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Health Technology Assessment

Volume 26 • Issue 26 • May 2022

ISSN 1366-5278

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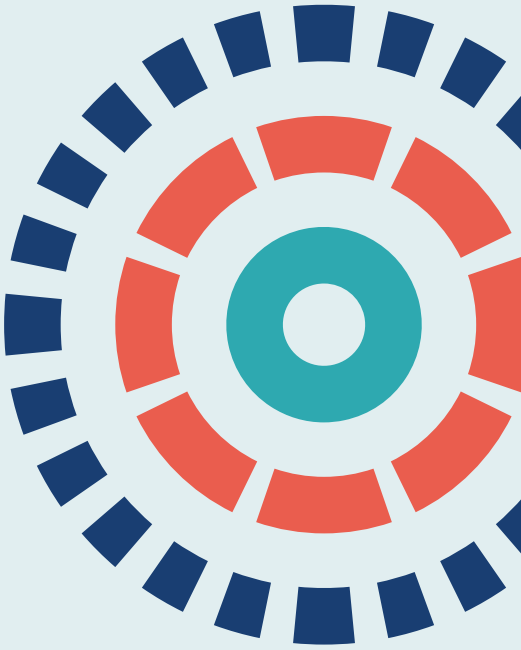

DOI 10.3310/OLUE3796

Colonoscopy surveillance following adenoma removal to reduce the risk of colorectal cancer: a retrospective cohort study

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Declared competing interests of authors: Amanda J Cross receives funding from Cancer Research UK (London, UK) (Population Research Committee – Programme Award C53889/A25004). Matthew D Rutter reports speaker honoraria from Swiss SCWeb AG (Lucerne, Switzerland) and PENTAX Medical (Tokyo, Japan), a grant from Olympus Corporation (Tokyo, Japan) and consultancy fees from Norgine BV (Amsterdam, the Netherlands) outside the submitted work. Brian P Saunders reports research grants, personal fees and non-financial support from Olympus Corporation, personal fees from Boston Scientific Corporation (Marlborough, MA, USA), Creo Medical Group plc (Chepstow, UK) and Norgine BV, a patent and royalty agreement with Diagmed Healthcare Ltd (Thirsk, UK) and Creo Medical Group plc, and equity in Creo Medical Group plc outside the submitted work. Alastair Gray is partly funded by the National Institute for Health and Care Research Biomedical Research Centre (Oxford, UK) and is a member of the UK National Screening Committee (London, UK) (2015–present).

Published May 2022
DOI: 10.3310/OLUE3796

This report should be referenced as follows:

Cross AJ, Robbins EC, Pack K, Stenson I, Kirby PL, Patel B, *et al*. Colonoscopy surveillance following adenoma removal to reduce the risk of colorectal cancer: a retrospective cohort study. *Health Technol Assess* 2022;**26**(26).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE, *Science Citation Index Expanded* (SciSearch®) and *Current Contents®*/ Clinical Medicine.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.014

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 15/80/13. The contractual start date was in March 2017. The draft report began editorial review in March 2020 and was accepted for publication in June 2020. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

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Abstract

Colonoscopy surveillance following adenoma removal to reduce the risk of colorectal cancer: a retrospective cohort study

Amanda J Cross,[1*] Emma C Robbins,[1] Kevin Pack,[1] Iain Stenson,[1] Paula L Kirby,[1] Bhavita Patel,[1] Matthew D Rutter,[2,3] Andrew M Veitch,[4] Brian P Saunders,[5] Matthew Little,[6] Alastair Gray,[6] Stephen W Duffy[7] and Kate Wooldrage[1]

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Background: Colonoscopy surveillance is recommended for some patients post polypectomy. The 2002 UK surveillance guidelines classify post-polypectomy patients into low, intermediate and high risk, and recommend different strategies for each classification. Limited evidence supports these guidelines.

Objectives: To examine, for each risk group, long-term colorectal cancer incidence by baseline characteristics and the number of surveillance visits; the effects of interval length on detection rates of advanced adenomas and colorectal cancer at first surveillance; and the cost-effectiveness of surveillance compared with no surveillance.

Design: A retrospective cohort study and economic evaluation.

Setting: Seventeen NHS hospitals.

Participants: Patients with a colonoscopy and at least one adenoma at baseline.

Main outcome measures: Long-term colorectal cancer incidence after baseline and detection rates of advanced adenomas and colorectal cancer at first surveillance.

Data sources: Hospital databases, NHS Digital, the Office for National Statistics, National Services Scotland and Public Health England.

Methods: Cox regression was used to compare colorectal cancer incidence in the presence and absence of surveillance and to identify colorectal cancer risk factors. Risk factors were used to stratify risk groups into higher- and lower-risk subgroups. We examined detection rates of advanced adenomas and colorectal cancer at first surveillance by interval length. Cost-effectiveness of surveillance compared with no surveillance was evaluated in terms of incremental costs per colorectal cancer prevented and per quality-adjusted life-year gained.

Results: Our study included 28,972 patients, of whom 14,401 (50%), 11,852 (41%) and 2719 (9%) were classed as low, intermediate and high risk, respectively. The median follow-up time was 9.3 years. Colorectal cancer incidence was 140, 221 and 366 per 100,000 person-years among low-, intermediate- and high-risk patients, respectively. Attendance at one surveillance visit was associated with reduced colorectal cancer incidence among low-, intermediate- and high-risk patients [hazard ratios were 0.56 (95% confidence interval 0.39 to 0.80), 0.59 (95% confidence interval 0.43 to 0.81) and 0.49 (95% confidence interval 0.29 to 0.82), respectively]. Compared with the general population, colorectal cancer incidence without surveillance was similar among low-risk patients and higher among high-risk patients [standardised incidence ratios were 0.86 (95% confidence interval 0.73 to 1.02) and 1.91 (95% confidence interval 1.39 to 2.56), respectively]. For intermediate-risk patients, standardised incidence ratios differed for the lower- (0.70, 95% confidence interval 0.48 to 0.99) and higher-risk (1.46, 95% confidence interval 1.19 to 1.78) subgroups. In each risk group, incremental costs per colorectal cancer prevented and per quality-adjusted life-year gained with surveillance were lower for the higher-risk subgroup than for the lower-risk subgroup. Incremental costs per quality-adjusted life-year gained were lowest for the higher-risk subgroup of high-risk patients at £7821.

Limitations: The observational design means that we cannot assume that surveillance caused the reductions in cancer incidence. The fact that some cancer staging data were missing places uncertainty on our cost-effectiveness estimates.

Conclusions: Surveillance was associated with reduced colorectal cancer incidence in all risk groups. However, in low-risk patients and the lower-risk subgroup of intermediate-risk patients, colorectal cancer incidence was no higher than in the general population without surveillance, indicating that surveillance might not be necessary. Surveillance was most cost-effective for the higher-risk subgroup of high-risk patients.

Future work: Studies should examine the clinical effectiveness and cost-effectiveness of post-polypectomy surveillance without prior classification of patients into risk groups.

Trial registration: This trial is registered as ISRCTN15213649.

Funding: This project was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 26, No. 26. See the NIHR Journals Library website for further project information.

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List of abbreviations

AA	advanced adenoma
BCSP	Bowel Cancer Screening Programme
CI	confidence interval
CRC	colorectal cancer
DSA	deterministic sensitivity analysis
EQ-5D	EuroQol-5 Dimensions
EQ-5D-3L	EuroQol-5 Dimensions, three-level version
EVPI	expected value of perfect information
FIT	faecal immunochemical test
HR	hazard ratio
IBD	inflammatory bowel disease
ICER	incremental cost-effectiveness ratio
IQR	interquartile range
LRT	likelihood ratio test
NIHR	National Institute for Health and Care Research
NSS	National Services Scotland
OR	odds ratio
PHE	Public Health England
PIAG	Patient Information Advisory Group
PPI	patient and public involvement
PROM	patient-reported outcome measure
PSA	probabilistic sensitivity analysis
QALY	quality-adjusted life-year
QoL	quality of life
SE	standard error
SIR	standardised incidence ratio
UK-ASG	UK adenoma surveillance guidelines

Plain English summary

Bowel cancers develop from polyps, also called adenomas, which are growths on the lining of the bowel. Removal of adenomas, therefore, helps prevent bowel cancer. Adenomas can be detected and removed during colonoscopy, when a thin tube with a camera on one end is used to examine the bowel lining. In the UK, patients with adenomas are divided into three risk groups. Low-risk patients (i.e. those with one or two adenomas that are < 10 mm in size) are thought to be unlikely to develop bowel cancer after adenoma removal and follow-up colonoscopy is not recommended in this group. Intermediate-risk patients (i.e. those with three or four adenomas that are < 10 mm in size, or one or two adenomas with at least one ≥ 10 mm in size) are recommended to have another colonoscopy 3 years after adenoma removal. High-risk patients (i.e. those with five or more adenomas that are < 10 mm in size, or three or more adenomas with at least one ≥ 10 mm in size) are recommended to have another colonoscopy after 1 year and then usually again after 3 years.

The number of follow-up colonoscopies carried out is stretching health-care resources and each procedure carries a small risk of complications for patients. It is possible that too many follow-up colonoscopies are being carried out. This study aimed to determine which patients require follow-up colonoscopies and how many are required to detect adenomas and prevent bowel cancer, while also being resource-efficient, cost-effective and not exposing patients to unnecessary risks.

The study used data from 17 hospitals and cancer registries in the UK. In each risk group, one follow-up colonoscopy after adenoma removal was associated with a 40–50% reduction in bowel cancer risk. However, even without any follow-up, bowel cancer risk was no higher in some low- and intermediate-risk patients than in the general population. These patients may not need as many follow-up colonoscopies as recommended. In the case of higher-risk patients, who even after adenoma removal have a higher bowel cancer risk than the general population, follow-up colonoscopies are necessary and cost-effective.

Scientific summary

Background

Adenomas are the precursors of most colorectal cancers and their removal by polypectomy reduces colorectal cancer incidence and mortality. However, some patients are thought to remain at increased risk of colorectal cancer following polypectomy and are recommended surveillance by colonoscopy. The 2002 UK adenoma surveillance guidelines were in place when this study started in 2006. These guidelines divide patients into low-, intermediate- and high-risk groups based on the number and size of baseline adenomas. No surveillance or 5-yearly surveillance is recommended for low-risk patients; however, 3-yearly surveillance is recommended for intermediate-risk patients and surveillance at 1 year and then usually every 3 years is recommended for high-risk patients. The evidence supporting the guidelines is limited as few high-quality data are available on post-polypectomy colorectal cancer risk or on the effects of surveillance on colorectal cancer risk.

Objectives

We aimed to examine the need for, and benefit of, post-polypectomy surveillance among each risk group in terms of detecting advanced adenomas and preventing colorectal cancer while being cost-effective and minimising exposure of patients to unnecessary colonoscopies.

The main objectives were to examine, for each risk group, heterogeneity of long-term colorectal cancer incidence by baseline characteristics and number of surveillance visits; detection rates of advanced adenomas and colorectal cancer at the first surveillance visit by surveillance interval length; and the cost-effectiveness of adopting surveillance compared with no surveillance.

Methods

We performed this retrospective multicentre cohort study using data from 17 hospitals in the UK. Participating hospitals were required to have electronically recorded endoscopy and pathology data for patients undergoing colonic examination for at least 6 years before the start of the study in 2006.

Hospital endoscopy databases were searched to identify patients who had undergone colonic examination before 31 December 2010. Pathology databases were then searched for reports of colorectal lesions. Endoscopy and pathology records were matched and pseudo-anonymised. Data from the records were entered into an Oracle database (Oracle Corporation, Redwood City, CA, USA). Patient, procedural and polyp data were coded using standard operating procedures. Summary values for polyp size, histology and location were assigned to polyps seen at more than one examination.

Once we had identified patients with a colonic examination before the end of 2010, we looked in these patients' records to identify the first diagnosis of an adenoma, which we defined as baseline. In some patients, multiple examinations were performed at baseline to achieve complete examination of the colon and remove all detected lesions. These examinations were grouped together and defined as the baseline visit. We grouped subsequent colonic examinations into surveillance visits. Surveillance interval was defined as the time between the latest most complete examination in one visit to the first examination in the next visit.

We included patients in whom colonoscopy was performed and at least one adenoma was diagnosed during the baseline visit. We excluded patients who had colorectal cancer at or before baseline; a bowel resection at or before baseline; Lynch syndrome or a family history of familial adenomatous polyposis; inflammatory bowel disease or colitis at baseline; polyposis, juvenile polyps or hamartomatous polyps; or colorectal carcinoma in situ reported in registry data > 3 years before baseline. We also excluded patients who had an examination without a date recorded or for whom information needed for risk group classification was missing.

We classified patients into three risk groups in accordance with the 2002 UK adenoma surveillance guidelines. Low-risk patients were those with one or two small (i.e. < 10 mm in size) adenomas. Intermediate-risk patients were those with three or four small adenomas or one or two adenomas of which at least one was ≥ 10 mm in size. High-risk patients were those with five or more small adenomas or three or more adenomas of which at least one was ≥ 10 mm in size.

Primary outcomes were long-term colorectal cancer incidence after baseline and the first surveillance visit, and detection rates of advanced adenomas and colorectal cancer at first surveillance. We defined advanced adenomas as adenomas ≥ 10 mm in size or with villous or tubulovillous histology or high-grade dysplasia. We included adenocarcinomas of the colorectum as colorectal cancer outcomes. Advanced adenomas and colorectal cancer were ascertained using pathology data stored on the study database. We also obtained data on colorectal cancer diagnoses and deaths from NHS Digital, the NHS Central Register and National Services Scotland through 2016. Primary exposures of interest were the number of surveillance visits and the length of the surveillance interval from baseline to first surveillance.

Cox proportional hazards models were used to compare long-term colorectal cancer incidence in the presence and absence of surveillance, with adjustment for baseline patient, procedural and polyp characteristics. Time at risk started from the latest most complete examination at baseline (for the analysis of incidence after baseline) or the last examination in the first surveillance visit (for the analysis of incidence after first surveillance). Exposure to successive surveillance visits started at the last examination in each visit. Time-to-event data were censored at first diagnosis of colorectal cancer or a condition affecting colonic surveillance regimen, bowel resection, death, emigration or date of complete ascertainment of cases in cancer registries.

Independent risk factors for colorectal cancer were identified in multivariable Cox proportional hazards models, using backward stepwise selection to retain variables with *p*-values of < 0.05 in the likelihood ratio test. Risk factors were used to stratify each risk group into higher- and lower-risk subgroups. One minus the Kaplan–Meier estimator of the survival function was used to show time to cancer diagnosis and estimate cumulative colorectal cancer incidence with 95% confidence intervals at 3, 5 and 10 years. Standardised incidence ratios were calculated to compare colorectal cancer incidence with that in the general population of England in 2007.

We examined detection rates of advanced adenomas and colorectal cancer at the first surveillance visit by surveillance interval length, overall and by risk subgroup.

We performed an economic evaluation to examine the cost-effectiveness of adopting surveillance compared with no surveillance for each risk group overall and by risk subgroup. In a within-study analysis, we used individual patient-level data recorded in the main study database to compare the costs and outcomes of patients who received surveillance with those who received no surveillance. In this analysis, cost-effectiveness was assessed in terms of the incremental costs per colorectal cancer prevented by adopting surveillance. We also performed a lifetime analysis in which we extrapolated the results from the within-study analysis over a lifetime horizon using a Markov model. Cost-effectiveness in this analysis was assessed in terms of the incremental costs per quality-adjusted life-year gained by adopting surveillance. We used a cost-effectiveness threshold of £20,000 per quality-adjusted life-year.

Results

A total of 28,972 patients were included in our study, of whom 14,401 (50%) were classed as low risk, 11,852 (41%) as intermediate risk and 2719 (9%) as high risk, according to the 2002 UK adenoma surveillance guidelines. The median follow-up time was 9.3 years. In the low-, intermediate- and high-risk groups colorectal cancer incidence per 100,000 person-years was 140 (95% confidence interval 122 to 162 per 100,000 person-years), 221 (95% confidence interval 195 to 251 per 100,000 person-years) and 366 (95% confidence interval 295 to 453 per 100,000 person-years), respectively. Compared with no surveillance, attendance at one surveillance visit was associated with reductions in colorectal cancer incidence in the low-, intermediate- and high-risk groups [hazard ratios 0.56 (95% confidence interval 0.39 to 0.80), 0.59 (95% confidence interval 0.43 to 0.81) and 0.49 (95% confidence interval 0.29 to 0.82), respectively].

