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Original Article

**Reduced risk of emergency admission for colorectal cancer associated with introduction of bowel cancer screening across England: retrospective national cohort study**

Author List:

J. Geraghty, M. Shawihdi, E. Devonport, S. Sarkar, M.G. Pearson and K. Bodger

Authors’ Address & Job Position:

Dr Joe Geraghty

*Postgraduate Research Student (Royal-Cook Endoscopy Fellow)*

*Department of Gastroenterology, Institute of Translational Medicine, University of Liverpool, UK*

Dr Mustafa Shawihdi

*Postdoctoral Research Associate*

*Institute of Psychology, Health and Society , University of Liverpool, UK*

Mrs Elizabeth Devonport

*Data Analyst*

*Aintree Health Outcomes Partnership, Aintree University Hospital, Liverpool, UK*

Dr Sanchoy Sarkar

*Consultant Gastroenterologist*

*Gastroenterology Department, Royal Liverpool Hospital, Liverpool, UK*

Prof Michael G Pearson

*Professor of Clinical Evaluation (Honorary)*

*Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, UK*

Dr Keith Bodger

*Senior Lecturer in Medicine & Consultant Gastroenterologist (Honorary)*

*Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, UK*

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CRC (colorectal cancer); FOBT (faecal occult blood test); BCSP (bowel cancer screening programme)

Correspondence to: Dr Keith Bodger

Room 3.14, Clinical Sciences Centre, Aintree University Hospital NHS Trust,

Lower Lane, Liverpool L9 7AL, United Kingdom.

E-mail: kbodger@liverpool.ac.uk

**ABSTRACT**

**Aim**: We examined whether roll out of the bowel cancer screening programme (BCSP) across England was associated with a reduced risk of emergency hospital admission for people presenting with colorectal cancer (CRC) during this period.

**Method**: This is a retrospective cohort study of 27,763 incident cases of CRC over a 1-year period during the roll-out of screening across parts of England.The primary outcome was the number of emergency (unplanned) hospital admissions during the diagnostic pathway. The primary exposure was to those living in an area where BCSP was active at the time of diagnosis. Patients were categorized into three exposure groups: BCSP not active (reference group), active <6 months or active ≥6 months.

**Results**: The risk of emergency admission for CRC in England was associated with increasing age, female gender, co-morbidity and social deprivation. After adjusting for these factors in logistic regression, the odds ratio for emergency admission in patients diagnosed ≥6 months after start-up of local screening was 0.83 (CI 0.76-0.90). The magnitude of risk reduction was greatest for cases of screening age (OR 0.75; CI 0.63-0.90) but this effect was apparent also for cases outside the 60-69 year age-group (OR: 0.85; CI 0.77-0.94). Living in an area with active BCSP conferred no reduction in risk of emergency admission for people diagnosed with oesophagogastric cancer during the same period.

**Conclusion**:The start-up of bowel cancer screening in England was associated with a substantial reduction in risk of emergency admission for CRC in people of all ages. This suggests that the roll-out of the programme had indirect benefits beyond those related directly to participation in screening.

What does this paper add to the existing literature?

This study provides evidence that the benefits of launching a screening programme for colorectal cancer are not limited to people of screening age with asymptomatic cancer but extend to the wider population. This is likely to reflect enhanced public and/or professional awareness of colon cancer in the symptomatic population.

**INTRODUCTION**

High rates of emergency admission at the time of cancer diagnosis have been a focus of concern in the UK despite over a decade of initiatives to promote earlier diagnosis.(1-3) In the case of colorectal cancer (CRC), emergency admission is associated with late-stage disease, reduced chance of curative surgery and poorer survival compared with patients diagnosed electively(4-7). The rate of emergency admission for CRC in England between 1999 and 2006 was estimated at 32.5%(8), consistent with the poorer outcomes observed for British patients relative to other European countries during this period.(9,10)

The roll out of the bowel cancer screening programme (BCSP) in England started in parts of the country in July 2006 and achieved nationwide coverage by January 2010. The programme offers faecal occult blood testing (FOBT) to all 60-69 years olds and colonoscopy for those with positive results. Screening programmes are intended to detect cancers earlier so that there is better chance of successful therapy and subsequent survival. Although this concept is straightforward, screening for some cancers has proved controversial with doubts about whether the overall gains from specific programmes warrant the cost or harm.(11-13)

In practice, quantifying the real-world benefits of population-based cancer screening is difficult. Survival benefit takes many years to realize(11,14) and a range of other healthcare advances may occur over this period to confound the interpretation of national trends in cancer incidence or survival. In the case of CRC screening, a recent meta-analysis of trial data estimated that it took 10.3 years before one death from CRC was prevented for 1000 patients screened.(14).

Our study examined whether introduction of the BCSP across England was associated with a reduction in overall risk of emergency admission for CRC in the general population. Although a process measure, emergency admission is linked strongly to bowel cancer outcome (5-7,15) and therefore a useful surrogate for evaluating the early impact of the programme. There are a number of ways in which the implementation of screening should improve rates of elective diagnosis and reduce risk of emergency admission. Firstly, the start-up of screening should lead to direct detection of asymptomatic cancers among people of screening age (screen-detected cases), thereby increasing the overall number of electively diagnosed cases in the population. Secondly, increased public and professional awareness of bowel cancer during the roll out period may bring additional indirect benefits to the wider population. Raising awareness of colon cancer may encourage symptomatic patients to seek routine healthcare more readily and/or primary care teams to refer more promptly for elective investigation. These indirect benefits may operate within a short timescale (months not years) and impact on people of all ages, not only those members of the public targeted directly by screening.

**METHODS**

**Participants and setting**

We studied patients of any age discharged with a diagnosis of colorectal cancer (CRC) from an English National Health Service (NHS) hospital between October 2006 and September 2007, a 1-year period when the BCSP was rolling out across parts of the country.

**Study design, data sources and timescales**

We used a retrospective cohort design (**Figures 1A** and **1B**). At the beginning of the year of case-ascertainment (October 2006), the BCSP was active already in parts of England and became active in some but not all additional areas during the study year. Hence, there was variation in exposure to start-up of BCSP between (and within) local populations during the period of study. This provided an opportunity for us to develop logistic regression models to estimate the association between start-up of BCSP in a patient’s area and risk of emergency admission during the diagnostic pathway.

