With participation reflecting that of the current UK national cancer screening programmes (approximately 60% and 80% in the most and least deprived groups, respectively), reductions in late-stage diagnoses were greater in the most deprived group compared with the least deprived group; MCED-based screening is therefore unlikely to exacerbate existing health inequalities.

⇒ The extent of the reduction in late-stage cancer diagnosis and subsequent cancer mortality with MCED screening in more deprived groups relative to less deprived groups varied by cancer type and was greatest in lung, head and neck, and colon/rectum cancers.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ By potentially enhancing informed uptake among those in more deprived groups, MCED screening may present an opportunity to reduce the deprivation gap associated with late-stage cancer diagnoses and outcomes.

INTRODUCTION

In England, the difference in life expectancy between those living in the most and least deprived areas is approximately 8 years for women and 10 years for men.[1] Cancer burden is one contributing factor, with an estimated 16 800 extra cancer cases each year attributable to deprivation, and a 16–19% gap in the incidence rate between groups experiencing the most and least deprivation.[2] Some cancers, including bladder, breast, colon, rectal, ovarian and prostate cancers and melanoma, are diagnosed at a later stage in groups with higher deprivation.[3]

The National Health Service (NHS) delivers nationally organised and quality-assured population screening programmes in the UK for breast, cervical and bowel cancers.[4] While screening (along with all other healthcare

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provisions) is free at the point of care, paid for by general taxation and National Insurance contributions, screening participation is lower in groups experiencing greater deprivation,[5–7] potentially due to psychosocial, logistic and economic barriers to participation.[8–11] This association between deprivation and screening participation increases health inequalities and reduces the overall impact of population screening. Furthermore, previous research has demonstrated greater frequencies of high-mortality cancer types among individuals living in more deprived communities.[12 13] These factors contribute to an increased cancer burden in groups experiencing the greatest deprivation: this must be addressed both to substantially improve cancer outcomes in general, and particularly to ensure existing inequalities are minimised rather than widened.

The NHS Long Term Plan for England[14] set a target of 75% of all cancers to be diagnosed at stage I or II, with a current target date of 2028, as early-stage cancers are generally easier to treat and manage than later stage cancers.[14] However, the proportion of cancers diagnosed early remains approximately 55%.[15] Over the last 20 years, NHS cancer strategies and approaches have also focused on addressing health inequalities,[16–19] yet the deprivation gaps in cancer incidence and mortality remain.[20] New approaches to screening and diagnosis are needed, both to contribute substantially to attaining an overall reduction in late-stage cancer diagnoses, and to reduce inequalities.

Blood-based multi-cancer early detection (MCED) tests are designed to simultaneously detect multiple cancer types through a single blood draw. An MCED-based screening programme could be used alongside current single-cancer screening modalities,[21–23] and may substantially increase the number of cancers screened for, while minimising the undue burden of multiple additional appointments on individuals and the NHS. One blood-based MCED test (Galleri (GRAIL, LLC, California, USA)) uses the methylation patterns of cell-free DNA (cfDNA) to detect a shared cancer signal across more than 50 cancer types and predict the tissue type or organ where the cancer signal originated (cancer signal origin, CSO).[24 25] The clinical utility of this previously validated MCED test[26] is currently being assessed in the prospective, randomised, controlled NHS-Galleri trial (NCT05611632).[27] Over 140 000 participants have been randomised and are now attending for their third annual blood sample. If successful in clinical trials, MCED tests may present an opportunity to reduce both the overall late-stage cancer burden and the greater relative cancer burden among more deprived individuals.[26]

In this modelling study, we estimated the potential differential reductions in late-stage cancer incidence and mortality with MCED screening in groups stratified by an area-based marker of relative deprivation (the Index of Multiple Deprivation (IMD)),[28] and the impact of screening participation on these benefits. To achieve this, we used a previously published multi-cancer screening model (interception model)[29 30] that incorporates MCED test sensitivity estimates based on a case–control study,[26] varying the proportion of people within each IMD group who participated in annual screening.

METHODS
Data
This work uses data provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Cancer Registration and Analysis Service (NCRAS), which is part of NHS England.[31 32]

NCRAS provided incidence and survival data for 24 cancer types and one 'other' category, as defined in the International Classification of Diseases for Oncology, Third Edition, First Revision (online supplemental table S1),[33] based on individuals aged 50–79 years who were diagnosed with cancer between 2013 and 2018. The age range of those included in this study reflects the inclusion criterion for enrolment in the NHS-Galleri trial (NCT05611632)[27]: 50–77 years of age at enrolment, plus 2 years to allow for ageing of the trial population during the screening period of the trial.