We identified higher- and lower-risk subgroups within each risk group based on the presence of baseline risk factors for colorectal cancer. In the low-risk group, the higher-risk subgroup comprised patients whose baseline colonoscopy had been incomplete or of unknown completeness, or who had a tubulovillous or villous adenoma or proximal polyps at baseline ($n = 9166$, 64%), and the lower-risk subgroup comprised patients with none of these baseline characteristics ($n = 5235$, 36%). In the intermediate-risk group, the higher-risk subgroup comprised patients whose baseline colonoscopy had been incomplete or of unknown completeness, or who had an adenoma with high-grade dysplasia or proximal polyps at baseline ($n = 7114$, 60%), and the lower-risk subgroup comprised patients with none of these baseline characteristics ($n = 4738$, 40%). In the high-risk group, patients whose baseline colonoscopy had been incomplete or of unknown completeness, or who had an adenoma with high-grade dysplasia at baseline, were classed as higher risk ($n = 902$, 33%), whereas patients with none of these characteristics were classed as lower risk ($n = 1817$, 67%).

In the whole low-risk group, colorectal cancer incidence after baseline was not significantly different as compared with the general population in the absence of surveillance (standardised incidence ratio 0.86, 95% confidence interval 0.73 to 1.02). This was also true for the higher-risk subgroup of low-risk patients (standardised incidence ratio 1.07, 95% confidence interval 0.88 to 1.28). In the lower-risk subgroup, colorectal cancer incidence without surveillance was lower than in the general population (standardised incidence ratio 0.51, 95% confidence interval 0.35 to 0.73).

Among all intermediate-risk patients, colorectal cancer incidence after baseline was not significantly higher than in the general population in the absence of surveillance (standardised incidence ratio 1.16, 95% confidence interval 0.97 to 1.37). In the lower-risk subgroup of intermediate-risk patients, colorectal cancer incidence without surveillance was lower than in the general population (standardised incidence ratio 0.70, 95% confidence interval 0.48 to 0.99). By contrast, in the higher-risk subgroup, colorectal cancer incidence without surveillance was higher than in the general population (standardised incidence ratio 1.46, 95% confidence interval 1.19 to 1.78). After the first surveillance visit, colorectal cancer incidence was no longer higher in the higher-risk subgroup than in the general population (standardised incidence ratio 1.00, 95% confidence interval 0.73 to 1.33).

In the whole high-risk group, colorectal cancer incidence after baseline was higher than in the general population without surveillance (standardised incidence ratio 1.91, 95% confidence interval 1.39 to 2.56). This was also true for the higher-risk subgroup of high-risk patients (standardised incidence ratio 3.55, 95% confidence interval 2.34 to 5.17). In the lower-risk subgroup, colorectal cancer incidence without surveillance was not significantly different from that in the general population (standardised incidence ratio 1.10, 95% confidence interval 0.64 to 1.76).

After first surveillance, colorectal cancer incidence was no longer significantly higher in the whole high-risk group than in the general population (standardised incidence ratio 1.34, 95% confidence interval 0.86 to 1.99), but it remained higher in the higher-risk subgroup of the high-risk group

(standardised incidence ratio 1.97, 95% confidence interval 1.02 to 3.44). After a second surveillance visit, colorectal cancer incidence was no longer higher in the higher-risk subgroup than in the general population (standardised incidence ratio 1.02, 95% confidence interval 0.41 to 2.09).

In all three risk groups, attendance at one or more surveillance visits, compared with no surveillance, was associated with reduced colorectal cancer incidence in the higher-risk subgroup, but not in the lower-risk subgroup. However, estimates for the lower-risk subgroups were imprecise because of the small number of colorectal cancer cases. In all three risk groups, colorectal cancer incidence was lower with attendance at two or more surveillance visits than with attendance at only one. This pattern was also observed in the higher-risk subgroups of each risk group, but not in the lower-risk subgroups. However, estimates for the lower-risk subgroups lacked precision.

At the first surveillance visit, detection rates of advanced adenomas and colorectal cancer were $< 10\%$ and $< 2\%$, respectively, with all intervals through to 6 years among low-risk patients and all intervals to 3 years among intermediate-risk patients. In the higher-risk subgroup of intermediate-risk patients, the detection rate of colorectal cancer increased from approximately 1–2% to 4% when the interval extended beyond 3 years. Among high-risk patients, advanced adenoma detection rates were $\geq 11\%$ with all intervals, whereas colorectal cancer detection rates were 1% with intervals < 1.5 years, increasing to 3% with an interval of 2 years.

In the within-study economic analysis, the incremental cost per colorectal cancer prevented by adopting surveillance was higher in the lower-risk subgroup of low-risk patients (£453,221) than in the higher-risk subgroup (£127,945). This pattern was also observed in the intermediate-risk group, in which equivalent costs in the lower- and higher-risk subgroups were £2,587,860 and £145,729, respectively. In the high-risk group, the incremental cost per colorectal cancer prevented was £568,719 in the lower-risk subgroup and £36,636 in the higher-risk subgroup.

In the lifetime economic analysis, the incremental cost per quality-adjusted life-year gained by adopting surveillance was £136,496 and £27,341, respectively, in the lower- and higher-risk subgroups of the low-risk group. In the intermediate-risk group, surveillance was dominated by (i.e. more costly and less effective than) no surveillance in the lower-risk subgroup, whereas the incremental cost per quality-adjusted life-year gained with surveillance in the higher-risk subgroup was £46,990. In the high-risk group surveillance was dominated in the lower-risk subgroup, whereas the incremental cost per quality-adjusted life-year gained with surveillance in the higher-risk subgroup was £7821.

Limitations

The study is an observational study and, therefore, we cannot assume that surveillance caused the observed reductions in colorectal cancer incidence. Limitations of the economic evaluation include missing cancer staging data and uncertainty around quality-of-life estimates, which place uncertainty on our cost-effectiveness estimates.

Conclusions

Implications for health care

In all three risk groups, surveillance was associated with reduced post-polypectomy colorectal cancer incidence. However, even without surveillance, colorectal cancer incidence following a complete baseline colonoscopy was no higher in the whole low-risk group or in the lower-risk subgroup of intermediate-risk patients (i.e. intermediate-risk patients without high-grade dysplasia or proximal polyps at baseline) than in the general population. This indicates that surveillance might not be necessary for these patients who could potentially be managed instead by routine colorectal cancer screening.

In contrast, we showed that surveillance is likely to be warranted for the higher-risk subgroup of intermediate-risk patients (i.e. those whose baseline colonoscopy was not complete or who had high-grade dysplasia or proximal polyps at baseline) and the whole high-risk group. These patients remained at increased risk of colorectal cancer following adenoma removal, compared with the general population, and benefited significantly from attending at least one surveillance visit. Our results suggest that a 3-year surveillance interval is likely to be appropriate for the higher-risk subgroup of intermediate-risk patients. The optimal surveillance interval for high-risk patients remains uncertain.

The results from our economic evaluation indicate that for each risk group surveillance is more cost-effective for the higher-risk subgroup than for the lower-risk subgroup, and surveillance is highly cost-effective for the higher-risk subgroup of high-risk patients.

Recommendations for research

- Large randomised controlled trials of post-polypectomy patients with long-term follow-up and additional economic evaluations are needed to determine the optimal number of, and interval between, surveillance visits for higher-risk patients.
- Future studies should examine the clinical effectiveness and cost-effectiveness of post-polypectomy surveillance in all patients with adenomas, without prior classification of patients into risk groups.
- Data are required on long-term colorectal cancer incidence following the removal of serrated polyps.
- Additional studies should gather quality-of-life data from patients with colorectal cancer.
- Research is required to understand barriers to and facilitators of patients' adherence to surveillance.
- Future studies should investigate surveillance strategies based on the faecal immunochemical test and other technologies and biomarkers.

Trial registration

This trial is registered as ISRCTN15213649.

Funding

This project was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 26, No. 26. See the NIHR Journals Library website for further project information.

Chapter 1 Introduction

Context and rationale for the research

Adenomas are the precursor lesions of most colorectal cancers (CRCs), and removal of adenomas by polypectomy prevents development of CRC.[1–5] However, as adenomas tend to recur, some patients remain at increased risk of CRC following polypectomy.[6] National guidelines, therefore, recommend surveillance by colonoscopy.[7–10]

The 2002 UK adenoma surveillance guidelines (UK-ASG) divide patients with adenomas into three risk groups according to the size and number of adenomas removed at baseline colonoscopy, and recommend different surveillance strategies for each group.[7] In the low-risk group, comprising patients with one or two small adenomas (i.e. < 10 mm in size), the guidelines recommend either no surveillance or surveillance at 5 years. In the intermediate-risk group, comprising patients with three or four small adenomas or one or two adenomas of which at least one is ≥ 10 mm in size, 3-yearly surveillance is recommended. In the high-risk group, comprising patients with five or more small adenomas or three or more adenomas of which at least one is ≥ 10 mm in size, surveillance is recommended at 1 year and then usually every 3 years.

The UK-ASG were developed at a time when few high-quality data were available to inform the risk group definitions. The risk groups were defined mostly based on evidence from studies that used detection rates of advanced adenomas (AAs) at follow-up colonoscopy as a proxy for CRC risk.[11–14] The use of AAs as a surrogate for CRC is limited because the malignant potential of AAs varies[6] and AAs are detected more frequently at follow-up than CRC, resulting in overestimations of risk.[14,15]

The evidence used to inform the surveillance recommendations was also limited. Namely, the recommendation for 3-yearly surveillance in intermediate-risk patients was based mainly on one trial[14] that showed that the detection rate of advanced colorectal neoplasia (AAs or CRC) was the same (i.e. 3%) among patients attending surveillance at 1 and 3 years, and at 3 years only. A second study[15] reported higher rates of advanced colorectal neoplasia among patients undergoing surveillance at 4 years (i.e. 9%) than in those examined at 2 years (i.e. 5%), but the difference was not significant. Additional evidence to inform optimal surveillance intervals was not available.

A further limitation of the UK-ASG was that they were developed prior to the significant improvements in colonoscopy quality seen over the past two decades. These improvements, driven by the implementation of colonoscopy quality improvement initiatives in 2001 and the introduction of new endoscopic technologies and techniques,[16,17] saw rates of post-colonoscopy CRCs fall by 30% from 2001 to 2007.[18] Therefore, it is likely that patients now receiving high-quality baseline colonoscopies are at lower risk of CRC and require less surveillance than is recommended in the 2002 UK-ASG.

In 2004, the Department of Health and Social Care issued a call for research proposals to examine the optimal frequency of post-polypectomy surveillance, specifically focusing on the intermediate-risk group, which accounts for the majority of surveillance colonoscopies.[19] This call was issued in anticipation that the introduction of the national Bowel Cancer Screening Programme (BCSP) in 2006 would lead to more individuals having adenomas detected and being funnelled into surveillance. There was concern that the increased demand for surveillance would overwhelm already overstretched endoscopy services.

In response to this call, we performed a retrospective cohort study assessing CRC incidence among intermediate-risk patients over a median of 7.9 years and estimated the effects of surveillance on CRC incidence.[20] Our findings suggested that the intermediate-risk group can be divided into higher- and lower-risk subgroups. The higher-risk subgroup comprised patients with an incomplete colonoscopy or colonoscopy of unknown completeness, poor bowel preparation, adenoma $\geq$ 20 mm in size or with high-grade dysplasia, or proximal polyps at baseline. These patients had a higher CRC risk than the general population following baseline colonoscopy and polypectomy, and they derived significant benefit from attending at least one surveillance visit. In contrast, among lower-risk patients without these baseline features, CRC risk was no higher than in the general population before any surveillance. We therefore suggested that surveillance might not be necessary for the lower-risk subgroup.

These findings suggest that adequate protection against the development of CRC can be achieved with less surveillance than is currently recommended. This is of timely importance as surveillance represents a substantial burden on endoscopy resources, accounting for 20% of all colonoscopies performed in the UK.[21] Additionally, as colonoscopy is an invasive procedure associated with a small risk of serious complications,[22] it is important that surveillance is directed to patients who remain at an increased CRC risk following polypectomy compared with the general population. It was, therefore, seen as a priority to revise the 2002 UK-ASG to minimise the number of unnecessary colonoscopies while ensuring that patients at increased CRC risk undergo surveillance.

Aims and objectives

The overall aim of the study was to examine the need for, and benefit of, post-polypectomy surveillance among each of the three risk groups defined in the UK-ASG, in terms of detecting AAs and preventing CRC, while being cost-effective and minimising exposure of patients to unnecessary colonoscopies.

The primary objectives were to examine, for each risk group, heterogeneity in long-term CRC incidence by baseline patient, procedural and polyp characteristics and number of surveillance visits, and detection rates of AAs and CRC at the first surveillance visit by surveillance interval length. The aim of the economic evaluation was to evaluate the cost-effectiveness of adopting surveillance compared with no surveillance for each risk group. The objectives of the within-study analysis and lifetime analysis were to assess cost-effectiveness in terms of incremental costs per CRC prevented and incremental costs per quality-adjusted life-year (QALY) gained, respectively.

Study design and setting

This was a retrospective multicentre cohort study, performed using data from 17 NHS hospitals. The hospitals included teaching and general hospitals and were located throughout the UK. We obtained endoscopy and pathology data from these hospitals on patients undergoing diagnostic and surveillance colonic examinations. For the economic evaluation, we conducted both a within-study analysis (using resource use and outcomes data from the main study) and a lifetime analysis (using a Markov model).

Structure of this report

We describe the methods in *Chapter 2*, the findings from the main analyses in *Chapter 3* and the economic evaluation in *Chapter 4*. We describe how patients and the public were involved in the study in *Chapter 5*. In *Chapter 6* we present a synthesis of all the findings and discuss the strengths and limitations, implications for practice and research recommendations.

Chapter 2 Methods

For the present study, the methods used to select hospitals for inclusion, collect data from participating hospitals; transform, clean and code data; and define study variables were the same as for our previous study[23] of the intermediate-risk group. These methods are described in full in the National Institute for Health and Care Research (NIHR) final report of this previous study[23] and are summarised in this chapter.

Hospital selection

To be selected for inclusion in the study, hospitals were required to have electronically recorded endoscopy and pathology data for lower gastrointestinal procedures for at least 6 years prior to the start of the study in 2006. We contacted endoscopy and pathology database manufacturers to identify potentially eligible hospitals. A total of 28 NHS hospitals were identified, and we contacted each of these to request their participation in the study. Of the 28 hospitals, 10 were excluded because of difficulties in obtaining research and development approval, problems with data extraction or missing data (see *Appendix 1*, *Table 23*).

These exclusions left 18 hospitals, two of which were subsequently merged into one site. Therefore, in total, 17 hospital sites were included in the study, which are listed in the *Acknowledgements*.

Data collection, matching and pseudo-anonymisation

We first searched hospital endoscopy databases for patients who had undergone colonic examination before 31 December 2010. We extracted data from relevant reports, including the date of examination, type of examination, name of endoscopist, indications, bowel preparation quality, colonic segment reached, polyp size, shape and location, information on any biopsies taken, complications, diagnoses and endoscopist comments. We also extracted the following pieces of patient-identifiable information: forename(s), surname, date of birth, sex, hospital number(s), NHS number and postcode. We removed duplicate patient identifiers and resolved any other inconsistencies and errors, and then assigned each patient a unique study number.

We searched pathology databases for reports of colorectal lesions using Systematized Nomenclature of Medicine codes (SNOMED) (versions 2 and 3), Systematized Nomenclature of Pathology codes (the first four digits of SNOMED version 2 codes), keywords or multiple search terms. We extracted data from relevant reports, including the date of the report, unique report number, type of examination at which the pathology specimen was collected, number of specimens and histopathology results.

We matched endoscopy and pathology extracts based on name, date of birth and hospital number. We removed all patient identifiers except for date of birth, and encrypted the data before removing it from the hospital. We stored patient identifiers with the corresponding unique study number in a patient-linking file in Microsoft Excel® (.xls or .xlsx format) (Microsoft Corporation, Redmond, WA, USA). We encrypted the patient-linking files and copied them onto compact discs, together with the raw endoscopy and pathology data. The compact discs were stored at each hospital in a secure location and were supervised by the local principal investigator.