Our analysis is based on patient-level data extracted from the Hospital Episode Statistics (HES) for England, a national data warehouse containing the information coded routinely at discharge for all inpatient care episodes occurring in NHS hospitals, including elective day case procedures, elective admissions and unplanned (emergency) admissions(3-7,16,17). We obtained administrative data for NHS hospitals for the two years relevant to the main period of roll-out of the English BCSP (2006/7 and 2007/8), merged the data and developed methods to identify a cohort of patients coded for the first time with colorectal cancer over the one year study period (1st October 2006 – 30th September 2007).

During the study period, general practices in England were grouped administratively and geographically into primary care trusts (PCTs) responsible for commissioning services for the local population. Information regarding the location and timing of start-up for each BCSP centre in England and the relevant Primary Care Trust populations served by each centre was obtained.(8,18) We generated a list identifying each PCT in England and the date when screening began in their local population. A small number of PCTs were associated with more than one screening centre, each having a different start-up date. As it was not possible to allocate the entire PCT population to a verified single start-up date for local screening, we excluded these PCTs (n=10). Hence, there were 142 PCTs included in the study, of which 17 PCTs had commenced screening before the beginning of the study period, 48 PCTs began active screening during the year of study and 77 PCTs had not yet started screening their local population by the end of the study period. The total adult population registered with general practitioners belonging to the study PCTs was 39,130,639.(9,10,19)

**Development of methods to extract incident cases of colorectal cancer (CRC)**

We developed linkage methods to extract a national cohort of CRC cases from the main HES dataset, identifying patients coded for the first time during the study period (**Figure 1A**). First, we identified all patients having one or more episodes containing a diagnostic code for CRC. Using the unique identifier for each cancer case we then extracted all of their care episodes from the main HES dataset and ordered them chronologically. Patients coded for the first time with CRC during the 1-year study period were identified as incident cases.

**Identification of first relevant hospital episode (index episode) for each patient**

HES data do not contain a precise diagnosis date and the first episode of care coded with a definitive cancer code is not a reliable starting point for the patient’s journey as it is not always the patient’s first relevant contact with the hospital.(11-13,17) Manual review of the sequence of hospital episodes for individual cancer cases revealed that some patients had relevant hospital admissions recorded in the weeks prior to the first (index) coding of cancer. Relevant episodes included elective day case endoscopic procedures or emergency admissions, where the recorded diagnosis was a non-specific symptom code (e.g. constipation) or a non-malignant diagnosis compatible with a patient undergoing investigation for cancer (e.g. iron deficiency anaemia). We created algorithms to identify the first “relevant” hospital episode for each patient, screening all coded primary diagnoses and procedures for any episodes recorded in the six months prior to first coding of cancer. Lists of primary diagnoses or procedures regarded as relevant to the CRC diagnostic pathway were generated, based on steering group review of all codes identified in earlier episodes. The admission date for the first relevant admission was recorded for each case of CRC.

**Primary outcome variable**

The outcome of interest is emergency hospital admission during the diagnostic pathway. For each case of CRC, we used the recorded admission method (ADMIMETH field) for the patient’s first relevant admission to define either an elective or emergency diagnostic pathway, as described previously.(11,14,17) HES data do not capture outpatient clinic attendances but any patient having only elective hospital episodes before cancer coding would be categorized as having an elective pathway, including those whose first relevant admission was for elective definitive surgery. Hence, patients were categorized as having an emergency admission pathway if their first relevant admission was an unplanned hospitalization.

**Patient exposure status (locally-active bowel cancer screening programme)**

The exposure of interest is thepresence (or absence) of an active BCSP in the patient’s local PCT area, quantified in terms of the duration of time that the programme had been active prior to the patient’s cancer diagnosis (**Figure 1B**). Each CRC case was assigned a variable to indicate whether or not they were living in a PCT that had active BCSP at the date of their first relevant admission. For those cases in which BCSP was active in the local population, we calculated the duration during which screening had been live in the area relative to the patient’s index admission. In the base-case analysis, we categorized patients into three groups according to exposure status: (1) No active local screening at the time of index admission (the reference or ‘unexposed’ group); (2) Local screening active for less than six months; and (3) Local screening active for more than 6 months.

To further evaluate any ‘dose-response’ effect, we undertook sensitivity analysis using an alternative continuous exposure variable (duration of locally active BCSP, expressed in months). In addition, a sub-group analysis was undertaken which excluded cases living in any of the 77 PCTs that had not yet rolled-out screening before the end of the study period. This sub-group analysis included only patients living in PCTs that had introduced local screening at some point prior to 30th September 2007.

**Patient demographic, co-morbidity and socioeconomic variables**

A number of patient-level confounders needed to be considered when exploring possible factors associated with risk of emergency admission for CRC. There is evidence to show that emergency admission is associated with increasing age, female gender, co-morbidity and socio-economic deprivation.(14,18,20) We extracted the relevant data from HES for these case-mix variables, as described previously.(5-7,15-17) Patients were allocated to the following age groups: <60, 60-69 (the target age-group for BCSP), 70-79 and ≥80 years. Co-morbidity was based on the weighted Charlson score,(17,21) excluding the CRC diagnosis and categorized into three groups (None, score of 1 or ≥2). Patients were allocated to quintiles of deprivation based on their area of residence and the index of multiple deprivation, as described.(8,9,22)

**Comparison with emergency admission rate for another form of cancer**

We wanted to verify that any association demonstrated between the exposure of interest (a locally active BCSP) and emergency admission during the diagnostic pathway was *specific* to bowel cancer. Increased public and professional awareness of colon cancer as a result of start-up of local screening might act to reduce emergency admissions for CRC *per se* but would not be expected to impact on unrelated types of cancer. Indeed, if we did find a generalized association between active local BCSP and emergency admission for another form of cancer then this would suggest confounding – the exposure variable might be simply a surrogate marker for areas with superior access to elective services.

To exclude this possibility, we examined whether there was any relationship between active local BCSP and emergency admission rates for oesophageal and gastric cancers (OG cancer) using data from our recent study.(15,17) The methods for extracting and validating the national data for OG cancer were similar to those described here for CRC and the study covered the relevant time period. Case-mix variables for OG cancer cases were comparable (age-group, gender, co-morbidity, deprivation quintile) and each case had their index admission defined as either elective or emergency. Using the same approach applied to the CRC cases, we determined “exposure” status for active BCSP for each OG cancer patient based on their PCT of residence and the date of their index admission. We predicted that there should be no association between the presence of local bowel cancer screening programme and rates of emergency admission for OG cancer.