We calculated crude incidence rates for each cancer type by stage, 5-year age band and IMD quintile (online supplemental table S2). The IMD is a set of relative measures of deprivation for small areas (lower layer super output areas) across England, based on indicators across seven different domains of deprivation: (1) income, (2) employment, (3) education, skills, and training, (4) health deprivation and disability, (5) crime, (6) barriers to housing and services and (7) living environment deprivation.[28] For the purposes of this model, we considered lymphoid leukaemia, myeloid neoplasm and plasma cell neoplasm unstageable. Incidence rates were calculated per 100 000 persons for all cancers apart from ovary, cervix, uterus and prostate cancers. For these sex-specific cancers, person rates were calculated by adjusting the rate according to the proportion of the relevant sex in the IMD group.

For each 5-year age band, 5-year net survival was calculated using the Pohar Perme estimator and a period approach.[34] Some of the numbers were small, so many of the calculations were unreliable when the data were split by both stage and IMD. We therefore split survival by stage alone (online supplemental table S3a) and provided the number of unreliable survival estimates in online supplemental table S3b. We also provided 5-year net survival by IMD to demonstrate the extent of the differences between groups (online supplemental figure S1). The analysis was censored on 5 January 2019, providing a minimum of 1 year of follow-up for all patients.

Interception model
The use of the interception model to estimate stage shift and associated potential mortality benefits is described in detail by Hubbell and colleagues[29]; it was modified in a subsequent publication to estimate potential benefits in England.[30] The code was written in R,[35] and data can be made available on request.

Briefly, the interception model is a state transition model that estimates the impact of an MCED-based screening programme when added to usual care, which refers to the standard screening, primary care referral, diagnostic work-up and treatment practices resulting in the incidence-by-stage and survival-by-stage data observed during the study period in England.[29] Starting from the number of incident cancers in usual care, the number of cancers that would have been present but not clinically diagnosed at earlier stages in the preceding years was calculated using dwell time estimates specific to each cancer type and stage, using an exponential distribution to model variation between individual cancers of the same type. From this, the number of cancers intercepted at each stage was calculated based on cancer type-specific and stage-specific sensitivity of an MCED test (Galleri), which were estimated in a case–control study[26] and adjusted using isotonic regression so that test sensitivity did not decrease by stage (online supplemental table S4). Throughout this report we use the generic term 'MCED screening' to reflect the fact that, while the results in this paper were calculated based on Galleri test sensitivity estimates (online supplemental table

S4),[26] different sensitivity estimates could be used in this model to broaden applicability to MCED tests in general.

The interception (detection) of a detectable cancer depends on the interval between MCED tests relative to the length of time the cancer spends in each stage (dwell time), such that a greater proportion of cancers are detected with shorter intervals between screening rounds. Naturally, if a person does not participate in screening, there is no opportunity for the cancer to be detected via MCED screening. The interception model can be used to estimate performance in both prevalent and incident screening rounds; however, here, we report results for an incident screening round in an annual screening programme, as the prevalent round is more susceptible to differences in cancer dwell time assumptions. We made the simplifying assumption that diagnostic resolution occurred shortly after screen detection. We did not explicitly model any complexity in the diagnostic pathway, for example, diagnostic odyssey following incorrect prediction of CSO(s), or missed cancers following insufficient investigations of single CSOs.

We extended the model by stratifying the incident population by IMD group and varying the proportion of individuals who participated in annual screening rounds. The model assumed everyone participated in the prevalent screening round. The proportion of those participating in incident screening rounds reflected the likelihood of participation for each individual within the group. For example, where participation was 60%, each person within the group had a 60% likelihood of attending for an MCED test in each screening round, rather than 60% of people in the group participating in every round of screening. This pattern of sporadic participation better reflects real-world patterns of participation, although some people never participate in screening.[5]

We assumed a survival HR of 3 and a fast cancer dwell time for each cancer type and stage (online supplemental table S5), with an exponential distribution to capture variation, as described previously.[29] [30] The survival HR reflects an assumption that cfDNA-detectable (cfDNA$^+$) tumours carry three times the risk of cancer death than cfDNA-non-detectable (cfDNA$^-$) tumours, based on recent findings.[36] Cancer survival by stage must match observed estimates, therefore, we assumed a reduced mortality for cfDNA$^-$ tumours to balance out the increased hazard for cfDNA$^+$ tumours. We did not modify survival by any deprivation index. Fast dwell times correspond to more rapid stage progression, increasing the likelihood of progression between screening rounds, with fewer cancers detected at earlier stages. These parameters reflect plausible scenarios that are adequate for this study. We produced a single set of estimates, in contrast to previous research that presented several scenarios,[29] to focus on the relative differences between groups and different levels of participation, rather than absolute values. We defined late-stage reduction as any shift from stage III or IV to stage I or II.