The study database

We developed a bespoke study database to store the patient data. We transformed, cleaned and automatically coded the data, when possible, so that these could be stored in a standardised, structured format. Data were classified as quantitative or qualitative variables. Reference data

(or look-up tables) were used to define the set of permissible values for the data fields. This helped to ensure that data from different hospitals were coded in the same way. We stored the transformed data on the study database together with the raw endoscopy and pathology data, in case data loss occurred during subsequent coding. We used programming techniques to identify ineligible patients and automatically exclude them. Approximately 17% of patients were excluded in this way.

Manual coding

We went through the records of the remaining patients who were not automatically excluded, checking that any automatic coding was correct and performing additional manual coding tasks. We developed a web-based coding application on which we performed these coding tasks. We developed standard operating procedures to describe the methods and rules for coding to ensure uniformity of coding. The standard operating procedures are detailed in the appendices of our previous NIHR final report.[23] Regular coding audits were carried out to check consistency.

Coding tasks included:

- checking that endoscopy and pathology reports were matched properly
- coding raw endoscopy and pathology data into structured data
- creating pathology-based endoscopy reports when pathology reports did not have a linked endoscopy report
- assigning polyps a unique polyp number if they were seen at more than one examination
- creating individual polyp records from endoscopy reports that described polyps as groups
- creating summary values for polyp characteristics that were described in multiple data fields
- coding the date, type and quality of endoscopic examination
- defining baseline and surveillance visits.

The final five coding tasks are discussed further below. For a full description of the first three tasks, please refer to the appendices of our previous NIHR final report.[23]

Polyp numbering

We assigned a unique polyp number to polyps seen at more than one examination so that different sightings could be linked. We thought that different sightings were likely to be of the same polyp when sightings were in the same or adjacent colonic segment, there was an indication that a polyp seen at an earlier examination had not been completely removed, bowel preparation quality at an earlier examination was poor and/or the grades of dysplasia and histology reported at the different sightings were similar. We assigned a match probability to sightings to indicate our confidence that they were of the same polyp. Match probabilities were estimated to the nearest 10%. We considered sightings matched with a probability of $\geq$ 70% to be of the same polyp.

Polyp groups

When polyps were described as groups rather than as individual polyps we created a single record for each polyp group. We then populated the record with information on the number, size, shape, histopathology and location of polyps in the group. We assigned a unique group number to each polyp group and a group-linking number to polyp groups seen at more than one examination. When information was recorded for an individual polyp within a group we created an individual polyp record and linked it to the group record.

Terms such as ‘some’, ‘several’ and ‘many’ were often used to describe the number of polyps in a group. We assigned numeric values to these descriptive terms (e.g. some = 3), using the median value calculated from endoscopy reports that gave both a descriptive term and an exact polyp number. Once we had an estimate for the number of polyps in each group we created individual polyp records from the group records. Information recorded for the group was replicated in the individual polyp records.

Summary values for polyp characteristics

Polyp characteristics were often described in multiple data fields on the study database, particularly if the polyp was seen at more than one examination. In such cases, we combined all available data to create summary values for polyp size, shape, histology and location, using hierarchies of rules.

Polyp size

We created three derived polyp size values: (1) derived-endoscopy-size, (2) derived-pathology-size and (3) derived-endoscopy-size-descriptor. Derived-endoscopy-sizes were created by combining the exact polyp size (in mm) on the endoscopy report with any reported minimum and maximum sizes, using a hierarchy of rules. Minimum and maximum sizes were reported when sizes were given as ranges (e.g. 7–10 mm). Most pathology reports gave an exact polyp size, which was used as the derived-pathology-size. Derived-endoscopy-size-descriptors were created by assigning numeric values to descriptors of polyp size that were qualitative or approximate; for example, for polyps described as 'tiny' or '< 10mm', we assigned values of 3 mm and 8 mm, respectively. In most cases, we assigned the median value calculated from endoscopy reports, which gave both a descriptive term and an exact polyp size.

For each polyp we identified the largest of each derived polyp size, comparing across examinations. We then compared the largest derived sizes and, in most cases, used the largest of these as the summary polyp size. However, when the largest size was the derived-endoscopy-size-descriptor, the largest derived-endoscopy-size or derived-pathology-size was used instead, if available.

Polyp shape

We used the first recorded description of the shape of a polyp as the summary value. We did this because polyp shape can change after a biopsy or resection is performed and so the first record is likely to be the most accurate. There were three shape values: (1) pedunculated (i.e. attached to the bowel wall by a stalk), (2) sessile (i.e. no stalk) and (3) flat. We used the polyp shape values, together with histopathology values described below, to classify polyps into different categories, such as hyperplastic polyps or adenomas (see *Appendix 1*, *Table 24*).

Polyp histopathology

Histopathological data were available for two-thirds of polyps. For the other one-third, histopathological data were missing because the polyp was not retrieved at endoscopy, the polyp was not described in the pathology report, a biopsy was not taken or we could not find a pathology report at the hospital.

For polyps with histopathological data we assumed that those with any villous features or dysplasia were adenomas. For polyps without histopathological data we assumed that those $\geq$ 10 mm in size were adenomas if the patient had at least one recorded sighting of an adenoma. Histopathology was coded as 'specimen not seen' or 'not able to diagnose' when histopathological data were not recorded at any polyp sighting.

Some adenomas sighted multiple times were not recorded as adenomas at the first sightings. In such cases, we mapped the diagnosis of an adenoma back to the earlier sightings, if the earlier sightings occurred within 3 years of the adenoma diagnosis. Polyps sighted multiple times also sometimes had different histopathological features recorded at each sighting. In these cases, we compared the records and gave precedence to the histopathological outcomes of interest (see *Appendix 1*, *Table 24*) over other histopathological outcomes.

Polyp location

Polyp location was defined according to the colonic segment in which the polyp was found. Colonic segments included the ileum, caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, rectosigmoid, rectum and anus. We used a number of rules to derive a summary value for polyp location:

- If a surgical procedure was performed, we used the segment recorded at that procedure.

- If a surgical procedure was not performed, we used the segment mentioned most frequently at other procedures.
- If no segment was mentioned more frequently than any other, we used the most distal segment. (Distal was defined as anus to sigmoid colon and proximal was defined as descending colon to terminal ileum.)
- If a segment range was given, we recorded this range on the study database.
- If more than one segment range was given, we recorded the narrowest segment range on the study database, provided that the most distal and proximal segments in the range were no more than two segments apart (see *Appendix 1*, *Table 25*). If the most distal and proximal segments were more than two segments apart, we manually reviewed the records to help reach a decision.

Colonic examinations

Examination date

In most cases, the date recorded on the endoscopy report was used as the examination date. However, when there was no endoscopy report, the examination date was derived from the pathology report. When multiple dates were given on the pathology report, precedence was given in the following order: (1) to the date that the biopsy was performed, (2) to the date that the biopsy sample arrived at the pathology laboratory and (3) to the date of the pathologist's report. We excluded the patient from the study when an examination date could not be derived.

Examination type

We determined the type of endoscopic examination that had been carried out by examining the hospital endoscopy report and, if this was not available, the pathology report. These reports covered a range of examination types, including colonoscopy, sigmoidoscopy and surgery.

When the type of examination was not specified, we assumed that examinations reaching the transverse colon or beyond were colonoscopies. If information on bowel preparation quality and depth of insertion was recorded, the examinations were assumed to be either a colonoscopy or flexible sigmoidoscopy, as were examinations at which a large lesion (i.e. $\geq$ 10 mm in size) or three or more adenomas were removed.

Examination quality

Examination completeness was determined based on the colonic segment reached, the most proximally recorded polyp, the quality of bowel preparation before the examination and whether or not the examination was recorded as incomplete. Examinations were defined as complete if the endoscope reached the caecum or polyps were found in the caecum or beyond. Bowel preparation quality was graded as excellent, good, satisfactory or poor.

Defining baseline and surveillance visits

We divided examinations into visits, defined as one or more examinations performed in close succession, to achieve a full examination of the colon and remove all detected lesions. The baseline visit included the earliest examination at which an adenoma was sighted and any examinations occurring within the following 11 months. A time period of 11 months was chosen because a longer period might have captured surveillance examinations performed in high-risk patients in whom surveillance at 1 year is recommended.

In some cases it was necessary to extend the baseline visit to capture examinations occurring within 6 months of the last baseline examination. We did this because examinations occurring so soon after baseline were unlikely to be surveillance examinations. In a few rare cases we extended the baseline a second time to capture examinations occurring 6–9 months after the last baseline examination. This was done in the below scenarios:

- The last baseline examination was incomplete or had poor bowel preparation.
- A polyp $\geq$ 15 mm in size was seen at the last baseline examination.

- The same polyp was seen at the last baseline examination and at the examination occurring within 6–9 months.
- A surgical procedure was performed shortly after the last baseline examination.

Surveillance visits included the first examination after baseline (or after a previous surveillance visit) and any examinations occurring within the following 11 months. When necessary, we extended the surveillance visit using the same criteria described previously for the extension of the baseline visit.

Once we had grouped examinations into baseline and surveillance visits, we defined examination completeness and bowel preparation quality according to the most complete examination and best bowel preparation achieved during a visit, respectively. Similarly, we defined adenoma histology and dysplasia according to the greatest degree of villous architecture and highest grade of dysplasia recorded in a visit, respectively.

It was important to determine whether or not patients had a colonoscopy during the baseline visit because this was necessary for inclusion in the study. Therefore, we reviewed the records of patients whose baseline visit was coded as 'colonoscopy or sigmoidoscopy'. In the case of patients diagnosed with three or more adenomas or an adenoma $\geq$ 10 mm in size or with tubulovillous or villous histology or high-grade dysplasia at baseline, we assumed that colonoscopy rather than sigmoidoscopy had been performed.

In the case of other patients it was clear that colonoscopy had been performed at the first surveillance visit but not during the baseline visit. In our previous study of intermediate-risk patients,[23] in all such cases the first surveillance visit was reassigned as the baseline visit and the original baseline visit was designated as a 'prior' visit. For patients in the present study this reassignment of baseline was applied only if the interval between the first examination in baseline and the first examination in the first surveillance visit was $<$ 3 years. The cut-off point of 3 years was used as it is the recommended surveillance interval for intermediate-risk patients.[7] When we came to stratify the patients into risk groups we considered any adenomas diagnosed at the prior visit in the determination of risk, in addition to those diagnosed at the new baseline visit.

Patient selection and follow-up

We included patients in whom colonoscopy was performed and at least one adenoma was diagnosed during the baseline visit. We excluded patients who had CRC at or before baseline; had undergone bowel resection at or before baseline; had Lynch syndrome or a family history of familial adenomatous polyposis; had inflammatory bowel disease (IBD) or colitis at baseline; had polyposis, juvenile polyps or hamartomatous polyps; had colorectal carcinoma in situ reported in registry data $>$ 3 years before baseline; or had undergone any examination without a date recorded. We also excluded patients for whom the information required for risk group classification was missing. In a sensitivity analysis we additionally excluded patients who did not have a complete colonoscopy at baseline.

We classified patients into low-, intermediate- and high-risk groups according to the characteristics of baseline adenomas, as per the 2002 UK-ASG.[7] Patients were classed as low risk if they had one or two small (i.e. $<$ 10 mm in size) adenomas. Patients were classed as intermediate risk if they had three or four small adenomas or one or two adenomas of which at least one was $\geq$ 10 mm in size. Patients were classed as high risk if they had five or more small adenomas, or three or more adenomas of which at least one was $\geq$ 10 mm in size.

We obtained data on CRC diagnoses and deaths occurring among our study cohort from NHS Digital, NHS Central Register and National Services Scotland (NSS) through 2016 and uploaded these data to the study database. We compared the cancer data with the pathology data already stored on the database and resolved any duplications and discrepancies.

Variables

Outcomes and exposures

The primary outcome measures were long-term CRC incidence after baseline and the first surveillance visit and detection rates of AAs and CRC at the first surveillance visit. Outcomes of AA and CRC were ascertained using pathology data stored on the study database and cancer data from national data sources (for CRC).

We defined AAs as adenomas ≥ 10 mm in size or with villous or tubulovillous histology, or high-grade dysplasia. We defined CRC sites by the *International Classification of Diseases* revisions 8, 9 and 10,[24–26] including codes C18–C20. We defined CRC morphology by the *Manual of Tumor Nomenclature and Coding*[27] and the *International Classification of Diseases for Oncology* revisions 1 and 2.[28,29] We included adenocarcinomas of the colorectum as CRC outcomes, as well as cancers with unspecified morphology but assumed to be adenocarcinomas (i.e. those located between the rectum and caecum). Cancers with unspecified morphology but assumed to be squamous cell carcinomas (i.e. those located around the anus) and in situ cancers were not included as CRC outcomes.

We excluded CRCs that we assumed had developed from lesions that were incompletely resected at baseline. We did this because we thought that their inclusion could bias our estimates of CRC risk and lead to inappropriate surveillance recommendations. We assumed that CRCs had arisen from an incompletely resected lesion if all of the below criteria were met:

- The CRC was found in the same or adjacent colonic segment to a baseline lesion.
- The baseline lesion was an adenoma.
- The baseline adenoma was ≥ 15 mm in size.
- The baseline adenoma was seen on two or more occasions within 5 years before the cancer diagnosis.

In a sensitivity analysis we excluded some additional cancers that met some but not all the criteria above that we thought were likely to have arisen from an incompletely resected baseline lesion.

For our analyses of findings at the first surveillance visit we excluded all AAs seen during the baseline visit. We did this because we had previously showed that adenomas detected at first surveillance that were also seen at baseline were likely to be under polypectomy site surveillance and that the inclusion of such adenomas confounded analyses.[23]

The primary exposures of interest were the number of surveillance visits and the length of the surveillance interval from baseline to the first surveillance visit. Patient follow-up was censored at first CRC diagnosis, first diagnosis of a condition affecting colonic surveillance regimen (including IBD, colitis, hyperplastic polyposis, proctitis or volvulus), performance of bowel resection, death, emigration, or the date when cancer registration data were considered complete (for patients matched to national data sources) or when the last examination was recorded on the study database (for patients not matched to national data sources).

In all analyses we excluded surveillance visits that fully occurred after censoring (i.e. if all examinations in the visit occurred after censoring). In our analyses of long-term CRC incidence, visits at which a censoring event occurred and visits with the last examination occurring after the date of censoring were not included as surveillance visits, as they did not offer protection against the development of CRC. By contrast, in our analyses of findings at first surveillance we included any first surveillance visits at which a censoring event occurred.

We defined the surveillance interval as the time period between the latest most complete examination in one visit to the first examination in the next visit. The surveillance interval was represented as a categorical variable and patients with the shortest surveillance interval were the reference group against which we compared patients exposed to a longer interval. In the case of the low- and intermediate-risk groups, the surveillance interval was categorised into the following: < 18 months, 2 years (± 6 months), 3 years (± 6 months), 4 years (± 6 months), 5 years (± 6 months), 6 years (± 6 months), 7 years (± 6 months), 8 years (± 6 months), 9 years (± 6 months) and ≥ 9.5 years. The following categories were used for the high-risk group: < 15 months, 1.5 years (± 3 months), 2 years (± 3 months), 2.5 years (± 3 months), 3 years (± 3 months), 3.5 years (± 3 months), 4 years (± 3 months), 4.5 years (± 3 months), 5 years (± 3 months) and ≥ 5.25 years.

Risk factors and confounders

We assessed the following patient, procedural and polyp characteristics as potential risk factors and confounders at baseline: age, sex, year of visit, length of visit (in days or months), examination completeness, bowel preparation quality, number of adenomas, adenoma size, histology, dysplasia, presence of proximal polyps, presence of hyperplastic polyps, presence of a large (i.e. ≥ 10 mm in size) hyperplastic polyp and family history of cancer/CRC. In a sensitivity analysis we additionally considered the hospital that patients attended as a confounding variable.

Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Of cases reported to have a 'family history of cancer', 72% came from a specialist hospital for colorectal diseases and we therefore assumed that these cases had a family history of CRC.

We created categorical variables for the following continuous quantitative variables: number of surveillance visits, age, length of visit, number of adenomas and adenoma size. We created an unknown category for variables with missing data.