**Analytical approach**

Descriptive statistics were used to describe the characteristics of CRC patients overall and according to exposure status. We used binary logistic regression to provide crude (unadjusted) odds ratio, adjusted odds ratio and 95% CI for emergency admission as the dependent variable, as described.(17) We explored the association between emergency admission and the exposure of interest in three separate models. Firstly, for all CRC patients (i.e. all ages), secondly for patients in the screening age-band specifically (60-69 yrs) and thirdly for those falling outside the age-band.

**RESULTS**

**National cohort of CRC cases identified from HES data**

We identified 32,299 incident cases of CRC in England during the study year, which is comparable to an independent estimate of 33,604 new cases reported nationally in 2007.(23) The patient characteristics of the national cohort are summarized in **Table 1**. The age and gender distributions are consistent with previous reports.(8,23) Based on our definition of emergency admission during the diagnostic pathway, there were 10,087 patients (36.5%) whose first relevant admission was an unplanned (emergency) hospitalization. This is comparable with an independent figure of 32.5% reported for England between 1999-2006.(8)

**CRC patients included in the study**

Of the 32,299 new cases of CRC nationally, 27,763 patients belonged to one of the 142 PCTs included in the study. The characteristics of the patients from these PCTs were indistinguishable from the national cohort (**Table 1**). With respect to the exposure of interest (local start-up of BCSP), 17,080 cases had their first relevant admission at a time when screening was *not* yet active in their local PCT population (“unexposed”) and 7,426 were diagnosed after the start-up date of screening in their locality (“exposed”). Of the “exposed” group, 4,222 patients had their first relevant admission within six months of the local start-up date and 3,204 patients over six months after screening had started in their area, with a mean exposure time overall of 5.7 months (ranging from 0.1 to 15.2 months). It should be noted that approximately only half the target population of 60-69 year olds would be offered screening in the first year of activation of the programme.

As shown in **Table 1**, there was a very small but significant difference in mean age of patients across the three groups (No exposure: 71.0 yrs; <6 months: 70.8 yrs; ≥6 months: 70.7 yrs; p<0.01 ANOVA). This is consistent with a trend for slightly younger age of CRC cases diagnosed in an area where BCSP had become active. This may be explained by the predictable finding that the proportion of total CRC cases aged 60-69 years was higher for exposed versus unexposed groups – this confirms enhanced detection of prevalent cases of CRC among people of screening age either in the programme (asymptomatic, screen-detected cases) or via normal diagnostic routes. There was no difference in gender mix or levels of co-morbidity across the exposure groups. With respect to deprivation, the ‘unexposed’ group had the lowest proportion of CRC cases living in socioeconomically disadvantaged areas (quintile 1) – i.e. they tended to be living in more affluent areas where risk of emergency admission would be expected to be lower.

**Crude rate of emergency admission by exposure status**

Despite the imbalance in deprivation across the three groups, the crude rate of emergency admission was lowest in the group of CRC patients diagnosed when the BCSP had been active in their local population for ≥6 months (32.7%) and highest in the unexposed group of patients diagnosed before screening began in their area (37.1%, p<0.001) (**Table 1**). Those cases of CRC diagnosed within six months of local start-up of BCSP had an intermediate rate of emergency admission.

The difference in unadjusted rates of emergency admission with respect to exposure group was greatest in magnitude for CRC patients of screening age (60-69 years) but was significant also in patients falling outside the age targeted by the screening programme (**Table 1**).

We exclude 4,332 patients from the study since they belonged to PCTs served by more than one screening centre with different start dates for each centre. Although the precise exposure status of each individual case in these PCTs could not be determined, we do know that all but one of the ten excluded PCTs had rolled out screening before or during the study period. Hence, most of the excluded cases of CRC would have been “exposed” to local BCSP. Consistent with this, the overall rate of emergency admission for excluded cases was 33.1%, significantly lower than that of the unexposed cases in the study cohort (37.1%).

**Identifying factors associated with emergency admission for CRC**

Logistic regression analysis (**Table 2**) confirmed that increasing age, female gender, increased levels of co-morbidity and socioeconomic deprivation were associated with increased risk of emergency admission for CRC nationally, consistent with previous research.(18,20) After adjusting for these case-mix factors in multiple regression, we were able to confirm that exposure status with respect to locally active BCSP was an independent patient-level factor associated with emergency admission for CRC in England. Overall, the adjusted odds ratio for emergency admission in patients diagnosed ≥6 months after start-up of local screening was 0.83 (CI: 0.76-0.90) compared with unexposed cases.

The “protective” effect of the BCSP in terms of risk for emergency admission was not restricted to people of screening age but extended across the whole population of bowel cancer cases presenting to the health service during this period. We constructed two separate models (**Supplementary Tables 2a & 2b**), one that included only the 6,719 CRC patients of *screening age* (60-69 years) and another that included the remaining 20,921 cases falling outside the target age for direct screening. For screening age cases, the adjusted odds ratio for emergency admission in patients diagnosed ≥6 months after screening started was 0.75 (CI: 0.63-0.90). It was to be expected that the magnitude of risk reduction would be greatest for those aged 60-69 years since some of these patients will had symptomless cancers detected within the screening programme, adding to any indirect effects that the launch of screening may have brought to symptomatic cases presenting via routine services. However, analysis of cases of CRC outside of screening age showed that the adjusted odds ratio for emergency admission in patients diagnosed ≥6 months after screening started in their area was 0.85 (CI: 0.77-0.94). This is consistent with our idea that local start-up of BCSP results in indirect, general benefits across the whole local population during this period.

**Sensitivity analyses**

We substituted the categorical exposure variable (No BCSP; <6 months; ≥6 months) for the actual duration (in months) that BCSP had been active at the time of the patient’s diagnosis. Using this continuous exposure variable, the adjusted odds ratio provides an estimate of risk reduction per month of exposure. These analyses confirmed an independent association between exposure time and risk of emergency admission for patients overall, those of screening age (60-69 years) and those outside this age-group (**Table 3**).