We modelled participation scenarios from 10% to 100%. Modelling 100% participation was required to fully understand the differential benefits between IMD groups without the confounding effect of participation. In practice, 100% participation is unrealistic, particularly given that there are people for whom MCED cancer screening would not be medically appropriate (eg, those on an end-of-life pathway). To inform possible participation levels, we extracted screening coverage statistics for England from the Cancer Services profile on Fingertips[37] for each of the screening programmes currently free at the point of care in the NHS (breast, cervix and bowel) by IMD group (with scores based on the 2019 index),[38] as shown in online supplemental table S6.

RESULTS

NCRAS data for England demonstrated an average annual cancer incidence of 1214 per 100 000 persons in 50–79 year-olds in the period 2013–2018. Of these cancers, 1164 per 100 000 were stageable and 973 per 100 000 were staged, with 450 per 100 000 diagnosed at a late stage (III or IV).

Cancer burden by IMD

Figure 1 shows the incidence rate by cancer stage by IMD for all cancers combined and 21 individual stageable cancer types diagnosed in adults aged 50–79 years between 2013 and 2018 in England (online supplemental table S2 shows the data underpinning figure 1, and online supplemental figure S2 shows incidence rates for the three unstageable cancer types by IMD). For all cancers combined, the most deprived IMD group had the greatest stage IV cancer incidence rate. This appears to be driven by several cancer types, including anus, bladder, cervix, colon/rectum, gallbladder, head and neck, kidney, liver/bile duct, lung, oesophagus, pancreas, stomach and urothelial tract cancers. For almost all cancer types, the least deprived group had the lowest incidence rates of stage IV disease. For melanoma, lymphoma and prostate cancers, the stage IV incidence rate was slightly higher in the least compared with the most deprived group, however, the difference was very small.

Late-stage cancer incidence and mortality benefits of MCED screening by IMD

We used a 100% participation model to isolate the impact of IMD on the benefits of MCED screening. The number of cancers found via usual care and MCED screening in an incident screening round ranged from 1107 to 1348 per 100 000 persons in the least and most deprived groups, respectively (table 1). Late-stage incidence was substantially reduced in all deprivation groups when MCED screening was added to usual care, but the benefit was greater in more deprived groups, with reductions in late-stage incidence ranging from 160 to 274 per 100 000 persons in the least and most deprived groups, respectively (table 1). The most deprived group still had the greatest number of late-stage diagnoses when MCED screening was added to usual care (370 per 100 000 persons compared with 266 per 100 000 persons in the least deprived group). Cancer mortality was consistently higher in more deprived groups under usual care, owing to the higher initial cancer burden. When MCED screening was added to usual care, cancer mortality was reduced by 60 and 99 per 100 000 persons in the least and most deprived groups, respectively (table 2).