Sample size calculations

We based our sample size calculation on obtaining estimates of CRC incidence with a coefficient of variation of approximately 30% [i.e. the standard error (SE) of the incidence estimate being approximately 30% of the value of the estimate]. We assumed an approximate Poisson distribution of incidence and a univariate estimate of the rate, and estimated that nine CRCs in any given risk subgroup would provide a coefficient of variation of 33%. Under these assumptions, only the number of CRCs diagnosed is relevant to the satisfaction of the stipulated criterion on the coefficient of variation (the number of person-years in the denominator has no bearing). Assuming that the size of the smallest subgroup would be 15% of the size of the whole corresponding risk group, we calculated that a minimum number of 60 CRCs were required in each risk group to ensure that the coefficient of variation was no higher than 33% in any of the risk subgroups.

At the time of applying for funding we estimated that approximately 120, 170 and 50 CRCs had been diagnosed during 6 years of follow-up in the low-, intermediate- and high-risk groups, respectively. With more than 3 additional years of follow-up anticipated we expected to accrue at least 60 CRCs in each risk group and thus achieve sufficient precision in all risk groups.

Statistical analyses

We conducted the statistical analyses in Stata®/IC 13.1 (StataCorp LP, College Station, TX, USA). We performed two-tailed tests and used a significance level of 0.05. All of the following analyses were performed separately for the low-, intermediate- and high-risk groups.

We compared the distribution of baseline characteristics (see *Risk factors and confounders*) among patients who attended at least one surveillance visit with that among those who did not attend any surveillance using the chi-squared test.

Long-term colorectal cancer incidence after baseline

We estimated the long-term incidence of CRC after baseline. Time at risk started from the last examination at baseline. Time-to-event data were censored at first CRC diagnosis; first diagnosis of IBD, colitis, hyperplastic polyposis, proctitis or volvulus; performance of bowel resection; death; emigration; or the date of complete case ascertainment in cancer registries. Patients who were not matched to national data sources were censored at the date of their last examination recorded on the study database rather than the date of complete case ascertainment.

We assessed the effects of baseline characteristics (see *Risk factors and confounders*) and surveillance on CRC incidence using Cox proportional-hazards models to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). Exposure to successive surveillance visits started at the last examination in each visit.

We used multivariable Cox proportional hazards models to identify baseline CRC risk factors (i.e. characteristics independently associated with increased long-term CRC incidence). This involved using a backward stepwise selection procedure to retain variables with p-values of < 0.05 in the likelihood ratio test (LRT). We included the number of surveillance visits as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits. We investigated interactions between the number of surveillance visits and age or sex by fitting the models with interaction parameters.

Higher- and lower-risk subgroups

We used the identified baseline CRC risk factors to divide each of the three risk groups into higher- and lower-risk subgroups. Patients with any of the baseline risk factors were assigned to the higher-risk subgroup, whereas those with none of the risk factors were assigned to the lower-risk subgroup. We did not include age in the risk classification criteria because older age is associated with poorer colonoscopy quality and greater risks of colonoscopy-related complications.[30] We also did not include the year or length of the baseline visit as these factors do not help define clinically meaningful patient subgroups.

We conducted a sensitivity analysis of the risk classification criteria for intermediate-risk patients. This involved using the baseline risk factors identified in our previous study of the intermediate-risk group in the classification of higher risk (i.e. incomplete colonoscopies or colonoscopies of unknown completeness, poor bowel preparation, adenomas ≥ 20 mm in size or with high-grade dysplasia, and proximal polyps).[20,23]

Cumulative incidence of colorectal cancer

We used one minus the Kaplan–Meier estimator of the survival function to show time to CRC diagnosis and to estimate cumulative incidence of CRC with 95% CIs at 3, 5 and 10 years. We used the log-rank test to compare cumulative incidence curves.

Comparisons with colorectal cancer incidence in the general population

We compared CRC incidence with that in the general population by calculating standardised incidence ratios (SIRs). These were calculated as the ratio of observed to expected cases of CRC, with exact Poisson 95% CIs. We estimated the number of expected cases by multiplying the observed sex- and 5-year age group-specific number of person-years by the corresponding CRC incidence in the general population of England in 2007.[31]

For our analyses of CRC incidence we divided each patient's follow-up time into four distinct blocks of time:

1. without surveillance (i.e. from start of time-at-risk, censored at any first surveillance)
2. after first surveillance (i.e. from first surveillance, censored at any second surveillance)
3. after second surveillance (i.e. from second surveillance, censored at any third surveillance)
4. after third surveillance (i.e. from third surveillance, censored at end of follow-up).

In some analyses we combined the last two blocks of time to show CRC incidence in the presence of two or more surveillance visits. We compared CRC incidence in the presence of one surveillance visit with two or more surveillance visits using univariable Cox proportional hazards models.

Findings at the first surveillance visit

We assessed detection rates of AAs and CRC at the first surveillance visit by interval length (from baseline to first surveillance), overall and by risk subgroup. A test for trend was used to test for association between detection rates and interval length. Univariable logistic regression was used to calculate unadjusted odds ratios (ORs) and 95% CIs, comparing the detection of AAs and CRC between risk subgroups.

For the analyses of AA detection rates we excluded patients in whom CRC was detected at first surveillance because we expected that their risk of having an AA detected would be different from that of patients without CRC and that their inclusion could therefore lead to biased estimates.

Selection of interval length cut-off point

For our analyses of findings at first surveillance we selected an interval length cut-off point for each risk group to determine which patients in whom a surveillance examination was recorded should actually be included as having had a surveillance examination.

In our main analysis we chose interval length cut-off points of 8.5 years for the low-risk group, 6.5 years for the intermediate-risk group and 3.75 years for the high-risk group. We used the surveillance intervals recommended in the 2002 UK-ASG to inform these cut-off points (i.e. 5 years, 3 years and 1 year for the low-, intermediate- and high-risk groups, respectively), although we allowed the period for the surveillance examination to occur within each risk group to extend to account for the long waits often experienced in endoscopy services and for any delays due to rescheduling.[32] We did not want to extend the intervals further, however, because this would have probably captured patients who were re-presenting, perhaps with symptoms, rather than attending a surveillance examination.

When we applied these cut-off points, low-risk patients were included as having had surveillance if the interval length to their first surveillance visit was < 8.5 years. Low-risk patients with interval lengths ≥ 8.5 years were not included as having undergone surveillance. By the same token, intermediate- and high-risk patients with interval lengths < 6.5 years and < 3.75 years, respectively, were included as having undergone surveillance, whereas those with interval lengths ≥ 6.5 years and ≥ 3.75 years, respectively, were not.

In a sensitivity analysis, we assessed the effects of a shorter interval cut-off point for the low-risk group, changing the cut-off point from 8.5 years to 6.5 years.

Economic evaluation

The aim of the economic evaluation was to evaluate the cost-effectiveness of adopting surveillance compared with no surveillance for each risk group. The economic evaluation involved a within-study analysis and a lifetime analysis.

Within-study analysis

We first conducted a within-study analysis using resource use and outcomes data from the main study. We considered resource use associated with both adenoma surveillance and treatment of CRC. Surveillance procedures included diagnostic and therapeutic colonoscopies, flexible sigmoidoscopies and rigid sigmoidoscopies. Unit costs for these procedures were taken from the NHS national schedule of reference costs for 2017–18.[33] We estimated the lifetime costs of CRC treatment using published estimates from a whole-disease model of CRC,[34] inflating these costs from 2012/13 to 2017/18 prices using the gross domestic product deflator. Treatment costs varied according to patient age and CRC stage at diagnosis. We handled missing CRC staging data by means of multiple imputation using an ordered logit model. We discounted costs and the number of CRC cases at a rate of 3.5% per year.

For each of the three main risk groups we calculated the following for the higher- and lower-risk subgroups:

- incremental cost associated with adopting surveillance compared with no surveillance per 1000 person-years
- incremental number of CRCs diagnosed among patients attending surveillance compared with those not attending surveillance
- incremental cost per CRC prevented by adopting surveillance compared with no surveillance.

Lifetime analysis

For the lifetime analysis we used an extrapolation model to extrapolate results from the within-study analysis over a lifetime horizon. We designed a Markov model that consisted of eight states: (1) no surveillance visits, (2) surveillance visits, (3) Dukes' stage A CRC, (4) Dukes' stage B CRC, (5) Dukes' stage C CRC, (6) Dukes' stage D CRC, (7) death from CRC and (8) death from other causes. We estimated time-homogeneous probabilities of transitions between states for each risk group. We used multiple data sources to estimate these probabilities, including the main study database, the 2013 *National Bowel Cancer Audit Annual Report*[35] and the Office for National Statistics.[36]

We assigned quality-of-life (QoL) estimates to each state. For the CRC states we used mean EuroQol-5 Dimensions (EQ-5D) scores from a study[37] that collected patient-reported outcome measures (PROMs) from patients with CRC. For the non-cancer states we used EQ-5D scores from a study[38] that pooled responses in the Health Survey for England from people without cancer.

We ran the Markov model for the higher- and lower-risk subgroups of each risk group. This allowed us to calculate the costs and QALYs associated with surveillance. We discounted future costs and QALYs at an annual rate of 3.5%. We calculated incremental cost-effectiveness ratios (ICERs) as the ratio between the mean difference in QALYs and the mean difference in costs. Cost-effectiveness was evaluated assuming a willingness-to-pay threshold of £20,000 per QALY gained.

Research governance

Previous approvals for our original study of the intermediate-risk group

We initially obtained research governance approvals to permit data collection from hospitals and national databases for our original study of the intermediate-risk group. These approvals are described in full in the NIHR final report for the original study[23] and are summarised below:

- Ethics approval was granted by the Royal Free Research Ethics Committee (reference 06/Q0501/45).
- Approval for the processing of patient-identifiable information without consent in England was granted by the Patient Information Advisory Group (PIAG) under Section 60 of the Health and Social Care Act 2001[39] (re-enacted by Section 251 of the NHS Act 2006[40]) (reference PIAG 1–05[e]/2006).

- Approval was granted by the Community Health Index Advisory Group of NSS to access the Community Health Index. This enabled the Information Services Division of the NSS to link patient-identifiable information with data from cancer and death registries.
- Research and development approval was obtained for all participating hospitals.

Approvals for the present study of all three risk groups

We subsequently obtained additional ethics approval from the London – Hampstead Research Ethics Committee and the Health Research Authority (reference 06/Q0501/45, IRAS ID 59943) for substantial amendments that extended the scope of the study protocol to examine the low- and high-risk groups, in addition to the intermediate-risk group previously analysed. Amendments and annual reviews of our approval to process patient-identifiable information without consent were approved by the Health Research Authority Confidentiality Advisory Group (reference PIAG 1–05[e]/2006).

Our data-sharing agreements with NHS Digital (reference DARS-NIC-147827-NC2TC) and NHS NSS (reference PBPP 1718–0048/SR244) were amended to include these additional analyses, and a new application was made to the Public Health England (PHE) Office for Data Release (reference ODR1718_326) to obtain cancer staging and treatment data for the health economic analysis.

We renewed our Data Access Agreements to allow continued access to data from the participating hospitals through December 2022.

To protect patient confidentiality, all information kept at the Cancer Screening and Prevention Group's office was pseudo-anonymised and no patient-identifiable information, except for date of birth, was stored on the study database (Oracle database, Oracle Corporation, Redwood City, CA, USA). Access controls to the study database are in place, including password control and a firewall that limited access to a subset of Cancer Screening and Prevention Group computers.

Role of the funding source

The NIHR stipulated that we use a retrospective cohort study design, but it had no involvement in data collection, analysis or interpretation, in the writing of the report or in the decision to submit the report for publication.

Chapter 3 Results

In total, 33,011 patients were identified as having had a colonoscopy performed and at least one adenoma diagnosed during the baseline visit. Indications for colonoscopy were various and included the presence of CRC symptoms (e.g. a change in bowel habit, abdominal pain, anaemia, rectal bleeding), a family history of CRC or a personal history of colorectal polyps (indications are listed in full in the appendices of our previous NIHR final report).[23]

Of the 33,011 potentially eligible patients, we excluded 3015. The 3015 patients excluded included 2859 patients who did not have a baseline colonoscopy, 125 patients who had CRC at or before baseline and/or another colonic condition associated with increased CRC risk, 15 patients whose baseline visit occurred after 2010, 12 patients who had colorectal carcinoma in situ reported in registry data > 3 years before their baseline visit, two patients who had examinations with missing dates and two patients who did not in fact have an adenoma. A further 980 patients were missing information needed for risk group assignment and were excluded and 44 patients were lost to follow-up. This left 28,972 patients for analysis, of whom 14,401 (50%) were classed as low risk, 11,852 (41%) as intermediate risk and 2719 (9%) as high risk (*Figure 1*). Baseline colonoscopies in these patients were performed from 1984 to 2010, with most (87%) occurring between 2000 and 2010.

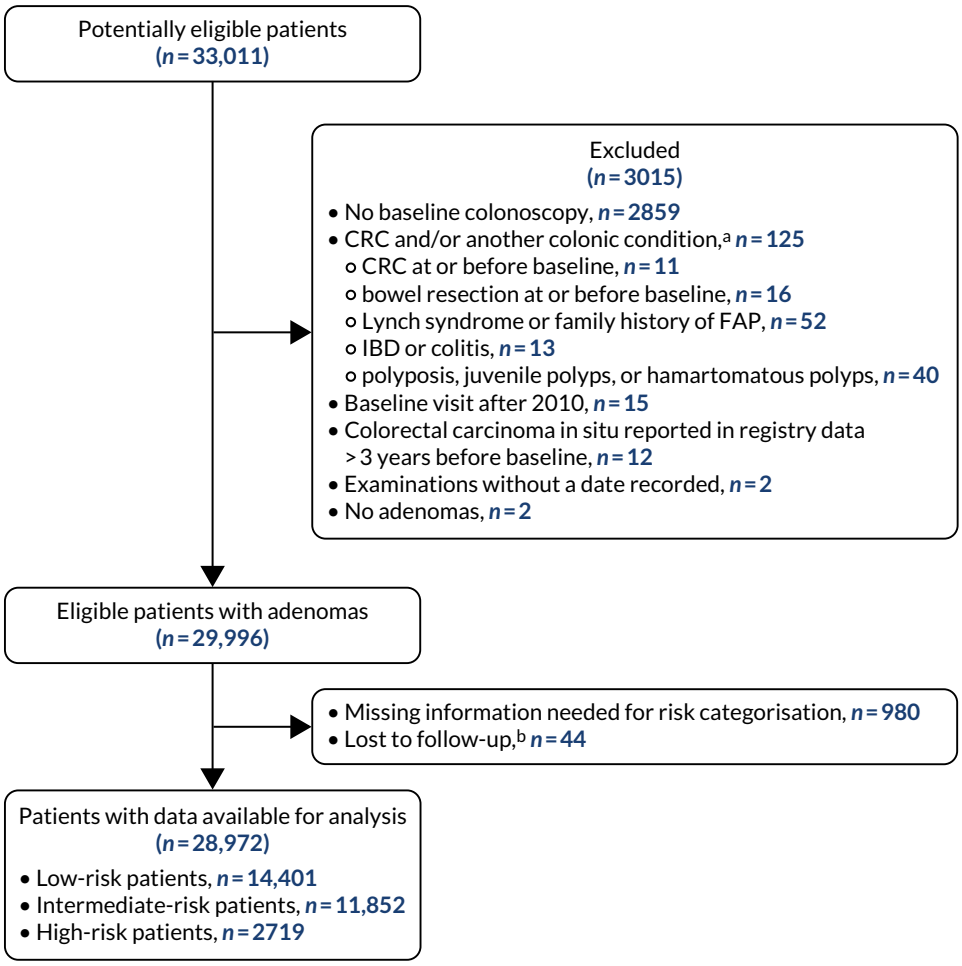

FIGURE 1 Participant flow diagram. a, Not mutually exclusive; and b, patients lost to follow-up included 22 patients who could not be traced in national data sources and who had no surveillance, 19 patients who underwent all their examinations after emigrating and three patients whose date of birth was not known. FAP, familial adenomatous polyposis.