To further explore potential confounding, we undertook a sub-group analysis in which we excluded all patients from the 77 PCTs that had not introduced screening at any point during the study period. The purpose of this analysis was to exclude any bias relating to possible systematic differences in rates of emergency admissions found in the 77 “*late adopter*” PCTs compared with the PCTs that had rolled-out bowel cancer screening before the end of our study period. Hence, in this sub-group analysis all patients belonged to one of the 65 PCTs that did roll out BCSP prior to the end of the study year (30th September 2007). In this analysis there were 10,683 patients from 65 PCTs and, again, we confirmed an independent association between exposure status for BCSP and risk of emergency admission for CRC. For patients diagnosed ≥6 months after local start-up of BCSP, the adjusted odds ratio for emergency admission was 0.76 overall (p<0.001), 0.70 for those aged 60-69 years (p=0.002) and 0.78 for other age-groups (p<0.001).

**Comparison with emergency admissions for oesophagogastric cancer**

The characteristics of 22,450 cases of OG cancer diagnosed in England over a two year period (2006-2008) have been described.(17) Of these patients, 9,319 belonged to the PCTs included in the present study and were diagnosed during the one year study period. Relative to their index admission, 6,787 OG cancer patients were diagnosed at a time when BCSP was not active in their PCT (“unexposed”) and 2,532 were diagnosed after the colon cancer screening programme started (“exposed”). Crude rates of emergency admission during the diagnostic pathway for OG cancer showed no difference across the exposure groups. The results of the binary logistic regression analysis are shown in **Table 4**. We found no association between emergency admission rates of OG cancer and our predictor variable defining “exposure” of the local population to BCSP. This suggests that exposure status is specifically associated with risk of emergency admission for CRC rather than for emergency admission for cancer or other conditions in general. This makes it unlikely that access to elective diagnosis in general was systematically “better” in primary care trust populations where the programme became active earlier in the course of the national roll out.

**DISCUSSION**

We have demonstrated that the roll out period of the BCSP across England was associated with a marked reduction in risk of emergency admission for colorectal cancer cases. The “effect” was greatest among patients of screening age, where the risk of emergency admission in those diagnosed more than six months after local start-up of the programme was 0.75 times that of someone diagnosed before screening became active in their locality. However, what is of particular interest is that the risk reduction was not confined to the 60-69 year age group – this suggests that indirect, population-wide benefits were operating as each area introduced screening. This is consistent with our hypothesis that the implementation of the BCSP would impact not only on individuals targeted for screening but would be associated with benefit across the local population by virtue of heightened public and professional awareness of bowel cancer. This is the first national study to show early and population-wide benefit arising from the introduction of the bowel cancer screening programme.

Previous reports from specific parts of the country explored the impact of bowel cancer screening on overall emergency admissions for CRC. A randomized controlled trial assessing FOBT screening (the Nottingham screening study) compared 75,253 patients in the screened group (60% response rate) and 74,998 well matched, unscreened controls (age range; 45 and 74 years). The emergency presentation rate was 23.9% in the screened group, compared with 27.9% in the control group, but the difference was not statistically significant (possibly due to lack of study power).(24) In an uncontrolled observational study from Coventry and North Warwickshire, where the bowel cancer screening pilot targeted a wider age group (50 to 69 years), the authors reported that 29.4% of CRC patients presented as an emergency in the year before the pilot (1999) but that the local rate had fallen to just 15.8% by 2004. Surprisingly, the proportion of Dukes stage cancers was unchanged over the study period and the annual number of cases did not rise as might be expected if extra screen-detected cases were contributing to the reported totals.(25) Expert commentators questioned whether screening itself, or other changes in local or national CRC care over the 5 year period was responsible for the time-trends reported.(26) Similar uncontrolled local data for sigmoidoscopy-based colon cancer screening have

shown a trend for reduced emergency admissions.(27)

Our study has the advantage of nationwide coverage, large numbers and a design that sought to control for sources of bias. The staged roll out of screening across the country meant that simple observation of temporal trends in annual emergency admission rates would not provide an accurate means of assessing the impact of the programme on unplanned care. Hence, we conceived a study design that took advantage of the variation in exposure between and within local populations to the potential benefits of start-up of BCSP during the roll out period. Although our logistic regression models included key potential confounders, we cannot entirely eliminate the possibility of residual confounding given the observational nature of the work. Nevertheless, we undertook sensitivity and sub-group analyses and found consistent results. Furthermore, our analysis of 9,319 cases of oesophageal and gastric cancer diagnosed during the study period found no association between risk of emergency admissions for this unrelated tumour type and the local roll-out of the BCSP. This excluded the possibility that our findings were due to non-specific, generalized differences in hospital emergency admission rates between PCTs that rolled out screening early versus late.

We are not able to selectively quantify the indirect (as opposed to direct) benefits of the programme in our study since we cannot identify or exclude cases of screen-detected cancer (i.e. patients diagnosed directly by the programme after positive FOBT). Screening status is not recorded in HES data. Hence, we cannot know how much of the observed reduction in risk of emergency admission is attributable to the elective diagnosis of symptomless cancers within the programme itself. However, relative to the total number of new CRC cases diagnosed nationally, the absolute numbers of screen-detected tumours is low. In a report of cumulative findings from the BCSP up until October 2008 (a full year after the end of our study period), only 1,772 screen-detected CRC cases had been recorded.(28) It follows that our study cohort of 27,763 cases will have contained only a few hundred screen-detected cancer patients.

Certainly, screen-detected cancers will have contributed in part to the reduced risk of emergency admission observed in the 60-69 year age group, but this cannot explain the fact that a major risk reduction is seen also in people outside of screening age. Moreover, we have shown a risk reduction within 6-12 months of start-up, a time-point when screening will have been offered to less than half of eligible 60-69 year olds and hence the direct benefits of screen-detected cancers not yet fully realized. We anticipated that indirect benefits would operate mostly during the start-up and early phase of screening when local publicity and awareness of colorectal cancer was heightened and we designed our study deliberately to focus on this period.

The full impact of the BCSP will take some years to quantify but the present study suggests that the introduction of screening brought benefits that extended beyond those people targeted by and participating in the programme. These indirect benefits are likely to have translated into savings in acute hospital bed days and improvement in cancer outcomes. This strengthens the case supporting the cost-effectiveness of introducing bowel cancer screening in the UK health service setting. The roll out of national screening based on FOBT has now completed and services in England are preparing for implementation of screening with flexible sigmoidoscopy. It will be interesting to see whether this next phase is associated with similar population-wide benefits.