Modelled benefits of MCED screening by cancer type

The extent of the reduction in late-stage cancer diagnosis and subsequent cancer mortality with MCED screening in more deprived groups relative to less deprived groups varied by cancer type (table 3). This reflects patterns of observed cancer incidence and late-stage burden, as well as differential MCED test sensitivity between cancer types and stages (online supplemental table S4). Substantial differences between IMD groups were noted for lung cancer (incidence rate, 277 vs 93 per 100 000 persons in the most vs least deprived groups, respectively, with corresponding reductions in late-stage diagnoses of 102 vs 34 per 100 000 persons); head and neck cancer (incidence rate, 65 vs 30 per 100 000 persons; reduction in late-stage diagnoses, 30 vs 13 per 100 000 persons); and colon/rectum cancer (incidence rate, 137 vs 123 per 100 000 persons; reduction in late-stage diagnoses, 48 vs 41 per 100 000 persons; table 3). There was
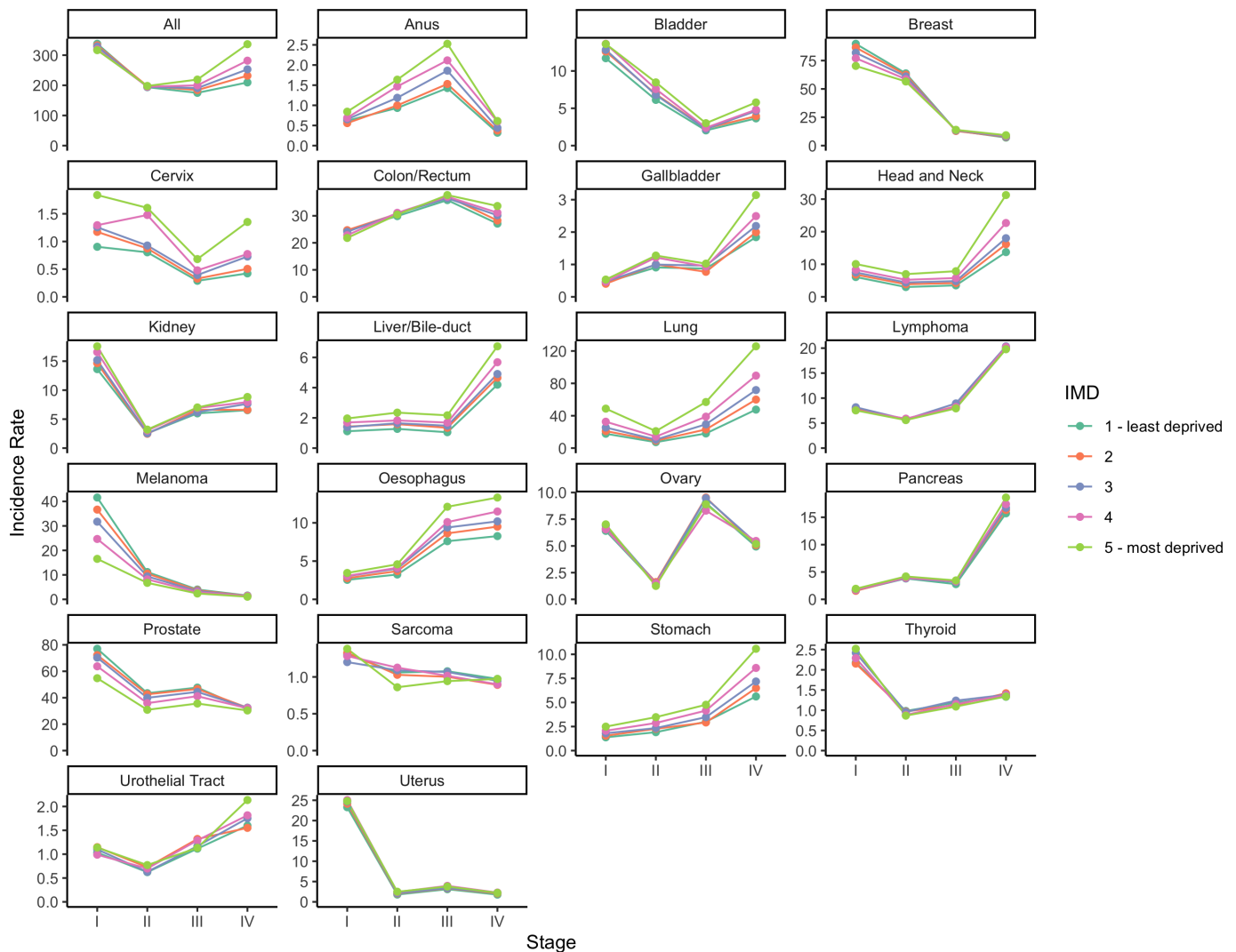
Figure 1 Crude incidence rates by cancer stage by Index of Multiple Deprivation (IMD) for all cancers combined and 21 stageable cancer types diagnosed between 2013 and 2018 in adults aged 50–79 years in England. Definitions for the cancer types are shown in online supplemental table S1.

also a steep gradient in cancers shifted earlier between the least and most deprived groups for liver/bile duct, oesophagus and stomach cancers. However, as these cancers are less prevalent, they contributed less to the overall result.