Baseline patient, procedural and polyp characteristics

The low-risk group

The median age of the low-risk group was 64 [interquartile range (IQR) 55–72] years, and 8019 (56%) patients were men. Approximately half of the group ($n = 7194$) were counted as having attended one or more surveillance visit in our analysis of long-term CRC incidence (*Table 1*). Patients who attended surveillance were younger and more likely to have had a baseline visit before 2005 or a baseline visit ≥ 6 months in length than those who did not attend surveillance. Non-attenders were more likely than attenders to have had an incomplete baseline colonoscopy and poor bowel preparation. Attenders were more likely to have had two adenomas (rather than one), an adenoma with tubulovillous or villous histology, an adenoma with high-grade dysplasia or hyperplastic polyps at baseline or to have a family history of cancer/CRC. The proportion of patients in whom data on adenoma histology, adenoma dysplasia, colonoscopy completeness and bowel preparation quality were missing was higher among attenders than among non-attenders (see *Table 1*).

TABLE 1 Comparison of baseline characteristics among low-risk patients according to attendance at surveillance

Baseline characteristic	All low-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		*p*-value[a]
	n	%	*n*	%	*n*	%	
Total	14,401	100.0	7194	50.0	7207	50.0	
Sex							0.32
Women	6382	44.3	3218	44.7	3164	43.9	
Men	8019	55.7	3976	55.3	4043	56.1	
Age (years)							< 0.0001
< 55	3569	24.8	2147	29.8	1422	19.7	
55–64	3991	27.7	2339	32.5	1652	22.9	
65–74	4258	29.6	2007	27.9	2251	31.2	
≥ 75	2583	17.9	701	9.7	1882	26.1	
Year of baseline visit							< 0.0001
1984–99	1640	11.4	1126	15.7	514	7.1	
2000–4	5168	35.9	2855	39.7	2313	32.1	
2005–10	7593	52.7	3213	44.7	4380	60.8	
Length of baseline visit							0.0075
1 day	11,354	78.8	5688	79.1	5666	78.6	
2 days to 3 months	1373	9.5	642	8.9	731	10.1	
3–6 months	950	6.6	469	6.5	481	6.7	
≥ 6 months	724	5.0	395	5.5	329	4.6	
Colonoscopy completeness							< 0.0001
Complete	11,719	81.4	5570	77.4	6149	85.3	
Incomplete	1140	7.9	481	6.7	659	9.1	
Unknown	1542	10.7	1143	15.9	399	5.5	

TABLE 1 Comparison of baseline characteristics among low-risk patients according to attendance at surveillance (*continued*)

Baseline characteristic	All low-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		*p*-value[a]
	n	%	*n*	%	*n*	%	
Bowel preparation quality							< 0.0001
Excellent or good	5145	35.7	2562	35.6	2583	35.8	
Satisfactory	2540	17.6	1122	15.6	1418	19.7	
Poor	968	6.7	388	5.4	580	8.0	
Unknown	5748	39.9	3122	43.4	2626	36.4	
Number of adenomas							< 0.0001
One	11,762	81.7	5753	80.0	6009	83.4	
Two	2639	18.3	1441	20.0	1198	16.6	
Adenoma histology							< 0.0001
Tubular	11,138	77.3	5430	75.5	5708	79.2	
Tubulovillous	2113	14.7	1149	16.0	964	13.4	
Villous	190	1.3	106	1.5	84	1.2	
Unknown	960	6.7	509	7.1	451	6.3	
Adenoma dysplasia							< 0.0001
Low grade	13,242	92.0	6507	90.5	6735	93.5	
High grade	357	2.5	224	3.1	133	1.8	
Unknown	802	5.6	463	6.4	339	4.7	
Proximal polyps							0.065
No	8133	56.5	4008	55.7	4125	57.2	
Yes	6268	43.5	3186	44.3	3082	42.8	
Hyperplastic polyps							< 0.0001
No	11,535	80.1	5597	77.8	5938	82.4	
Yes	2866	19.9	1597	22.2	1269	17.6	
Hyperplastic polyp ≥ 10 mm in size							0.39
No	14,263	99.0	7120	99.0	7143	99.1	
Yes	138	1.0	74	1.0	64	0.9	
Family history of cancer/CRC[b]							< 0.0001
No	12,936	89.8	6106	84.9	6830	94.8	
Yes	1465	10.2	1088	15.1	377	5.2	

a *p*-values were calculated with the chi-squared test to compare patients attending surveillance with those not attending surveillance.
b Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

The intermediate-risk group

The median age of the intermediate-risk group was 66 (IQR 58–74) years, and 6581 (56%) were men. A total of 7169 (60%) patients attended one or more surveillance visit during the long-term CRC incidence analysis (*Table 2*). Compared with patients who did not attend surveillance, attenders included a higher proportion of men and patients aged < 75 years, and were more likely to have had a baseline visit before 2005 and to have had a longer baseline visit (> 1 day). Non-attenders were more likely than attenders to have had an incomplete colonoscopy or poor bowel preparation at baseline. Attenders were more likely to have had an adenoma ≥ 20 mm in size, with tubulovillous histology, or with high-grade dysplasia, hyperplastic polyps, a hyperplastic polyp ≥ 10 mm in size at baseline or to have a family history of cancer/CRC. A greater proportion of attenders than of non-attenders were missing data for adenoma histology, adenoma dysplasia, colonoscopy completeness and bowel preparation quality (see *Table 2*).

TABLE 2 Comparison of baseline characteristics among intermediate-risk patients according to attendance at surveillance

	All intermediate-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		
Baseline characteristic	***n***	**%**	***n***	**%**	***n***	**%**	***p*-value[a]**
Total	11,852	100.0	7169	60.5	4683	39.5	
Sex							0.023
Women	5271	44.5	3128	43.6	2143	45.8	
Men	6581	55.5	4041	56.4	2540	54.2	
Age (years)							< 0.0001
< 55	2097	17.7	1537	21.4	560	12.0	
55–64	3158	26.7	2278	31.8	880	18.8	
65–74	3915	33.0	2460	34.3	1455	31.1	
≥ 75	2682	22.6	894	12.5	1788	38.2	
Year of baseline visit							< 0.0001
1984–99	1870	15.8	1335	18.6	535	11.4	
2000–4	4222	35.6	2591	36.1	1631	34.8	
2005–10	5760	48.6	3243	45.2	2517	53.7	
Length of baseline visit							0.0001
1 day	6697	56.5	3944	55.0	2753	58.8	
2 days to 3 months	2343	19.8	1428	19.9	915	19.5	
3–6 months	1403	11.8	897	12.5	506	10.8	
≥ 6 months	1409	11.9	900	12.6	509	10.9	
Colonoscopy completeness							< 0.0001
Complete	8967	75.7	5362	74.8	3605	77.0	
Incomplete	1321	11.2	605	8.4	716	15.3	
Unknown	1564	13.2	1202	16.8	362	7.7	
Bowel preparation quality							< 0.0001
Excellent or good	3974	33.5	2392	33.4	1582	33.8	
Satisfactory	1903	16.1	995	13.9	908	19.4	

TABLE 2 Comparison of baseline characteristics among intermediate-risk patients according to attendance at surveillance (*continued*)

Baseline characteristic	All intermediate-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		*p*-value[a]
	n	%	*n*	%	*n*	%	
Poor	660	5.6	280	3.9	380	8.1	
Unknown	5315	44.8	3502	48.8	1813	38.7	
Number of adenomas							0.78
One	7793	65.8	4701	65.6	3092	66.0	
Two	3053	25.8	1863	26.0	1190	25.4	
Three or four	1006	8.5	605	8.4	401	8.6	
Adenoma size (mm)							0.0003
< 10	1006	8.5	605	8.4	401	8.6	
10–19	6802	57.4	4018	56.0	2784	59.4	
≥ 20	4044	34.1	2546	35.5	1498	32.0	
Adenoma histology							0.0007
Tubular	4694	39.6	2762	38.5	1932	41.3	
Tubulovillous	5537	46.7	3395	47.4	2142	45.7	
Villous	1134	9.6	683	9.5	451	9.6	
Unknown	487	4.1	329	4.6	158	3.4	
Adenoma dysplasia							< 0.0001
Low grade	9399	79.3	5596	78.1	3803	81.2	
High grade	1979	16.7	1236	17.2	743	15.9	
Unknown	474	4.0	337	4.7	137	2.9	
Proximal polyps							0.34
No	8254	69.6	5016	70.0	3238	69.1	
Yes	3598	30.4	2153	30.0	1445	30.9	
Hyperplastic polyps							< 0.0001
No	9793	82.6	5783	80.7	4010	85.6	
Yes	2059	17.4	1386	19.3	673	14.4	
Hyperplastic polyp ≥ 10 mm in size							0.0006
No	11,668	98.4	7035	98.1	4633	98.9	
Yes	184	1.6	134	1.9	50	1.1	
Family history of cancer/CRC[b]							< 0.0001
No	11,366	95.9	6790	94.7	4576	97.7	
Yes	486	4.1	379	5.3	107	2.3	

a *p*-values were calculated with the chi-squared test to compare patients attending surveillance with those not attending surveillance.
b Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

The high-risk group

The median age of the high-risk group was 67 (IQR 61–74) years, and 1920 (71%) patients were men. In total, 1808 (66%) patients attended one or more surveillance visit during the long-term CRC incidence analysis (*Table 3*). Patients who attended surveillance were, on average, younger than non-attenders and more likely to have had a baseline visit before 2000 and a longer baseline visit (≥ 3 months). Non-attenders were more likely than attenders to have had an incomplete colonoscopy or poor bowel preparation at baseline. Attenders were more likely to have had six or more adenomas or hyperplastic polyps at baseline, and were more likely to have a family history of cancer/CRC. The proportion of patients for whom data for colonoscopy completeness and bowel preparation quality were missing was higher among attenders than among non-attenders (see *Table 3*).

TABLE 3 Comparison of baseline characteristics among high-risk patients according to attendance at surveillance

	All high-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		
Baseline characteristic	***n***	**%**	***n***	**%**	***n***	**%**	***p*-value[a]**
Total	2719	100.0	1808	66.5	911	33.5	
Sex							0.46
Women	799	29.4	523	28.9	276	30.3	
Men	1920	70.6	1285	71.1	635	69.7	
Age (years)							< 0.0001
< 55	283	10.4	221	12.2	62	6.8	
55–64	750	27.6	602	33.3	148	16.2	
65–74	1065	39.2	719	39.8	346	38.0	
≥ 75	621	22.8	266	14.7	355	39.0	
Year of baseline visit							0.021
1984–99	329	12.1	241	13.3	88	9.7	
2000–4	874	32.1	575	31.8	299	32.8	
2005–10	1516	55.8	992	54.9	524	57.5	
Length of baseline visit							< 0.0001
1 day	1184	43.6	773	42.8	411	45.1	
2 days to 3 months	562	20.7	334	18.5	228	25.0	
3–6 months	442	16.3	316	17.5	126	13.8	
≥ 6 months	531	19.5	385	21.3	146	16.0	
Colonoscopy completeness							< 0.0001
Complete	2354	86.6	1574	87.1	780	85.6	
Incomplete	123	4.5	56	3.1	67	7.4	
Unknown	242	8.9	178	9.8	64	7.0	
Bowel preparation quality							< 0.0001
Excellent or good	1119	41.2	768	42.5	351	38.5	
Satisfactory	411	15.1	246	13.6	165	18.1	
Poor	143	5.3	74	4.1	69	7.6	
Unknown	1046	38.5	720	39.8	326	35.8	

TABLE 3 Comparison of baseline characteristics among high-risk patients according to attendance at surveillance (*continued*)

Baseline characteristic	All high-risk patients		Patients attending one or more surveillance visits		Patients not attending surveillance		*p*-value[a]
	n	%	*n*	%	*n*	%	
Number of adenomas							0.0015
Three	1227	45.1	788	43.6	439	48.2	
Four	557	20.5	367	20.3	190	20.9	
Five	454	16.7	297	16.4	157	17.2	
Six or more	481	17.7	356	19.7	125	13.7	
Adenoma size (mm)							0.13
< 10	264	9.7	189	10.5	75	8.2	
10–19	1344	49.4	870	48.1	474	52.0	
≥ 20	1084	39.9	732	40.5	352	38.6	
Unknown	27	1.0	17	0.9	10	1.1	
Adenoma histology							0.95
Tubular	1038	38.2	684	37.8	354	38.9	
Tubulovillous	1293	47.6	867	48.0	426	46.8	
Villous	328	12.1	217	12.0	111	12.2	
Unknown	60	2.2	40	2.2	20	2.2	
Adenoma dysplasia							0.43
Low grade	2035	74.8	1340	74.1	695	76.3	
High grade	616	22.7	420	23.2	196	21.5	
Unknown	68	2.5	48	2.7	20	2.2	
Proximal polyps							0.35
No	663	24.4	431	23.8	232	25.5	
Yes	2056	75.6	1377	76.2	679	74.5	
Hyperplastic polyps							< 0.0001
No	1929	70.9	1230	68.0	699	76.7	
Yes	790	29.1	578	32.0	212	23.3	
Hyperplastic polyp ≥ 10 mm in size							0.11
No	2650	97.5	1756	97.1	894	98.1	
Yes	69	2.5	52	2.9	17	1.9	
Family history of cancer/CRC[b]							< 0.0001
No	2621	96.4	1724	95.4	897	98.5	
Yes	98	3.6	84	4.6	14	1.5	

a *p*-values were calculated with the chi-squared test to compare patients attending surveillance with those not attending surveillance.
b Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

Long-term colorectal cancer incidence after baseline

The low-risk group

In the low-risk group, 195 CRCs were diagnosed during 138,903 person-years of follow-up (median 9.6 years, IQR 7.2–12.4 years), giving an incidence rate of 140 per 100,000 person-years (95% CI 122 to 162 per 100,000 person-years). In multivariable regression analysis, number of surveillance visits, age, completeness of colonoscopy, adenoma histology and proximal polyps were independently associated with CRC incidence. Adjusting for these factors, one surveillance visit was associated with a 44% reduction in CRC incidence compared with no surveillance (HR 0.56, 95% CI 0.39 to 0.80). Even greater reductions in incidence were seen with attendance at two visits (HR 0.27, 95% CI 0.13 to 0.56) and three or more visits (HR 0.18, 95% CI 0.05 to 0.58) (*Table 4*).

Being aged ≥ 55 years and having an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with tubulovillous or villous histology or proximal polyps at baseline were independent risk factors for CRC (see *Table 4*).

The intermediate-risk group

In the intermediate-risk group, 246 CRCs were diagnosed during 111,270 person-years of follow-up (median 9.1 years, IQR 6.6–12.4 years), giving an incidence rate of 221 per 100,000 person-years (95% CI 195 to 251 per 100,000 person-years). In multivariable regression analysis, number of surveillance visits, age, year of baseline visit, length of baseline visit, completeness of colonoscopy, adenoma dysplasia and proximal polyps were independently associated with CRC incidence. Adenoma histology was not included in the final multivariable model because the association between adenoma histology and CRC incidence was driven by the unknown histology category. Adjusting for the other factors, CRC incidence was 41% lower with attendance at one surveillance visit than with none (HR 0.59, 95% CI 0.43 to 0.81). Incidence rates did not fall much further with attendance at a second surveillance visit (HR 0.56, 95% CI 0.36 to 0.85), but fell again with attendance at three or more visits (HR 0.44, 95% CI 0.26 to 0.77) (*Table 5*).

Independent risk factors for CRC included age ≥ 65 years, having a baseline visit before 2000 or a baseline visit that spanned between 2 days and 3 months or ≥ 6 months, and having an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline (see *Table 5*).

The high-risk group

In the high-risk group, 84 CRCs were diagnosed during 22,961 person-years of follow-up (median 8.4 years, IQR 5.7–11.2 years), giving an incidence rate of 366 per 100,000 person-years (95% CI 295 to 453 per 100,000 person-years). In multivariable regression analysis, number of surveillance visits, completeness of colonoscopy and adenoma dysplasia were independently associated with CRC incidence. Adjusting for these factors, one surveillance visit was associated with a halving of CRC incidence (HR 0.49, 95% CI 0.29 to 0.82), compared with no surveillance. Attendance at subsequent surveillance visits was associated with further reductions in CRC incidence (HR 0.30, 95% CI 0.15 to 0.62 for two visits and HR 0.29, 95% CI 0.11 to 0.73 for three or more visits) (*Table 6*).