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**Contributors**

JG undertook the data extraction, linkages and data analysis, contributed to study design and assisted in drafting the manuscript. KB was responsible for the study conception and design, directed and supervised the analysis and drafted the manuscript. ET was responsible for data management and advised on extraction and linkage methodologies. MP contributed to review and revision of the manuscript. SS contributed to the clinical steering group for the study and reviewed the manuscript. All authors read and approved the final manuscript**.**

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**Competing Interests**

None declared.

**References**

1. National Cancer Intelligence Network .

2. Quarter of all cancers found late, according to study. The Guardian.

3. Burns EM, Rigby E, Mamidanna R, Bottle A, Aylin P, Ziprin P, et al. Systematic review of discharge coding accuracy. J Public Health (Oxf). 2012 Mar;34(1):138–48.

4. Tekkis PP, Poloniecki JD, Thompson MR, Stamatakis JD. Operative mortality in colorectal cancer: prospective national study. BMJ. 2003 Nov 22;327(7425):1196–201.

5. McArdle CS, Hole DJ. Emergency presentation of colorectal cancer is associated with poor 5-year survival. Br J Surg. John Wiley & Sons, Ltd; 2004 Jan 1;91(5):605–9.

6. Bass G, Fleming C, Conneely J, Martin Z, Mealy K. Emergency first presentation of colorectal cancer predicts significantly poorer outcomes: a review of 356 consecutive Irish patients. Dis Colon Rectum. 2009 Apr;52(4):678–84.

7. Scott NA, Jeacock J, Kingston RD. Risk factors in patients presenting as an emergency with colorectal cancer. Br J Surg [Internet]. 1995 Mar;82(3):321–3. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id= 7795995&retmode=ref&cmd=prlinks

8. Raine R, Wong W, Scholes S, Ashton C, Obichere A, Ambler G. Social variations in access to hospital care for patients with colorectal, breast, and lung cancer between 1999 and 2006: retrospective analysis of hospital episode statistics. BMJ. 2010;340:b5479.

9. Morris EJA, Sandin F, Lambert PC, Bray F, Klint A, Linklater K, et al. A population-based comparison of the survival of patients with colorectal cancer in England, Norway and Sweden between 1996 and 2004. Gut. 2011 Aug;60(8):1087–93.

10. Gatta G, Capocaccia R, Sant M, Bell CM, Coebergh JW, Damhuis RA, et al. Understanding variations in survival for colorectal cancer in Europe: a EUROCARE high resolution study. Gut. 2000 Oct;47(4):533–8.

11. Baum M. Harms from breast cancer screening outweigh benefits if death caused by treatment is included. BMJ. 2013;346:f385.

12. Sandblom G, Varenhorst E, Rosell J, Lofman O, Carlsson P. Randomised prostate cancer screening trial: 20 year follow-up. BMJ. 2011;342:d1539.

13. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. Cochrane Database Syst Rev. 2013;1:CD004720.

14. Lee SJ, Boscardin WJ, Stijacic-Cenzer I, Conell-Price J, O'Brien S, Walter LC. Time lag to benefit after screening for breast and colorectal cancer: meta-analysis of survival data from the United States, Sweden, United Kingdom, and Denmark. BMJ. 2013;346:e8441.

15. Rabeneck L, Paszat LF, Li C. Risk factors for obstruction, perforation, or emergency admission at presentation in patients with colorectal cancer: a population-based study. Am J Gastroenterol. 2006 May;101(5):1098–103.

16. Bodger K, Bowering K, Sarkar S, Thompson E, Pearson MG. All-cause mortality after first ERCP in England: clinically guided analysis of hospital episode statistics with linkage to registry of death. Gastrointest Endosc. 2011 Oct;74(4):825–33.

17. Shawihdi M, Thompson E, Kapoor N, Powell G, Sturgess RP, Stern N, et al. Variation in gastroscopy rate in English general practice and outcome for oesophagogastric cancer: retrospective analysis of Hospital Episode Statistics. Gut. 2013 Feb.

18. BCSP Intranet [Internet]. Available from: http://www.bcsp.nhs.uk/pi/statistics\_documents

19. Statistics OFN. Primary Care Organisations Population Estimates (experimental) [Internet]. Available from: http://www.ons.gov.uk/ons/rel/sape/pco-pop-est-exp/mid-2010-release/pco-mid-2010.html

20. Moller H, Sandin F, Robinson D, Bray F, Klint S, Linklater KM, et al. Colorectal cancer survival in socioeconomic groups in England: variation is mainly in the short term after diagnosis. Eur J Cancer. 2012 Jan;48(1):46–53.

21. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol. 2004 Dec;57(12):1288–94.

22. Centre TI. Summary Hospital-level Mortality Indicator [Internet]. Available from: http://www.ic.nhs.uk/SHMI

23. Statistics OFN. Office for National Statistics [Internet]. 2010 ed. Available from: http://www.ons.gov.uk/ons/search/index.html?newquery=cancer+registrations

24. Scholefield JH, Robinson MH, Mangham CM, Hardcastle JD. Screening for colorectal cancer reduces emergency admissions. Eur J Surg Oncol. 1998 Feb;24(1):47–50.

25. Goodyear SJ, Stallard N, Gaunt A, Parker R, Williams N, Wong L. Local impact of the English arm of the UK Bowel Cancer Screening Pilot study. Br J Surg. 2008 Sep;95(9):1172–9.

26. Logan RFA. The effects of population-based faecal occult blood test screening upon emergency colorectal cancer admissions in Coventry and north Warwickshire. Gut. 2008 Sep;57(9):1333–authorreply1333–4.

27. Davies RJ, Collins CD, Vickery CJ, Eyre-Brook I, Welbourn R. Reduction in the proportion of patients with colorectal cancer presenting as an emergency following the introduction of fast-track flexible sigmoidoscopy: a three-year prospective observational study. Colorectal Dis. 2004 Jul;6(4):265–7.

28. Logan RFA, Patnick J, Nickerson C, Coleman L, Rutter MD, Wagner von C. Outcomes of the Bowel Cancer Screening Programme (BCSP) in England after the first 1 million tests. Gut. 2012 Oct;61(10):1439–46.