Assuming 100% participation, MCED screening did not appear to increase health inequalities. There were some cancer types for which the reduction in late-stage cancer diagnosis and subsequent cancer mortality were equivalent between least and most deprived groups, including lymphoma, gallbladder and breast cancers. At realistic participation levels (online supplemental table S6) reflecting socioeconomic gradients in participation, it is likely there would be greater benefit to the least deprived groups for these cancer types. For melanoma, thyroid and urothelial tract cancers, there was no benefit to either the

Table 1 Modelled late-stage cancer incidence reduction by Index of Multiple Deprivation (IMD) group in an incident round of multi-cancer early detection (MCED) screening

	IMD group				
	1 (Least deprived)	2	3	4	5 (Most deprived)
Found via usual care and MCED (%)	1107 (100)	1144 (100)	1178 (100)	1238 (100)	1348 (100)
Found via usual care (%)	809 (73)	819 (72)	827 (70)	845 (68)	879 (65)
MCED detected (%)	298 (27)	325 (28)	351 (30)	393 (32)	469 (35)
Late-stage diagnosis with usual care	427 (39)	460 (40)	496 (42)	551 (45)	645 (48)
Late-stage diagnosis with MCED (%)	266 (24)	283 (25)	301 (26)	328 (26)	370 (27)
Reduction in late-stage diagnosis with MCED (%)	160 (38)	178 (39)	195 (39)	223 (40)	274 (43)

MCED screening participation was assumed to be 100%. MCED test sensitivity estimates were from a case–control study (online supplemental table S4).[26] Results are presented as the rate per 100 000 persons.

Table 2 Modelled cancer mortality rate reductions by Index of Multiple Deprivation (IMD) group in an incident round of multi-cancer early detection (MCED) screening

	IMD group				
	1 (Least deprived)	2	3	4	5 (Most deprived)
Cancer mortality rate with usual care	358	394	430	489	594
Cancer mortality rate with MCED	299	329	358	407	495
Reduction in cancer mortality with MCED (%)	60 (17)	66 (17)	72 (17)	81 (17)	99 (17)

Participation was assumed to be 100%. MCED test sensitivity estimates were from a case–control study (online supplemental table S4).[26] Results are presented as the rate per 100 000 persons.

most or least deprived group. This is due to the low sensitivity of the MCED test for these cancer types in the early stages (online supplemental table S4), and the relatively low prevalence of thyroid and urothelial tract cancers. The patterns of reductions in late-stage diagnosis were generally reflected in the cancer mortality rate reductions with MCED screening.

Effects of screening participation on the benefits of MCED screening

Figure 2 shows the reductions in late-stage diagnoses and cancer mortality rates due to MCED screening for each IMD group at each participation level. As expected, the benefits of screening were attenuated by non-participation. At each participation level, the percentage reduction in late-stage diagnoses with MCED screening was greater in more versus less deprived groups, with the greatest benefit to the most deprived group (figure 2A). The magnitude of this benefit was greater with higher rates of participation. With participation rates reflecting approximately those of the current England national cancer screening programmes

(online supplemental table S6), 60% and 80% in the most and least deprived groups, respectively, reductions in late-stage diagnoses were greater in the most deprived group compared with the least deprived group. This was reflected in the percentage reduction in cancer mortality rates with MCED screening (figure 2B). These results indicate a greater benefit from MCED screening to more deprived groups under more realistic participation-level assumptions. The data presented in these figures are provided in online supplemental tables S7 and S8.

DISCUSSION

Our work demonstrates that MCED screening, with sensitivity as estimated in a case–control study (online supplemental table S4),[26] has the potential to reduce overall late-stage cancer diagnoses and subsequent cancer mortality, and to partially address deprivation-associated inequity. To our knowledge, this is the first study to model the potential differential benefits of a cancer screening intervention by IMD group.

Table 3 Modelled cancer incidence rates, reductions in late-stage diagnoses and reductions in cancer mortality rates with multi-cancer early detection (MCED) screening for 21 stageable cancer types

	Incidence rate		Reduction in late-stage diagnosis with MCED		Reduction in cancer mortality rate with MCED	
Cancer type	IMD 1	IMD 5	IMD 1	IMD 5	IMD 1	IMD 5
Anus	4	6	1	2	0	1
Bladder	25	36	1	2	1	2
Breast	185	163	7	8	3	4
Cervix	3	8	1	2	1	1
Colon/rectum	123	137	41	48	21	26
Gallbladder	5	9	1	1	0	0
Head and neck	30	65	13	30	5	10
Kidney	33	43	1	2	1	1
Liver/bile duct	17	30	7	13	3	5
Lung	93	277	34	102	10	29
Lymphoma	50	50	14	14	2	2
Melanoma	65	31	0	0	0	0
Oesophagus	24	39	7	12	1	2
Ovary	25	27	10	10	6	6
Pancreas	29	36	11	14	2	2
Prostate	209	169	3	2	1	1
Sarcoma	9	9	2	2	1	1
Stomach	14	26	3	5	1	1
Thyroid	8	9	0	0	0	0
Urothelial tract	5	7	0	0	0	0
Uterus	32	37	1	1	1	1