Independent risk factors for CRC included age (≥ 75 years) and having an incomplete colonoscopy, colonoscopy of unknown completeness or an adenoma with high-grade dysplasia at baseline (see *Table 6*).

In each of the three risk groups there were no significant interactions between the number of surveillance visits and age or sex. The results from the interaction analyses are presented in *Appendix 2*, *Table 26*.

TABLE 4 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	14,401 (100)	138,903	195	140 (122 to 162)				
Number of surveillance visits[c]						< 0.0001		< 0.0001
Zero	7207 (50.0)	84,591	143	169 (143 to 199)	1		1	
One	3959 (27.5)	34,507	41	119 (87 to 161)	0.55 (0.39 to 0.79)		0.56 (0.39 to 0.80)	
Two	1943 (13.5)	12,986	8	62 (31 to 123)	0.26 (0.12 to 0.54)		0.27 (0.13 to 0.56)	
Three or more	1292 (9.0)	6818	3	44 (14 to 136)	0.17 (0.05 to 0.57)		0.18 (0.05 to 0.58)	
Sex						0.67		0.99
Women	6382 (44.3)	63,337	92	145 (118 to 178)	1		1	
Men	8019 (55.7)	75,567	103	136 (112 to 165)	0.94 (0.71 to 1.25)		1.00 (0.75 to 1.32)	
Age (years)						< 0.0001		< 0.0001
< 55	3569 (24.8)	40,422	21	52 (34 to 80)	1		1	
55–64	3991 (27.7)	42,121	46	109 (82 to 146)	2.12 (1.26 to 3.55)		2.05 (1.22 to 3.44)	
65–74	4258 (29.6)	38,799	76	196 (156 to 245)	3.87 (2.38 to 6.28)		3.52 (2.17 to 5.73)	
≥ 75	2583 (17.9)	17,561	52	296 (226 to 389)	6.12 (3.67 to 10.20)		5.02 (3.00 to 8.39)	
Year of baseline visit						0.71		0.45
1984–99	1640 (11.4)	23,185	32	138 (98 to 195)	1		1	
2000–4	5168 (35.9)	56,134	86	153 (124 to 189)	1.06 (0.69 to 1.62)		0.93 (0.60 to 1.43)	
2005–10	7593 (52.7)	59,585	77	129 (103 to 162)	0.92 (0.59 to 1.44)		0.77 (0.48 to 1.23)	
Length of baseline visit						0.74		0.64
1 day	11,354 (78.8)	110,143	152	138 (118 to 162)	1		1	
2 days to 3 months	1373 (9.5)	12,314	19	154 (98 to 242)	1.12 (0.70 to 1.81)		1.13 (0.70 to 1.84)	
3–6 months	950 (6.6)	9309	16	172 (105 to 281)	1.24 (0.74 to 2.07)		1.39 (0.82 to 2.33)	
≥ 6 months	724 (5.0)	7137	8	112 (56 to 224)	0.81 (0.40 to 1.65)		0.91 (0.45 to 1.87)	

continued

TABLE 4 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Colonoscopy completeness[d]						0.17		0.027
Complete	11,719 (81.4)	108,319	144	133 (113 to 157)	1		1	
Incomplete	1140 (7.9)	10,674	26	244 (166 to 358)	1.26 (0.91 to 1.74)[d]		1.47 (1.05 to 2.04)[d]	
Unknown	1542 (10.7)	19,910	25	126 (85 to 186)	1.26 (0.91 to 1.74)[d]		1.47 (1.05 to 2.04)[d]	
Bowel preparation quality						0.15		0.32
Excellent or good	5145 (35.7)	52,129	84	161 (130 to 200)	1		1	
Satisfactory	2540 (17.6)	22,051	30	136 (95 to 195)	0.85 (0.56 to 1.29)		0.81 (0.53 to 1.23)	
Poor	968 (6.7)	7970	15	188 (113 to 312)	1.18 (0.68 to 2.04)		1.09 (0.63 to 1.88)	
Unknown	5748 (39.9)	56,754	66	116 (91 to 148)	0.72 (0.52 to 1.00)		0.76 (0.55 to 1.05)	
Number of adenomas						0.30		0.69
One	11,762 (81.7)	113,729	154	135 (116 to 159)	1		1	
Two	2639 (18.3)	25,175	41	163 (120 to 221)	1.20 (0.85 to 1.70)		1.07 (0.76 to 1.53)	
Adenoma histology[e]						0.0093		0.0067
Tubular	11,138 (77.3)	107,018	132	123 (104 to 146)	1		1	
Tubulovillous	2113 (14.7)	20,130	44	219 (163 to 294)	1.69 (1.21 to 2.37)[e]		1.71 (1.21 to 2.40)[e]	
Villous	190 (1.3)	1906	2	105 (26 to 420)	1.69 (1.21 to 2.37)[e]		1.71 (1.21 to 2.40)[e]	
Unknown	960 (6.7)	9849	17	173 (107 to 278)	1.39 (0.84 to 2.30)		1.52 (0.92 to 2.52)	
Adenoma dysplasia						0.054		0.078
Low grade	13,242 (92.0)	125,812	171	136 (117 to 158)	1		1	
High grade	357 (2.5)	3469	11	317 (176 to 573)	2.32 (1.26 to 4.28)		2.20 (1.18 to 4.10)	
Unknown	802 (5.6)	9623	13	135 (78 to 233)	0.99 (0.56 to 1.74)		0.93 (0.52 to 1.66)	

TABLE 4 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Proximal polyps						0.0046		0.0020
No	8133 (56.5)	80,118	93	116 (95 to 142)	1		1	
Yes	6268 (43.5)	58,785	102	174 (143 to 211)	1.50 (1.13 to 1.99)		1.57 (1.18 to 2.10)	
Hyperplastic polyps						0.34		0.17
No	11,535 (80.1)	110,804	150	135 (115 to 159)	1		1	
Yes	2866 (19.9)	28,099	45	160 (120 to 214)	1.18 (0.84 to 1.65)		1.27 (0.91 to 1.78)	
Hyperplastic polyp $\geq$ 10 mm in size						0.85		0.87
No	14,263 (99.0)	137,656	193	140 (122 to 161)	1		1	
Yes	138 (1.0)	1247	2	160 (40 to 641)	1.14 (0.28 to 4.60)		1.13 (0.28 to 4.54)	
Family history of cancer/CRC[f]						0.15		0.36
No	12,936 (89.8)	121,702	177	145 (126 to 169)	1		1	
Yes	1465 (10.2)	17,201	18	105 (66 to 166)	0.71 (0.44 to 1.16)		1.28 (0.77 to 2.11)	

a *p*-values were calculated with the LRT.
b The final multivariable model included number of surveillance visits, age, completeness of colonoscopy, adenoma histology and proximal polyps. For these variables the adjusted HRs are from the final multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the final multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e For the adenoma histology variable the HRs for the tubulovillous and villous categories are for these two categories combined.
f Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 5 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	11,852 (100)	111,270	246	221 (195 to 251)				
Number of surveillance visits[c]						0.0004		0.0009
Zero	4683 (39.5)	53,927	135	250 (211 to 296)	1		1	
One	3343 (28.2)	33,284	62	186 (145 to 239)	0.58 (0.42 to 0.79)		0.59 (0.43 to 0.81)	
Two	2279 (19.2)	15,477	31	200 (141 to 285)	0.53 (0.35 to 0.81)		0.56 (0.36 to 0.85)	
Three or more	1547 (13.1)	8582	18	210 (132 to 333)	0.45 (0.26 to 0.77)		0.44 (0.26 to 0.77)	
Sex						0.28		0.055
Women	5271 (44.5)	51,049	105	206 (170 to 249)	1		1	
Men	6581 (55.5)	60,221	141	234 (199 to 276)	1.15 (0.89 to 1.48)		1.28 (0.99 to 1.66)	
Age (years)						< 0.0001		< 0.0001
< 55	2097 (17.7)	24,995	28	112 (77 to 162)	1		1	
55–64	3158 (26.6)	33,530	52	155 (118 to 204)	1.44 (0.91 to 2.28)		1.41 (0.89 to 2.24)	
65–74	3915 (33.0)	35,391	98	277 (227 to 338)	2.74 (1.80 to 4.19)		2.66 (1.74 to 4.06)	
≥ 75	2682 (22.6)	17,354	68	392 (309 to 497)	4.25 (2.71 to 6.65)		3.64 (2.31 to 5.74)	
Year of baseline visit						0.0044		0.0078
1984–99	1870 (15.8)	25,329	83	328 (264 to 406)	1		1	
2000–4	4222 (35.6)	42,957	92	214 (175 to 263)	0.66 (0.48 to 0.90)		0.63 (0.46 to 0.87)	
2005–10	5760 (48.6)	42,983	71	165 (131 to 208)	0.57 (0.40 to 0.80)		0.59 (0.40 to 0.85)	
Length of baseline visit						0.018		0.0082
1 day	6697 (56.5)	63,453	117	184 (154 to 221)	1		1	
2 days to 3 months	2343 (19.8)	21,669	60	277 (215 to 357)	1.53 (1.12 to 2.08)		1.65 (1.20 to 2.26)	
3–6 months	1403 (11.8)	13,277	32	241 (170 to 341)	1.32 (0.89 to 1.95)		1.34 (0.90 to 1.99)	
≥ 6 months	1409 (11.9)	12,871	37	287 (208 to 397)	1.57 (1.09 to 2.27)		1.58 (1.08 to 2.30)	

TABLE 5 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Colonoscopy completeness[d]						0.0007		0.0022
Complete	8967 (75.7)	80,572	150	186 (159 to 218)	1		1	
Incomplete	1321 (11.2)	11,545	49	424 (321 to 562)	1.58 (1.22 to 2.06)[d]		1.55 (1.18 to 2.06)[d]	
Unknown	1564 (13.2)	19,152	47	245 (184 to 327)	1.58 (1.22 to 2.06)[d]		1.55 (1.18 to 2.06)[d]	
Bowel preparation quality						0.13		0.14
Excellent or good	3974 (33.5)	37,493	71	189 (150 to 239)	1		1	
Satisfactory	1903 (16.1)	15,451	36	233 (168 to 323)	1.28 (0.86 to 1.92)		1.47 (0.98 to 2.22)	
Poor	660 (5.6)	4840	17	351 (218 to 565)	1.92 (1.13 to 3.25)		1.67 (0.98 to 2.85)	
Unknown	5315 (44.8)	53,485	122	228 (191 to 272)	1.17 (0.88 to 1.57)		1.13 (0.84 to 1.53)	
Number of adenomas						0.37		0.20
One	7793 (65.8)	74,791	168	225 (193 to 261)	1		1	
Two	3053 (25.8)	27,502	64	233 (182 to 297)	1.06 (0.79 to 1.41)		0.92 (0.68 to 1.25)	
Three or four	1006 (8.5)	8977	14	156 (92 to 263)	0.71 (0.41 to 1.23)		0.61 (0.34 to 1.08)	
Adenoma size (mm)						0.087		0.18
< 10	1006 (8.5)	8977	14	156 (92 to 263)	1		1	
10–19	6802 (57.4)	64,716	134	207 (175 to 245)	1.30 (0.75 to 2.26)		1.53 (0.87 to 2.70)	
≥ 20	4044 (34.1)	37,577	98	261 (214 to 318)	1.64 (0.94 to 2.88)		1.69 (0.94 to 3.04)	
Adenoma histology						< 0.0001		0.0025
Tubular	4694 (39.6)	44,369	71	160 (127 to 202)	1		1	
Tubulovillous	5537 (46.7)	51,211	114	223 (185 to 267)	1.40 (1.04 to 1.88)		1.29 (0.95 to 1.75)	
Villous	1134 (9.6)	10,108	31	307 (216 to 436)	1.93 (1.27 to 2.95)		1.44 (0.93 to 2.24)	
Unknown	487 (4.1)	5581	30	538 (376 to 769)	3.23 (2.10 to 4.98)		2.76 (1.64 to 4.64)	

continued

TABLE 5 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.0002		0.0038
Low grade	9399 (79.3)	87,581	166	190 (163 to 221)	1		1	
High grade	1979 (16.7)	17,402	53	305 (233 to 399)	1.62 (1.19 to 2.21)		1.47 (1.07 to 2.02)	
Unknown	474 (4.0)	6287	27	429 (295 to 626)	2.11 (1.39 to 3.20)		1.86 (1.21 to 2.86)	
Proximal polyps						0.028		0.0025
No	8254 (69.6)	79,798	162	203 (174 to 237)	1		1	
Yes	3598 (30.4)	31,471	84	267 (216 to 331)	1.35 (1.04 to 1.76)		1.54 (1.17 to 2.02)	
Hyperplastic polyps						0.63		0.66
No	9793 (82.6)	91,902	204	222 (194 to 255)	1		1	
Yes	2059 (17.4)	19,367	42	217 (160 to 293)	0.99 (0.71 to 1.38)		1.06 (0.75 to 1.49)	
Hyperplastic polyp ≥ 10 mm in size						0.95		0.75
No	11,668 (98.4)	109,499	243	222 (196 to 252)	1		1	
Yes	184 (1.6)	1771	3	169 (55 to 525)	0.77 (0.25 to 2.39)		0.78 (0.25 to 2.46)	
Family history of cancer/CRC[e]						0.31		0.78
No	11,366 (95.9)	105,842	237	224 (197 to 254)	1		1	
Yes	486 (4.1)	5428	9	166 (86 to 319)	0.72 (0.37 to 1.40)		1.10 (0.56 to 2.16)	

a *p*-values were calculated with the LRT.
b The final multivariable model included number of surveillance visits, age, year of baseline visit, length of baseline visit, completeness of colonoscopy, adenoma dysplasia and proximal polyps. For these variables the adjusted HRs are from the final multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the final multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 6 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	2719 (100)	22,961	84	366 (295 to 453)				
Number of surveillance visits[c]						0.0019		0.0009
Zero	911 (33.5)	9243	44	476 (354 to 640)	1		1	
One	695 (25.6)	7144	24	336 (225 to 501)	0.51 (0.30 to 0.85)		0.49 (0.29 to 0.82)	
Two	593 (21.8)	4018	10	249 (134 to 463)	0.32 (0.16 to 0.67)		0.30 (0.15 to 0.62)	
Three or more	520 (19.1)	2555	6	235 (105 to 523)	0.31 (0.12 to 0.78)		0.29 (0.11 to 0.73)	
Sex						0.32		0.56
Women	799 (29.4)	6997	30	429 (300 to 613)	1		1	
Men	1920 (70.6)	15,963	54	338 (259 to 442)	0.79 (0.51 to 1.24)		0.87 (0.56 to 1.37)	
Age (years)						0.012		0.083
< 55	283 (10.4)	3191	6	188 (84 to 418)	1		1	
55–64	750 (27.6)	7082	20	282 (182 to 438)	1.53 (0.61 to 3.81)		1.68 (0.67 to 4.19)	
65–74	1065 (39.2)	8735	34	389 (278 to 545)	2.13 (0.89 to 5.09)		2.17 (0.91 to 5.19)	
≥ 75	621 (22.8)	3953	24	607 (407 to 906)	3.42 (1.39 to 8.42)		2.79 (1.13 to 6.89)	
Year of baseline visit						0.41		0.36
1984–99	329 (12.1)	3948	10	253 (136 to 471)	1		1	
2000–4	874 (32.1)	8250	34	412 (294 to 577)	1.62 (0.78 to 3.38)		1.65 (0.78 to 3.47)	
2005–10	1516 (55.8)	10,762	40	372 (273 to 507)	1.48 (0.70 to 3.13)		1.65 (0.75 to 3.62)	
Length of baseline visit						0.60		0.88
1 day	1184 (43.5)	10,106	33	327 (232 to 459)	1		1	
2 days to 3 months	562 (20.7)	4556	18	395 (249 to 627)	1.20 (0.68 to 2.14)		1.02 (0.57 to 1.82)	
3–6 months	442 (16.3)	3738	12	321 (182 to 565)	0.98 (0.51 to 1.89)		0.89 (0.46 to 1.74)	
≥ 6 months	531 (19.5)	4561	21	460 (300 to 706)	1.42 (0.82 to 2.45)		1.19 (0.67 to 2.10)	