**Table 1 Characteristics of colorectal cancer patients diagnosed in English NHS hospitals over a one year period (October 2006 to September 2007)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Patient characteristics** | **Total** | **Study cohort** | **No BCSP** | **BCSP**  **<6 months** | **BCSP**  **≥6 months** | **p value** |
| **Number of cases** | 32,299 | 27,640 | 20,498 | 4,151 | 2,991 | - |
| **Age**, mean [sd] | 71.0 [12.1] | 70.9 [12.1] | 71.0 [12.3]\* | 70.8 [11.6] | 70.7 [11.8]\* | <0.001 |
| **Age groups**, n (%) |  |  |  |  |  |  |
| <60 | 5,347 (16.6) | 4,583 (16.6) | 3,435 (16.8) | 684 (16.5) | 464 (15.5) |  |
| 60 to 69 | 7,868 (24.4) | 6,719 (24.3) | 4,825 (23.5)\* | 1,078 (26.0) | 816 (27.3)\* | <0.001 |
| 70 to 79 | 10,651 (33.0) | 9,134 (33.0) | 6,748 (32.9) | 1,374 (33.1) | 1,012 (33.8) |  |
| >79 | 8,433 (26.1) | 7,204 (26.1) | 5,490 (26.8) | 1,015 (24.5) | 699 (23.4) |  |
| **Gender**, n (%) |  |  |  |  |  |  |
| Male | 17,981 (55.7) | 15,437 (55.9) | 11,337 (55.3)\* | 2,387 (57.5) | 1,713 (57.3)\* | n/s |
| Female | 14,318 (44.3) | 12,203 (44.1) | 9,161 (44.7) | 1,764 (42.5) | 1,278 (42.7) |  |
| **Co-morbidity score**, n (%) |  |  |  |  |  |  |
| 0 | 21,847 (67.6) | 18,760 (67.9) | 13,933 (68.0)\* | 2,781 (67.0) | 2,046 (68.4)\* | n/s |
| 1 | 2,383 (7.4) | 2,067 (7.5) | 1,513 (7.4) | 323 (7.8) | 231 (7.7) |  |
| ≥2 | 8,069 (25.0) | 6,813 (24.6) | 5,052 (24.6) | 1,047 (25.2) | 714 (23.9) |  |
| **Deprivation quintile**, n (%) |  |  |  |  |  |  |
| 1 (Most deprived) | 5,516 (17.1) | 5,197 (18.8) | 3,567 (17.4)\* | 1,012 (24.4) | 618 (20.7)\* | <0.001 |
| 2 | 6,044 (18.7) | 5,324 (19.3) | 3,851 (18.8) | 873 (21.0) | 600 (20.1) |  |
| 3 | 6,844 (21.2) | 5,794 (21.0) | 4,279 (20.8) | 846 (20.4) | 669 (22.4) |  |
| 4 | 6,980 (21.6) | 5,897 (21.3) | 4,472 (21.8) | 823 (19.8) | 602 (20.1) |  |
| 5 (Least deprived) | 6,593 (20.4) | 5,428 (19.6) | 4,329 (21.1) | 597 (14.4) | 502 (16.8) |  |
| **Emergency admission**, n (%) |  |  |  |  |  |  |
| All patients (n=27,640)  - *Screening age* (n=6,719) | 11,651 (36.1)  2,293 (29.1) | 10,087 (36.5)  1,975 (29.4) | 7,595 (37.1)\*  1,460 (30.3)\* | 1,513 (36.4)  313 (29.0) | 979 (32.7)\*  202 (24.8)\* | <0.001  <0.001 |
| - *Other ages* (n=20,921) | 9,358 (38.3) | 8,112 (38.8) | 6,135 (39.1)\* | 1,200 (39.0) | 777 (35.7)\* | <0.001 |

\*denotes the comparator groups for the given p value

Of the total national cohort, 322 (1.0%) of patients had missing IMD (deprivation) status and were excluded from the analysis.

There was a small but significant difference in age across the exposure groups (p<0.001, ANOVA). As expected, the proportion of total cancer cases aged 60-69 yrs (screening age) was higher in the “exposed” groups. The proportion of people living in least deprived areas was highest in the unexposed (No BCSP) group (p<0.001, Chi Square). The crude rate of emergency admission was significantly lower in those diagnosed ≥6 months after start-up of BCSP in their local population.

**Table 2 Factors associated with emergency admission during the diagnostic pathway for colorectal cancer in England**. Binary logistic regression analysis of 27,763 cases diagnosed between October 2006 to September 2007, a period when bowel cancer screening was being rolled out across the country.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Emergency admissions/total (%)** | **Unadjusted (univariate)** | | | **Adjusted (multivariate)** | | |
| **OR** | **CI** | **p value** | **OR** | **CI** | **p value** |
| **Age group** (years) |  |  |  |  |  |  |  |
| <60 years | 1,440/4583 (31.4) | 1 | - | - | 1 | - | - |
| 60-69 years | 1,975/6,719 (29.4) | 0.91 | 0.84-0.99 | 0.021 | 0.90 | 0.83-0.98 | 0.019 |
| 70-79 years | 3,087/9,134 (33.8) | 1.11 | 1.03-1.20 | 0.005 | 1.08 | 1.00-1.17 | 0.063 |
| >79 years | 3,585/7,204 (49.8) | 2.16 | 2.00-2.34 | <0.001 | 2.09 | 1.93-2.27 | <0.001 |
| **Gender** |  |  |  |  |  |  |  |
| Male | 5,320/15,437 (34.5) | 1 | - | - | 1 | - | - |
| Female | 4,767/12,203 (39.1) | 1.22 | 1.16-1.28 | <0.001 | 1.17 | 1.11-1.24 | <0.001 |
| **Co-morbidity score** |  |  |  |  |  |  |  |
| 0 | 5,085/18,760 (27.1) | 1 | - | - | 1 | - | - |
| 1 | 914/2,067 (44.2) | 2.13 | 1.94-2.34 | <0.001 | 2.02 | 1.84-2.22 | <0.001 |
| ≥2 | 4,088/6,813 (60.0) | 4.03 | 3.81-4.28 | <0.001 | 4.06 | 3.83-4.31 | <0.001 |
| **Deprivation** |  |  |  |  |  |  |  |
| 1 most deprived | 2,194/5,197 (42.2) | 1 | - | - | 1 | - | - |
| 2 | 2,013/5,324 (37.8) | 0.83 | 0.77-0.90 | <0.001 | 0.80 | 0.73-0.87 | <0.001 |
| 3 | 2,122/5,794 (36.6) | 0.79 | 0.73-0.85 | <0.001 | 0.76 | 0.70-0.83 | <0.001 |
| 4 | 2,012/5,897 (34.1) | 0.71 | 0.66-0.77 | <0.001 | 0.67 | 0.62-0.73 | <0.001 |
| 5 least deprived | 1,746/5,428 (32.2) | 0.65 | 0.60-0.70 | <0.001 | 0.64 | 0.59-0.70 | <0.001 |
| **BCSP Exposure** |  |  |  |  |  |  |  |
| Control | 7,595/20,498 (37.1) | 1 | - | - | 1 | - | - |
| BCSP <6 months | 1,513/4,151 (36.4) | 0.97 | 0.91-1.04 | 0.463 | 0.95 | 0.88-1.02 | 0.170 |
| BCSP ≥6 months | 979/2,991 (32.7) | 0.83 | 0.76-0.90 | <0.001 | 0.83 | 0.76-0.90 | <0.001 |