All numbers are presented to the nearest whole number per 100 000 persons. The 'other' cancer category is not presented here; totals therefore do not necessarily sum to the results for all cancers combined. MCED test sensitivity estimates were from a case–control study (online supplemental table S4).[26]
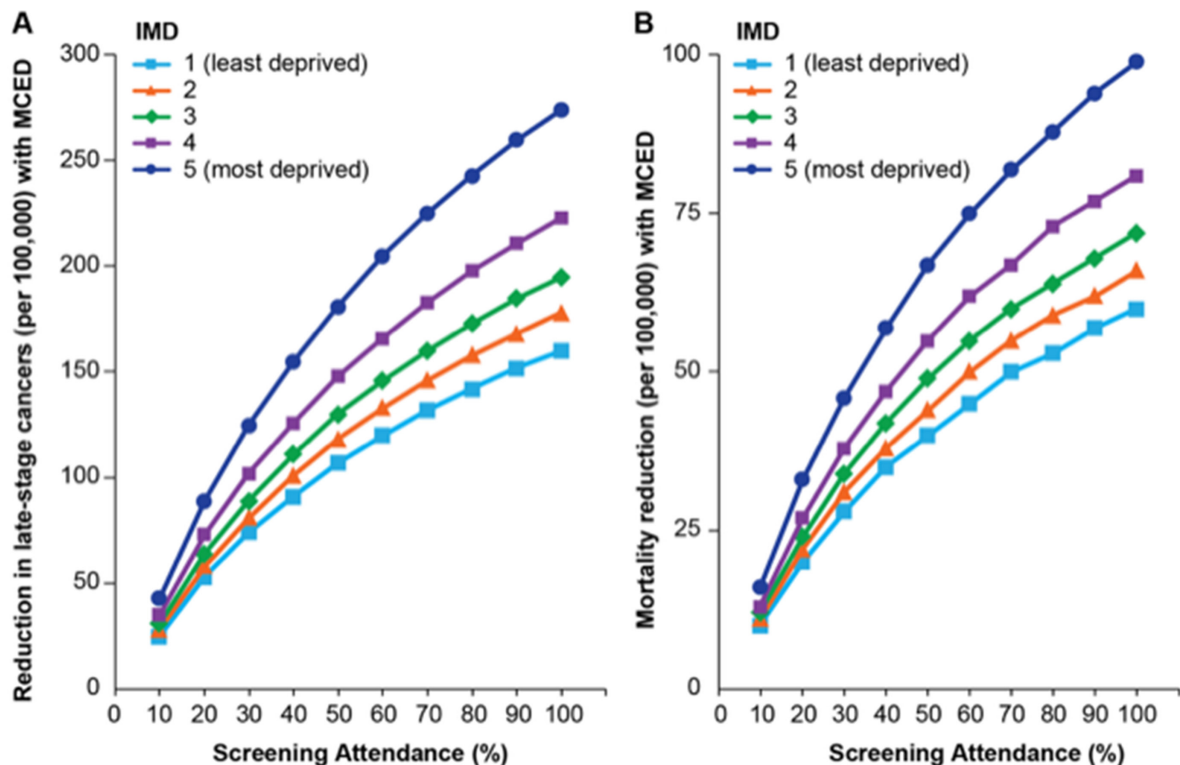IMD, Index of Multiple Deprivation (where 1 is the least and 5 the most deprived group).

Figure 2 Reductions in late-stage cancer diagnoses (A) and cancer mortality (B) per 100 000 persons available to be screened, by screening participation rate and Index of Multiple Deprivation (IMD) group. Multi-cancer early detection (MCED) test sensitivity estimates were from a case–control study (online supplemental table S4).[26]

The observation that there is lower screening participation among individuals experiencing greater deprivation has been well replicated[5–7] and likely contributes to health inequalities. Here, we demonstrate that, owing to the increased late-stage cancer diagnoses and cancer mortality burden in more deprived groups, and the performance of the MCED test, more deprived groups stand to benefit the most from an MCED-based screening programme. The differential benefits of MCED screening alone, even in the artificial 100% participation scenario, are not enough to eliminate the differences in late-stage diagnosis and cancer mortality rates between different IMD groups; however, they may contribute to reducing them alongside other approaches to reduce health inequalities at the national and system levels, such as NHS Core20PLUS5.[19]

It is clear that to achieve the greatest population impact from an MCED-based screening programme, public health policy should focus on improving equitable and informed participation. Our modelling of the benefits of MCED screening by cancer type demonstrated that in a 100% participation scenario (used to isolate the impact of IMD, rather than as an expectation for real-world screening participation), there were no cancer types for which the benefit to the least deprived group was greater than the most deprived group. Moreover, we identified a subset of cancers for which there were substantially greater predicted benefits of MCED screening to the most deprived group.