continued

TABLE 6 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Colonoscopy completeness[d]						0.061		0.044
Complete	2354 (86.6)	19,266	64	332 (260 to 424)	1		1	
Incomplete	123 (4.5)	1009	7	694 (331 to 1456)	1.66 (1.00 to 2.76)[d]		1.73 (1.04 to 2.89)[d]	
Unknown	242 (8.9)	2686	13	484 (281 to 833)	1.66 (1.00 to 2.76)[d]		1.73 (1.04 to 2.89)[d]	
Bowel preparation quality						0.89		0.89
Excellent or good	1119 (41.2)	9788	35	358 (257 to 498)	1		1	
Satisfactory	411 (15.1)	3106	12	386 (219 to 680)	1.08 (0.56 to 2.08)		1.03 (0.53 to 1.99)	
Poor	143 (5.3)	980	5	510 (212 to 1226)	1.46 (0.57 to 3.72)		1.42 (0.55 to 3.64)	
Unknown	1046 (38.5)	9086	32	352 (249 to 498)	0.99 (0.61 to 1.59)		0.95 (0.59 to 1.53)	
Number of adenomas						0.49		0.38
Three	1227 (45.1)	10,577	38	359 (261 to 494)	1		1	
Four	557 (20.5)	4704	13	276 (160 to 476)	0.77 (0.41 to 1.45)		0.81 (0.43 to 1.53)	
Five	454 (16.7)	3697	18	487 (307 to 773)	1.35 (0.77 to 2.36)		1.45 (0.83 to 2.54)	
Six or more	481 (17.7)	3983	15	377 (227 to 625)	1.05 (0.58 to 1.92)		1.24 (0.68 to 2.27)	
Adenoma size (mm)						0.30		0.69
< 10	264 (9.7)	2374	6	253 (114 to 562)	1		1	
10–19	1344 (49.4)	11,361	36	317 (229 to 439)	1.25 (0.53 to 2.97)		1.08 (0.45 to 2.57)	
≥ 20	1084 (39.9)	8951	41	458 (337 to 622)	1.82 (0.77 to 4.28)		1.41 (0.58 to 3.39)	
Unknown	27 (1.0)	275	1	364 (51 to 2585)	1.41 (0.17 to 11.76)		1.22 (0.14 to 10.31)	
Adenoma histology						0.19		0.48
Tubular	1038 (38.2)	8994	31	345 (242 to 490)	1		1	
Tubulovillous	1293 (47.6)	10,701	36	336 (243 to 466)	0.99 (0.61 to 1.59)		0.89 (0.55 to 1.45)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Villous	328 (12.1)	2648	16	604 (370 to 986)	1.77 (0.97 to 3.23)		1.40 (0.75 to 2.61)	
Unknown	60 (2.2)	619	1	162 (23 to 1147)	0.47 (0.06 to 3.41)		0.54 (0.07 to 4.09)	
Adenoma dysplasia						0.0027		0.0009
Low grade	2035 (74.8)	17,109	51	298 (227 to 392)	1		1	
High grade	616 (22.7)	5080	32	630 (445 to 891)	2.12 (1.36 to 3.30)		2.23 (1.43 to 3.47)	
Unknown	68 (2.5)	772	1	130 (18 to 919)	0.44 (0.06 to 3.21)		0.35 (0.05 to 2.57)	
Proximal polyps						0.96		0.47
No	663 (24.4)	5934	22	371 (244 to 563)	1		1	
Yes	2056 (75.6)	17,027	62	364 (284 to 467)	0.99 (0.61 to 1.61)		1.21 (0.73 to 2.00)	
Hyperplastic polyps						0.40		0.24
No	1929 (70.9)	16,037	55	343 (263 to 447)	1		1	
Yes	790 (29.1)	6923	29	419 (291 to 603)	1.22 (0.78 to 1.91)		1.32 (0.84 to 2.07)	
Hyperplastic polyp $\geq$ 10 mm in size						0.94		0.93
No	2650 (97.5)	22,388	82	366 (295 to 455)	1		1	
Yes	69 (2.5)	573	2	349 (87 to 1395)	0.95 (0.23 to 3.87)		1.07 (0.26 to 4.36)	
Family history of cancer/CRC[e]						0.072		0.17
No	2621 (96.4)	21,902	83	379 (306 to 470)	1		1	
Yes	98 (3.6)	1059	1	94 (13 to 670)	0.24 (0.03 to 1.76)		0.32 (0.04 to 2.31)	

a *p*-values were calculated with the LRT.
b The final multivariable model included number of surveillance visits, completeness of colonoscopy and adenoma dysplasia. For these variables the adjusted HRs are from the final multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the final multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

Higher- and lower-risk subgroups

We then divided each risk group into higher- and lower-risk subgroups using the baseline CRC risk factors identified in each group.

The low-risk group

The higher-risk subgroup of the low-risk group comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline ($n = 9166$, 64%). Patients without any of these factors were assigned to the lower-risk subgroup ($n = 5235$, 36%). Patients in the higher-risk subgroup were older and more likely to have had their baseline visit before 2005 than those in the lower-risk subgroup. Higher-risk patients had more surveillance than lower-risk patients (see *Appendix 2*, *Table 27*).

The intermediate-risk group

The higher-risk subgroup of the intermediate-risk group comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline ($n = 7114$, 60%). The lower-risk subgroup comprised patients who had none of these factors ($n = 4738$, 40%). Patients in the higher-risk subgroup were older, more likely to have had their baseline visit before 2005 and attended more surveillance visits than patients in the lower-risk subgroup (see *Appendix 2*, *Table 27*).

The high-risk group

The higher-risk subgroup of the high-risk group comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline ($n = 902$, 33%). Patients without any of these factors were assigned to the lower-risk subgroup ($n = 1817$, 67%). Patients in the two subgroups were comparable in terms of sex, age and number of surveillance visits. Higher-risk patients were more likely to have had their baseline visit before 2005 than lower-risk patients (see *Appendix 2*, *Table 27*).

Incidence of colorectal cancer by risk subgroup and number of surveillance visits

The low-risk group

Among low-risk patients, attendance at one surveillance visit was associated with reduced CRC incidence in the higher-risk subgroup (HR 0.52, 95% CI 0.35 to 0.78) and even greater reductions were seen with attendance at two or more visits (HR 0.18, 95% CI 0.08 to 0.37). By comparison, in the lower-risk subgroup, surveillance was not associated with significantly reduced CRC incidence rates (HR 0.54, 95% CI 0.25 to 1.20, for one visit and HR 0.42, 95% CI 0.12 to 1.48, for two or more visits). However, it is important to note that the HR estimates for the lower-risk subgroup have wide 95% CIs, as few CRC cases occurred in each stratum (*Table 7*).

The intermediate-risk group

Among intermediate-risk patients, attendance at one surveillance visit was associated with reduced CRC incidence in the higher-risk subgroup (HR 0.53, 95% CI 0.37 to 0.76) and CRC incidence was even lower with attendance at two or more visits (HR 0.42, 95% CI 0.27 to 0.65). In the lower-risk subgroup of intermediate-risk patients, surveillance was not associated with reduced CRC incidence rates (HR 0.66, 95% CI 0.35 to 1.23 for one visit and HR 0.63, 95% CI 0.31 to 1.29 for two or more visits). As above, however, the HR estimates for the lower-risk subgroup are imprecise, as few CRC cases occurred in each stratum (see *Table 7*).

TABLE 7 Incidence of CRC after baseline by risk subgroup and number of surveillance visits

Risk group/ subgroup	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
Low-risk group						
Whole risk group						< 0.0001
Zero visits	7207 (50.0)	84,591	143	169 (143 to 199)	1	
One visit	3959 (27.5)	34,507	41	119 (87 to 161)	0.55 (0.39 to 0.79)	
Two or more visits	3235 (22.5)	19,805	11	56 (31 to 100)	0.23 (0.12 to 0.44)	
Total	14,401 (100)	138,903	195	140 (122 to 162)		
Higher-risk subgroup[c]						< 0.0001
Zero visits	4403 (48.0)	51,688	112	217 (180 to 261)	1	
One visit	2527 (27.6)	23,097	33	143 (102 to 201)	0.52 (0.35 to 0.78)	
Two or more visits	2236 (24.4)	14,332	8	56 (28 to 112)	0.18 (0.08 to 0.37)	
Total	9166 (63.6)	89,118	153	172 (147 to 201)		
Lower-risk subgroup[c]						0.15
Zero visits	2804 (53.6)	32,903	31	94 (66 to 134)	1	
One visit	1432 (27.4)	11,410	8	70 (35 to 140)	0.54 (0.25 to 1.20)	
Two or more visits	999 (19.1)	5472	3	55 (18 to 170)	0.42 (0.12 to 1.48)	
Total	5235 (36.4)	49,785	42	84 (62 to 114)		
Intermediate-risk group						
Whole risk group						0.0001
Zero visits	4683 (39.5)	53,927	135	250 (211 to 296)	1	
One visit	3343 (28.2)	33,284	62	186 (145 to 239)	0.58 (0.42 to 0.79)	
Two or more visits	3826 (32.3)	24,059	49	204 (154 to 269)	0.50 (0.34 to 0.73)	
Total	11,852 (100)	111,270	246	221 (195 to 251)		
Higher-risk subgroup[d]						0.0001
Zero visits	2751 (38.7)	30,690	102	332 (274 to 404)	1	
One visit	1956 (27.5)	20,133	46	228 (171 to 305)	0.53 (0.37 to 0.76)	
Two or more visits	2407 (33.8)	15,977	36	225 (163 to 312)	0.42 (0.27 to 0.65)	
Total	7114 (60.0)	66,800	184	275 (238 to 318)		
Lower-risk subgroup[d]						0.30
Zero visits	1932 (40.8)	23,237	33	142 (101 to 200)	1	
One visit	1387 (29.3)	13,151	16	122 (75 to 199)	0.66 (0.35 to 1.23)	
Two or more visits	1419 (30.0)	8082	13	161 (93 to 277)	0.63 (0.31 to 1.29)	
Total	4738 (40.0)	44,470	62	139 (109 to 179)		

continued

TABLE 7 Incidence of CRC after baseline by risk subgroup and number of surveillance visits (*continued*)

Risk group/ subgroup	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
High-risk group						
Whole risk group						0.0006
Zero visits	911 (33.5)	9243	44	476 (354 to 640)	1	
One visit	695 (25.6)	7144	24	336 (225 to 501)	0.51 (0.30 to 0.85)	
Two or more visits	1113 (40.9)	6574	16	243 (149 to 397)	0.32 (0.17 to 0.60)	
Total	2719 (100)	22,961	84	366 (295 to 453)		
Higher-risk subgroup[e]						0.0006
Zero visits	305 (33.8)	3017	27	895 (614 to 1305)	1	
One visit	221 (24.5)	2378	12	505 (287 to 889)	0.41 (0.20 to 0.82)	
Two or more visits	376 (41.7)	2535	7	276 (132 to 579)	0.21 (0.08 to 0.51)	
Total	902 (33.2)	7929	46	580 (435 to 775)		
Lower-risk subgroup[e]						0.26
Zero visits	606 (33.4)	6226	17	273 (170 to 439)	1	
One visit	474 (26.1)	4766	12	252 (143 to 443)	0.66 (0.31 to 1.41)	
Two or more visits	737 (40.6)	4039	9	223 (116 to 428)	0.49 (0.20 to 1.18)	
Total	1817 (66.8)	15,032	38	253 (184 to 347)		

a The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
b *p*-values were calculated with the LRT.
c The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline; patients who did not have any of these factors were assigned to the lower-risk subgroup.
d The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia, or proximal polyps at baseline; patients who did not have any of these factors were assigned to the lower-risk subgroup.
e The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline; patients who did not have any of these factors were assigned to the lower-risk subgroup.

The high-risk group

Among high-risk patients, attendance at one surveillance visit was associated with reduced CRC incidence in the higher-risk subgroup (HR 0.41, 95% CI 0.20 to 0.82). Attendance at subsequent visits was associated with further reductions in CRC incidence in this higher-risk subgroup (HR 0.21, 95% CI 0.08 to 0.51 for two or more visits). By contrast, surveillance was not associated with reduced CRC incidence rates in the lower-risk subgroup of high-risk patients (HR 0.66, 95% CI 0.31 to 1.41 for one visit and HR 0.49, 95% CI 0.20 to 1.18 for two visits). However, estimates for the lower-risk subgroup again lack precision (see *Table 7*).

Cumulative incidence of colorectal cancer at 10 years

The low-risk group

Without surveillance, cumulative CRC incidence at 10 years was 1.7% (95% CI 1.4% to 2.1%) in the low-risk group overall, but differed significantly between the lower-risk subgroup, at 1.2% (95% CI 0.8% to 1.7%), and the higher-risk subgroup, at 2.1% (95% CI 1.7% to 2.6%). After one surveillance visit, cumulative CRC incidence at 10 years was 1.5% (95% CI 1.0% to 2.3%) in the low-risk group overall and was no longer significantly different in the lower-risk subgroup (0.6%, 95% CI 0.2% to 1.4%) when compared with higher-risk subgroup (2.0%, 95% CI 1.3% to 3.0%) (*Table 8* and *Figure 2*).

The intermediate-risk group

Without surveillance, cumulative CRC incidence at 10 years was 2.6% (95% CI 2.1% to 3.3%) in the intermediate-risk group overall, but differed significantly between the lower-risk subgroup, at 1.3% (95% CI 0.8% to 2.1%), and the higher-risk subgroup, at 3.7% (95% CI 2.9% to 4.7%). After one surveillance visit, cumulative CRC incidence at 10 years was 2.6% (95% CI 1.9% to 3.6%) in the intermediate-risk group overall, still differing significantly between the lower-risk subgroup (1.9%, 95% CI 1.0% to 3.4%) and the higher-risk subgroup (3.1%, 95% CI 2.2% to 4.5%) (*Figure 3*; see also *Table 8*).

The high-risk group

Without surveillance, cumulative CRC incidence at 10 years was 5.7% (95% CI 4.0% to 8.3%) in the high-risk group overall, differing significantly between the lower-risk subgroup, at 3.8% (95% CI 2.1% to 6.8%), and the higher-risk subgroup, at 9.9% (95% CI 6.2% to 15.7%). After one surveillance visit, CRC incidence at 10 years was 5.6% (95% CI 3.1% to 9.8%) in the high-risk group overall and was no longer significantly different in the lower-risk subgroup (4.4%, 95% CI 1.8% to 10.6%) when compared with the higher-risk subgroup (7.8%, 95% CI 3.8% to 15.4%) (*Figure 4*; see also *Table 8*).

Comparisons with colorectal cancer incidence in the general population

The low-risk group

Compared with the general population, CRC incidence in the absence of surveillance was not significantly different in the low-risk group overall (SIR 0.86, 95% CI 0.73 to 1.02) or in the higher-risk subgroup (SIR 1.07, 95% CI 0.88 to 1.28), but was lower in the lower-risk subgroup (SIR 0.51, 95% CI 0.35 to 0.73). After one surveillance visit, CRC incidence was significantly lower in both subgroups than in the general population and SIRs were 0.38 (95% CI 0.16 to 0.74) and 0.70 (95% CI 0.48 to 0.98) for the lower- and higher-risk subgroups, respectively (see *Table 8*).

The intermediate-risk group

Without surveillance, CRC incidence was not significantly different in the intermediate-risk group overall (SIR 1.16, 95% CI 0.97 to 1.37) compared with the general population, but was lower in the lower-risk subgroup (SIR 0.70, 95% CI 0.48 to 0.99) and higher in the higher-risk subgroup (SIR 1.46, 95% CI 1.19 to 1.78). After one surveillance visit, CRC incidence was no longer higher in the higher-risk subgroup than in the general population (SIR 1.00, 95% CI 0.73 to 1.33) (see *Table 8*).

The high-risk group

Without surveillance, CRC incidence was higher in the high-risk group overall (SIR 1.91, 95% CI 1.39 to 2.56) and in the higher-risk subgroup (SIR 3.55, 95% CI 2.34 to 5.17) than in the general population, but was not significantly different in the lower-risk subgroup (SIR 1.10, 95% CI 0.64 to 1.76). After first surveillance, CRC incidence was not significantly different in the high-risk group overall (SIR 1.34, 95% CI 0.86 to 1.99) than in the general population, but remained higher in the higher-risk subgroup (SIR 1.97, 95% CI 1.02 to 3.44). Following a second surveillance visit, CRC incidence was no longer higher in the higher-risk subgroup than in the general population (SIR 1.02, 95% CI 0.41 to 2.09) (see *Table 8*). It is worth noting that the estimates from our analyses of the high-risk group have low precision because of the small number of CRC cases.