**Table 3 Sensitivity analyses testing the association between locally active bowel cancer screening programme and emergency admission for colorectal cancer:** Exposure was expressed as the number of months that screening was active at the time of the patients diagnosis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Emergency admissions / total cases (%)** | **Unadjusted (univariate)** | | | **Adjusted (multivariate)** | | |
| **OR** | **CI** | **p value** | **OR** | **CI** | **p value** |
| **BCSP exposure (months)** |  |  |  |  |  |  |  |
| *All age-groups*  No BCSP | 7,599/20,520 (37.0) | 1 | - | - | 1 | - | - |
| BCSP (per month) | 2,488/7,120 (34.9) | 0.98 | 0.97-0.99 | <0.001 | 0.98 | 0.97-0.99 | <0.001 |
| *Screening age only (60-69)*  No BCSP | 1,460/4,826 (30.3) | 1 | - | - | 1 | - | - |
| BCSP (per month) | 515/1,893 (27.2) | 0.97 | 0.96-0.99 | 0.002 | 0.97 | 0.96-0.99 | 0.003 |
| *Other age groups*  No BCSP | 6,135/15,673 (39.1) | 1 | - | - | 1 | - | - |
| BCSP (per month) | 1,977/5,248 (37.7) | 0.98 | 0.97-0.99 | <0.001 | 0.98 | 0.97-0.99 | <0.001 |

Results from three separate models (all age-groups combined; screening age only; and other age groups). In all analyses, an association between exposure and reduced risk of emergency admission was confirmed after adjusting for age, gender, co-morbidity and deprivation in multivariate binary logistic regression. The odds ratio expresses the reduction in risk per month of locally active screening.

**Table 4 Factors associated with emergency admission during the diagnostic pathway for oesophagogastric cancers in England**. Binary logistic regression analysis of 9,319 cases diagnosed between October 2006 to September 2007.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Emergency admissions/ total (%)** | **Unadjusted (univariate)** | | | **Adjusted (multivariate)** | | |
| **OR** | **CI** | **p value** | **OR** | **CI** | **p value** |
| **Age group** (years) |  |  |  |  |  |  |  |
| <60 years | 293/1,454 (20.2) | 1 | - | - | 1 | - | - |
| 60-69 years | 460/2,171 (21.2) | 1.07 | 0.90-1.26 | 0.451 | 1.06 | 0.89-1.26 | 0.498 |
| 70-79 years | 769/3,023 (25.4) | 1.35 | 1.16-1.57 | <0.001 | 1.32 | 1.12-1.55 | 0.001 |
| >79 years | 1,110/2,671 (41.6) | 2.82 | 2.43-3.27 | <0.001 | 3.02 | 2.57-3.54 | <0.001 |
| **Gender** |  |  |  |  |  |  |  |
| Male | 1,634/6,090 (26.8) | 1 | - | - | 1 | - | - |
| Female | 998/3,229 (30.9) | 1.22 | 1.11-1.34 | <0.001 | 1.10 | 0.99-1.22 | 0.070 |
| **Co-morbidity** |  |  |  |  |  |  |  |
| 0 | 1,345/6,757 (19.9) | 1 | - | - | 1 | - | - |
| 1 | 770/1,744 (44.2) | 3.18 | 2.85-3.56 | <0.001 | 3.14 | 2.80-3.52 | <0.001 |
| ≥2 | 517/818 (63.2) | 6.91 | 5.92-8.06 | <0.001 | 7.72 | 6.58-9.05 | <0.001 |
| **Deprivation** |  |  |  |  |  |  |  |
| 1 most deprived | 676/2,130 (31.7) | 1 | - | - | 1 | - | - |
| 2 | 551/1,936 (28.5) | 0.86 | 0.75-0.98 | 0.023 | 0.87 | 0.75-1.00 | 0.052 |
| 3 | 522/1,830 (28.5) | 0.86 | 0.75-0.98 | 0.028 | 0.84 | 0.72-0.92 | 0.019 |
| 4 | 494/1,840 (26.8) | 0.79 | 0.69-0.91 | 0.001 | 0.76 | 0.65-0.88 | <0.001 |
| 5 least deprived | 389/1,583 (24.6) | 0.70 | 0.61-0.82 | <0.001 | 0.65 | 0.55-0.76 | <0.001 |
| **BCSP Exposure** |  |  |  |  |  |  |  |
| Control | 1,900/6,787 (28.0) | 1 | - | - | 1 | - | - |
| BCSP <6 months | 417/1,406 (29.7) | 1.08 | 0.96-1.23 | 0.207 | 1.07 | 0.93-1.22 | 0.350 |
| BCSP ≥6 months | 315/1,126 (28.0) | 1.00 | 0.87-1.15 | 0.989 | 0.95 | 0.82-1.11 | 0.510 |

**Figure 1A Selection of an incident cohort of cases presenting to NHS hospitals in England over a defined one year period (October 2006 to September 2007)**

*Figure 1A*

SEP 2007

OCT 2006

**Selection of a one-year cohort of incident cases of colorectal cancer in England**

(Included)

**Patient C**

Patient D

(Excluded)

Study period

(Included)

**Patient B**

Patient A

(Excluded)

The cohort included all patients discharged with a diagnosis of colorectal cancer for the first time within the study period ( ), thereby excluding cases whose first hospital episode was before or after this period ( ).