Invariably, with lower participation, the modelled benefits of MCED screening were attenuated. Based on current screening programme participation (online supplemental table S6), participation in the most deprived group (approximately 60%) would be substantially lower than the least deprived group (approximately 80%). We demonstrated that, despite this inequality in real-world screening uptake in England, an MCED population screening intervention is unlikely to exacerbate health inequalities overall. However, for cancer types in which IMD groups benefit equally

from MCED screening, this may still be the case if participation is lower in the most deprived group. Optimal informed participation, particularly among individuals living in areas of higher deprivation, must be supported to decrease the overall burden of cancer mortality and to ensure the deprivation gap is reduced.

This modelling study has limitations. In a previous study, some of the assumptions that underpin the interception model were discussed in detail,[29] and results for a range of plausible scenarios were generated to estimate their impact on late-stage cancer incidence and mortality outcomes. Nevertheless, there remains uncertainty regarding these assumptions; we hope that some of this can be resolved using the results of the NHS-Galleri trial, and the growing evidence base for the mechanisms and clinical significance of cfDNA shedding. In this study, we chose to model a single set of conservative dwell times and cfDNA-based survival differential assumptions, enabling us to focus on the relative late-stage cancer incidence and mortality-related benefits of MCED testing to each IMD group, and how participation may impact these benefits. The model structure and assumptions should be reviewed and updated in future to reflect findings from the NHS-Galleri trial and insights into tumour biology, especially regarding cfDNA, as these become available. The NHS-Galleri trial design precludes understanding differential uptake by sociodemographic factors[27]; participation in blood-based multi-cancer screening programmes can only be understood following further roll-out of a screening programme. Uptake in MCED screening programmes, and the factors that affect uptake, are currently unknown and unknowable, because no such programmes have yet been implemented. Uptake and participation will depend on the approach to implementation,[39] and whether MCED screening is made as accessible as possible to a wide range of groups. This is likely to depend on the choice of screening settings and locations,[40] communications about screening,[40 41] alignment and coordination with other screening programmes[42] and

ensuring general practitioner (GP) understanding of and buy-in to the programme,[40 41] among other factors. Blood-based MCED tests present the opportunity for more innovative service delivery models, which may improve access for people in more socioeconomically deprived groups relative to screening programmes based on more complex and less portable equipment, such as imaging or endoscopy. The size of the potential deprivation gradient in participation could differ substantially in either direction from that of established cancer screening programmes. In addition, although the NHS-Galleri trial is not statistically powered for subgroup analyses, the model could be calibrated with trial data to examine the potential benefits of MCED screening in groups stratified by factors such as deprivation.

A key strength of this study is the national population coverage of the NCRAS dataset, which enables full characterisation of the population, including by metrics such as IMD. Research has shown that, although IMD is widely used and accepted, concordance between area-level (eg, IMD) and individual measures of deprivation may be limited.[43] This suggests that further research using person-level deprivation metrics is needed to better understand the impact of MCED screening on inequalities, and to better describe variations in participation. Further research could include other factors known to be associated with inequalities in screening, such as ethnicity,[44–47] and adopt an intersectional approach to understand how characteristics interact.

The data used in this study were available at a high level of granularity, enabling analyses by cancer type and stage; however, net survival analysis in a population of this size yielded some unreliable estimates due to small numbers (online supplemental table S3b), particularly for lower prevalence cancers. Mortality reductions for some cancer types should therefore be interpreted with caution. Owing to the small numbers issue, it was also not possible to calculate survival by stage by IMD. However, survival differences between IMD groups by cancer type were small (online supplemental figure S1). Using aggregate survival by stage for all IMD groups is therefore unlikely to substantially influence results; however, it is possible that aggregate survival estimates may mask some important effects of cancer stage. Timely access to guideline-recommended treatment is critical to enable patients with cancer to have the best chance of survival. Research on socioeconomic inequalities in access to treatment is less clear-cut than for inequalities in stage at diagnosis, with some indicating no difference in access to treatment by deprivation,[48] and others suggesting worse access to treatment among individuals experiencing higher deprivation.[49 50] As such, the relationship between stage shift and mortality benefit in each IMD group is not likely to be as straightforward as estimated in our model. This reiterates the importance of measuring real-world outcomes to ensure all socioeconomic groups are benefiting from interventions as anticipated.

There are many potential reasons why individuals experiencing greater deprivation may be less likely to participate in screening,[9] which can be categorised using an established framework of health-related behaviour resulting from individuals' capabilities, opportunities and motivations (COM-B).[51] Capability-based reasons include lack of confidence in interacting with healthcare systems, difficulty travelling to appointments, and competing life stressors[9–11]; opportunity-based reasons include more logistic and economic barriers to attending screening appointments,[8 10 11] as well as community or primary care endorsement; and motivation-based reasons include greater fear or dislike of test procedures, and more pessimistic beliefs about cancer outcomes.[9]

Research on public attitudes towards genetic screening in general is limited, especially in the UK; however, one study suggested that attitudes were generally positive.[52] A meta-analysis of 41 studies in the USA and Australia also indicated generally positive attitudes towards genetic testing for cancer specifically.[53] However, it also highlighted some negative attitudes, including cancer stigma, and worry about the possibility of getting a high-risk result, particularly among ethnic minority groups.[53] These factors may affect uptake in an MCED screening programme, although MCED tests are designed to detect cancer at the time of screening, rather than predict future risk. The relative non-invasiveness of the MCED test compared with current screening approaches may result in higher uptake in general. Given that blood-based MCED tests are not as resource intensive as other screening modalities, and could be delivered in mobile or community settings, transport-related and other logistic barriers could also be minimised.[22 27] However, needle phobia is prevalent, and may be a barrier to MCED screening[39] as it is for other public health interventions such as COVID-19 vaccination.[54] The general population's appetite for being tested for multiple types of cancer at the same time is also relatively unknown.

The information on MCED screening made available to the public and health professionals involved in its delivery will also impact screening uptake. This in turn depends on the extent to which the results from the NHS-Galleri trial are unambiguous.[27] If the benefits are marginal, or vary substantially by cancer type, the messaging from healthcare professionals regarding this intervention, for example, in screening invitation letters and at GP appointments, may be less straightforward.[55–58] Indeed, research shows that the perceived uncertainty of information can lead to information distrust, particularly among individuals with lower levels of numeracy.[56]

When a new screening programme is introduced, participation may be low to begin with and subsequently increase over a period of years.[59] It is not yet clear whether an MCED screening programme would be able to capitalise on the successes of existing programmes, or whether it will take substantial time for the use of this new technology to become embedded and for MCED screening to be considered a standard component of NHS healthcare provisions by the general population. Research to understand the downstream behavioural implications of initiating an MCED screening programme could help inform strategies to optimise screening uptake in general: for example, joined up, consistent public-facing communications across screening programmes and coordination between screening programmes. In addition, participation for cervical and breast cancer screening has declined in recent years.[42] Uptake, along with the effectiveness of interventions designed to increase uptake, should therefore be closely monitored across screening programmes if an MCED test-based national screening programme is introduced. The approach to MCED test delivery as a novel screening modality, and the impact of any changes or additions to the current range of recommended NHS single-cancer population screening programmes and modalities, should be evaluated. This could help inform the introduction of similar programmes in the UK and other countries.

CONCLUSIONS

MCED screening is a promising intervention for the reduction of late-stage cancer diagnosis and consequent cancer mortality. Here, we have shown that it is also a potentially powerful means of reducing socioeconomic inequalities in early-stage diagnosis, which should translate into reduced disparities in cancer mortality rates. To achieve the greatest possible population benefit from MCED screening and to reduce cancer-related health inequalities, there should be a focus on optimising informed uptake in communities experiencing higher deprivation.

and investigation process. RS, SLQ, CvW, RS, EH and LL developed the methodology. RS and EH implemented the computer code and supporting algorithms. RS, SLQ, CvW and LL provided oversight and leadership of the study. RS carried out the validation of the results. RS, SLQ, CvW and LL prepared data visualisations. RS acts as the guarantor for this paper. All authors were involved in drafting and revision of this manuscript, have read and approved this version of the manuscript for publication and agree to be accountable for all aspects of the work.

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