**Figure 1B Exposure status for each patient in the cohort was determined relative to the start-up date of the bowel cancer screening programme in their local Primary Care Trust population**. Patients were categorized into three groups: No BCSP (i.e. programme not yet active in the area at the time of patient’s first relevant admission), active <6 months and active ≥6 months.

SEP 2007

OCT 2006

*Exposure time*

START-UP DATE

BCSP is now active in local population

BCSP is not yet active in local population

**Exposure status based on the start-up date of the local bowel cancer screening programme**

*Figure 1B*

**Patient 2**

(“Exposed”)

**Patient 1**

(“Unexposed”)

ONLINE ONLY SUPPORTING INFORMATION

**Supplementary Tables (online only)**

**Table 2a Factors associated with emergency admission during the diagnostic pathway for colorectal cancer cases of screening age (60-69 years) in England**. Binary logistic regression analysis of 6,719 cases diagnosed between October 2006 to September 2007.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Emergency admissions/ total (%)** | **Unadjusted (univariate)** | | | **Adjusted (multivariate)** | | |
| **OR** | **CI** | **p value** | **OR** | **CI** | **p value** |
| **Age group** (years) |  |  |  |  |  |  |  |
| 60-69 years | 1,975/6,719 (29.4) | 1 | - | - | 1 | - | - |
| **Gender** |  |  |  |  |  |  |  |
| Male | 1,180/4,142 (28.5) | 1 | - | - | 1 | - | - |
| Female | 795/2,577 (30.8) | 1.12 | 1.01-1.25 | 0.039 | 1.10 | 0.98-1.23 | 0.096 |
| **Co-morbidity score** |  |  |  |  |  |  |  |
| 0 | 1,006/4,739 (21.2) | 1 | - | - | 1 | - | - |
| 1 | 153/453 (33.8) | 1.89 | 1.54-2.33 | <0.001 | 1.87 | 1.52-2.30 | <0.001 |
| ≥2 | 816/1,527 (53.4) | 4.26 | 3.77-4.81 | <0.001 | 4.24 | 3.75-4.79 | <0.001 |
| **Deprivation** |  |  |  |  |  |  |  |
| 1 most deprived | 444/1,310 (33.9) | 1 | - | - | 1 | - | - |
| 2 | 377/1,271 (29.7) | 0.82 | 0.70-0.97 | 0.021 | 0.79 | 0.67-0.95 | 0.009 |
| 3 | 409/1,381 (29.6) | 0.82 | 0.70-0.97 | 0.017 | 0.80 | 0.68-0.95 | 0.011 |
| 4 | 413/1,450 (28.5) | 0.78 | 0.66-0.91 | 0.002 | 0.78 | 0.66-0.93 | 0.005 |
| 5 least deprived | 332/1,307 (25.4) | 0.66 | 0.56-0.79 | <0.001 | 0.67 | 0.56-0.80 | <0.001 |
| **BCSP Exposure** |  |  |  |  |  |  |  |
| Control | 1,460/4,825 (30.3) | 1 | - | - | 1 | - | - |
| BCSP <6 months | 313/1,078 (29.0) | 0.94 | 0.82-1.09 | 0.428 | 0.92 | 0.79-1.07 | 0.270 |
| BCSP ≥6 months | 202/816 (24.8) | 0.76 | 0.64-0.90 | 0.001 | 0.75 | 0.63-0.90 | 0.002 |

**Supplementary Tables (online only)**

**Table 2b Factors associated with emergency admission during the diagnostic pathway for colorectal cancer cases outside the screening age targeted for BCSP in England**. Binary logistic regression analysis of 20,921 cases diagnosed between October 2006 to September 2007

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Emergency admissions/ total (%)** | **Unadjusted (univariate)** | | | **Adjusted (multivariate)** | | |
| **OR** | **CI** | **p value** | **OR** | **CI** | **p value** |
| **Age group** (years) |  |  |  |  |  |  |  |
| <60 years | 1,440/4,583 (31.4) | 1 | - | - | 1 | - | - |
| 70-79 years | 3,087/9,134 (33.8) | 1.11 | 1.03-1.20 | 0.005 | 1.08 | 1.00-1.17 | 0.063 |
| >79 years | 3,585/7,204 (49.8) | 2.16 | 2.00-2.34 | <0.001 | 2.09 | 1.92-2.27 | <0.001 |
| **Gender** |  |  |  |  |  |  |  |
| Male | 4,140/11,295 (36.7) | 1 | - | - | 1 | - | - |
| Female | 3,972/9,626 (41.3) | 1.21 | 1.15-1.28 | <0.001 | 1.20 | 1.13-1.27 | <0.001 |
| **Co-morbidity score** |  |  |  |  |  |  |  |
| 0 | 4,079/14,021 (29.1) | 1 | - | - | 1 | - | - |
| 1 | 761/1,614 (47.1) | 2.17 | 1.96-2.41 | <0.001 | 2.07 | 1.86-2.30 | <0.001 |
| ≥2 | 3,272/5,286 (61.9) | 3.96 | 3.71-4.23 | <0.001 | 4.01 | 3.75-4.29 | <0.001 |
| **Deprivation** |  |  |  |  |  |  |  |
| 1 most deprived | 1,750/3,887 (45.0) | 1 | - | - | 1 | - | - |
| 2 | 1,636/4,053 (40.4) | 0.83 | 0.76-0.90 | <0.001 | 0.80 | 0.73-0.88 | <0.001 |
| 3 | 1,713/4,413 (38.8) | 0.78 | 0.71-0.85 | <0.001 | 0.75 | 0.69-0.83 | <0.001 |
| 4 | 1,599/4,447 (36.0) | 0.69 | 0.63-0.75 | <0.001 | 0.64 | 0.59-0.71 | <0.001 |
| 5 least deprived | 1,414/4,121 (34.3) | 0.64 | 0.58-0.70 | <0.001 | 0.63 | 0.58-0.70 | <0.001 |
| **BCSP Exposure** |  |  |  |  |  |  |  |
| Control | 6,135/15,673 (39.1) | 1 | - | - | 1 | - | - |
| BCSP <6 months | 1,200/3.073 (39.0) | 1.00 | 0.92-1.08 | 0.922 | 0.96 | 0.88-1.04 | 0.337 |
| BCSP ≥6 months | 777/2,175 (35.7) | 0.86 | 0.79-0.95 | 0.002 | 0.85 | 0.77-0.94 | 0.001 |