TABLE 8 Cumulative incidence of CRC at 3, 5 and 10 years and age- and sex-SIRs, by risk subgroup

Risk group/ subgroup	Number of patients (%)	Number of person-years	Questionnaire, *n* (%)						*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			3 years		5 years		10 years					
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
Low-risk group												
After baseline, with no surveillance[d]									< 0.0001			
Whole risk group	14,401 (100)	84,591	45	0.4 (0.3 to 0.5)	77	0.7 (0.6 to 0.9)	124	1.7 (1.4 to 2.1)		143	165	0.86 (0.73 to 1.02)
Higher-risk subgroup[e]	9166 (63.6)	51,688	39	0.5 (0.4 to 0.7)	66	1.0 (0.8 to 1.3)	95	2.1 (1.7 to 2.6)		112	105	1.07 (0.88 to 1.28)
Lower-risk subgroup[e]	5235 (36.4)	32,903	6	0.1 (0.1 to 0.3)	11	0.3 (0.2 to 0.5)	29	1.2 (0.8 to 1.7)		31	60	0.51 (0.35 to 0.73)
After first surveillance, with one surveillance visit[f]									0.069			
Whole risk group	7194 (100)	34,507	14	0.2 (0.1 to 0.4)	27	0.6 (0.4 to 0.8)	40	1.5 (1.0 to 2.3)		41	69	0.60 (0.43 to 0.81)
Higher-risk subgroup[e]	4763 (66.2)	23,097	9	0.2 (0.1 to 0.4)	20	0.7 (0.4 to 1.0)	32	2.0 (1.3 to 3.0)		33	47	0.70 (0.48 to 0.98)
Lower-risk subgroup[e]	2431 (33.8)	11,410	5	0.2 (0.1 to 0.6)	7	0.4 (0.2 to 0.8)	8	0.6 (0.2 to 1.4)		8	21	0.38 (0.16 to 0.74)
After second surveillance, with two or more surveillance visits[g]									0.90			
Whole risk group	3235 (100)	19,805	1	0.04 (0.01 to 0.3)	4	0.2 (0.1 to 0.5)	8	0.6 (0.3 to 1.3)		11	42	0.26 (0.13 to 0.47)
Higher-risk subgroup[e]	2236 (69.1)	14,332	1	0.1 (0.01 to 0.4)	4	0.3 (0.1 to 0.7)	6	0.6 (0.2 to 1.4)		8	32	0.25 (0.11 to 0.50)
Lower-risk subgroup[e]	999 (30.9)	5472	0		0		2	0.7 (0.2 to 3.0)		3	10	0.29 (0.06 to 0.84)
Intermediate-risk group												
After baseline, with no surveillance[d]									< 0.0001			
Whole risk group	11,852 (100)	53,927	57	0.6 (0.5 to 0.8)	88	1.3 (1.0 to 1.6)	121	2.6 (2.1 to 3.3)		135	117	1.16 (0.97 to 1.37)
Higher-risk subgroup[h]	7114 (60.0)	30,690	44	0.8 (0.6 to 1.1)	68	1.7 (1.3 to 2.2)	94	3.7 (2.9 to 4.7)		102	70	1.46 (1.19 to 1.78)
Lower-risk subgroup[h]	4738 (40.0)	23,237	13	0.4 (0.2 to 0.6)	20	0.7 (0.4 to 1.1)	27	1.3 (0.8 to 2.1)		33	47	0.70 (0.48 to 0.99)

Risk group/ subgroup	Number of patients (%)	Number of person-years	Questionnaire, *n* (%)						*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			3 years		5 years		10 years					
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
After first surveillance, with one surveillance visit[f]									0.029			
Whole risk group	7169 (100)	33,284	17	0.3 (0.2 to 0.5)	34	0.8 (0.6 to 1.2)	57	2.6 (1.9 to 3.6)		62	73	0.85 (0.65 to 1.08)
Higher-risk subgroup[h]	4363 (60.9)	20,133	14	0.4 (0.2 to 0.7)	26	1.0 (0.7 to 1.5)	42	3.1 (2.2 to 4.5)		46	46	1.00 (0.73 to 1.33)
Lower-risk subgroup[h]	2806 (39.1)	13,151	3	0.1 (0.04 to 0.4)	8	0.5 (0.2 to 1.0)	15	1.9 (1.0 to 3.4)		16	27	0.59 (0.34 to 0.96)
After second surveillance, with two or more surveillance visit[g]									0.39			
Whole risk group	3826 (100)	24,059	10	0.3 (0.2 to 0.6)	19	0.7 (0.4 to 1.1)	36	2.0 (1.4 to 2.9)		49	56	0.87 (0.65 to 1.16)
Higher-risk subgroup[h]	2407 (62.9)	15,977	7	0.3 (0.2 to 0.7)	13	0.7 (0.4 to 1.2)	26	2.2 (1.4 to 3.3)		36	38	0.95 (0.67 to 1.31)
Lower-risk subgroup[h]	1419 (37.1)	8082	3	0.3 (0.1 to 0.8)	6	0.6 (0.3 to 1.5)	10	1.7 (0.8 to 3.3)		13	18	0.72 (0.38 to 1.22)
High-risk group												
After baseline, with no surveillance[d]									0.0001			
Whole risk group	2719 (100)	9243	17	1.0 (0.6 to 1.7)	32	3.1 (2.1 to 4.4)	41	5.7 (4.0 to 8.3)		44	23	1.91 (1.39 to 2.56)
Higher-risk subgroup[i]	902 (33.2)	3017	10	1.9 (1.0 to 3.6)	19	5.6 (3.5 to 9.0)	24	9.9 (6.2 to 15.7)		27	8	3.55 (2.34 to 5.17)
Lower-risk subgroup[i]	1817 (66.8)	6226	7	0.6 (0.3 to 1.4)	13	1.9 (1.0 to 3.4)	17	3.8 (2.1 to 6.8)		17	15	1.10 (0.64 to 1.76)
After first surveillance, with one surveillance visit[f]									0.086			
Whole risk group	1808 (100)	7144	9	0.6 (0.3 to 1.2)	16	1.8 (1.1 to 3.1)	23	5.6 (3.1 to 9.8)		24	18	1.34 (0.86 to 1.99)
Higher-risk subgroup[i]	597 (33.0)	2378	4	0.9 (0.3 to 2.3)	8	2.9 (1.4 to 6.1)	12	7.8 (3.8 to 15.4)		12	6	1.97 (1.02 to 3.44)
Lower-risk subgroup[i]	1211 (67.0)	4766	5	0.5 (0.2 to 1.3)	8	1.3 (0.6 to 2.9)	11	4.4 (1.8 to 10.6)		12	12	1.01 (0.52 to 1.76)

continued

TABLE 8 Cumulative incidence of CRC at 3, 5 and 10 years and age- and sex-SIRs, by risk subgroup (*continued*)

Risk group/ subgroup	Number of patients (%)	Number of person-years	Questionnaire, *n* (%)						*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			3 years		5 years		10 years					
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
After second surveillance, with two or more surveillance visits[g]									0.74			
Whole risk group	1113 (100)	6574	3	0.3 (0.1 to 1.0)	9	1.2 (0.6 to 2.3)	15	2.6 (1.5 to 4.4)		16	18	0.91 (0.52 to 1.47)
Higher-risk subgroup[i]	376 (33.8)	2535	2	0.6 (0.2 to 2.4)	3	1.0 (0.3 to 3.1)	6	2.7 (1.2 to 6.2)		7	7	1.02 (0.41 to 2.09)
Lower-risk subgroup[i]	737 (66.2)	4039	1	0.2 (0.02 to 1.2)	6	1.3 (0.6 to 2.8)	9	2.4 (1.2 to 4.7)		9	11	0.83 (0.38 to 1.58)

a *p*-values were calculated with the log-rank test to compare cumulative incidence curves of the higher- and lower-risk subgroups.
b Total number of observed CRCs at end of follow-up.
c The number of expected CRCs were calculated by multiplying the sex- and 5-year age group-specific observed person-years by the corresponding sex- and age-specific incidence rates in the general population of England in 2007.
d Data were censored at first surveillance visit.
e The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
f Data were censored at second surveillance visit.
g Data were censored at end of follow-up.
h The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
i The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.

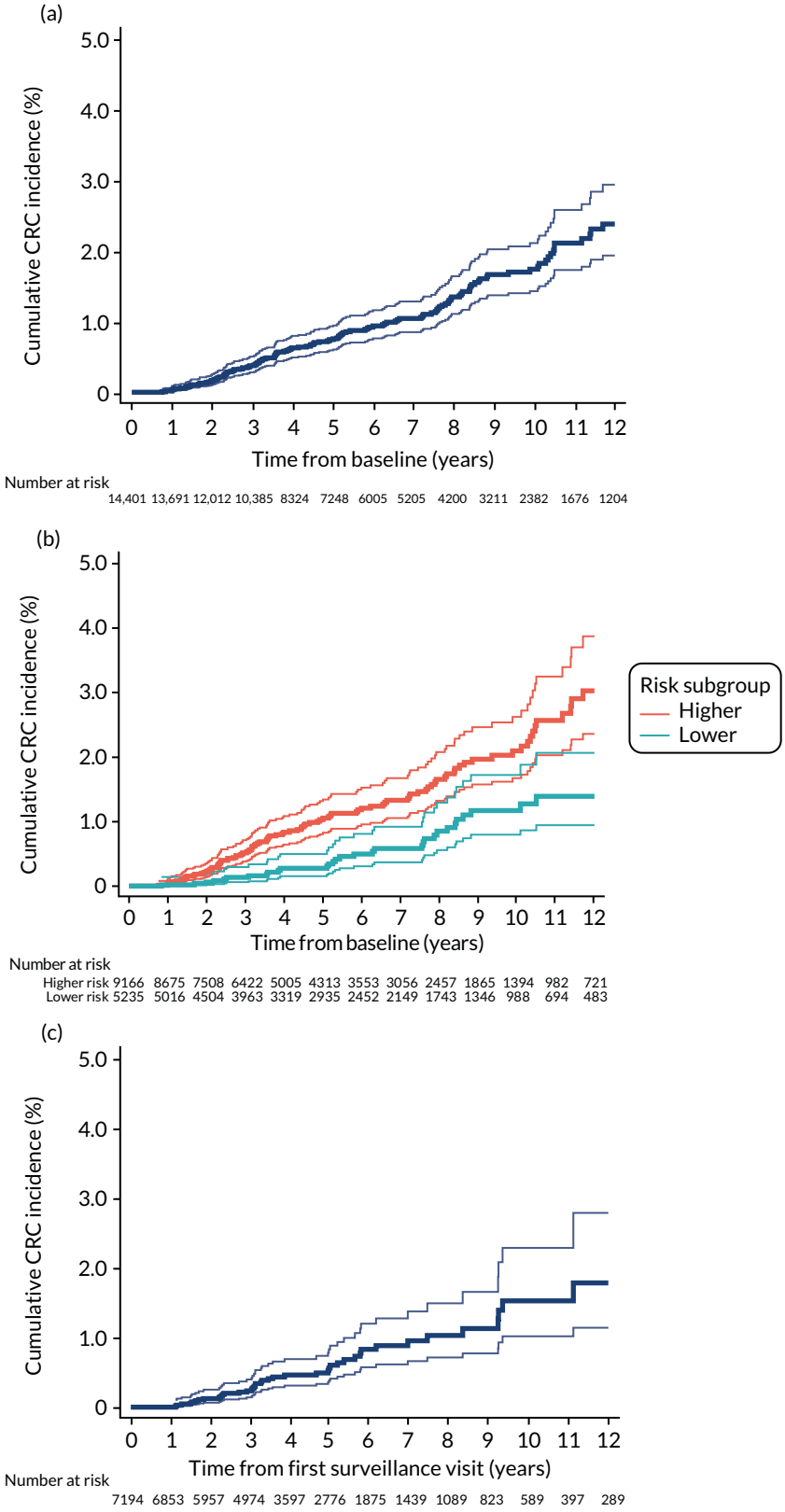

FIGURE 2 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the low-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole low-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole low-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole low-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups. (*continued*)

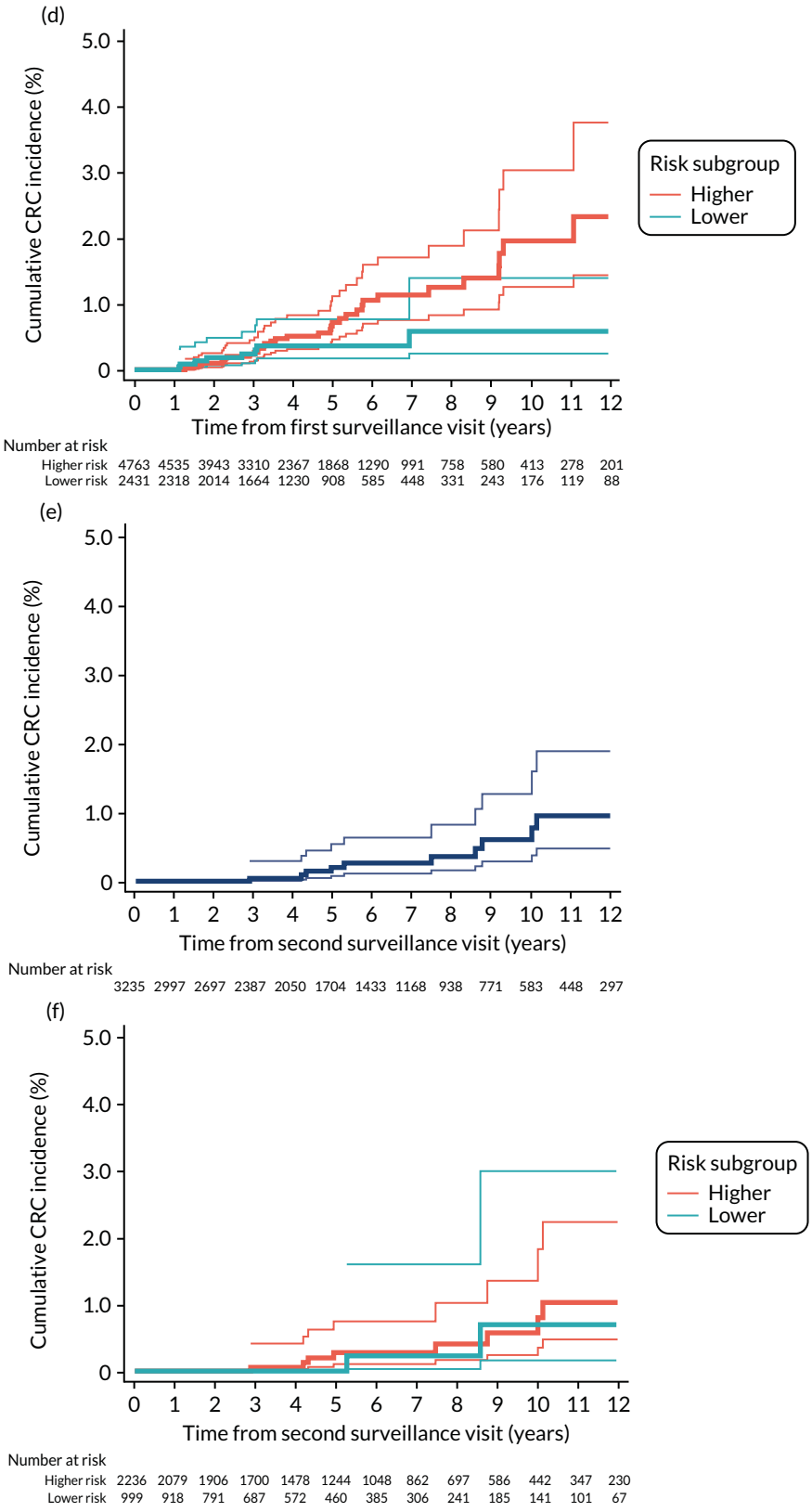

FIGURE 2 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the low-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole low-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole low-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole low-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups.

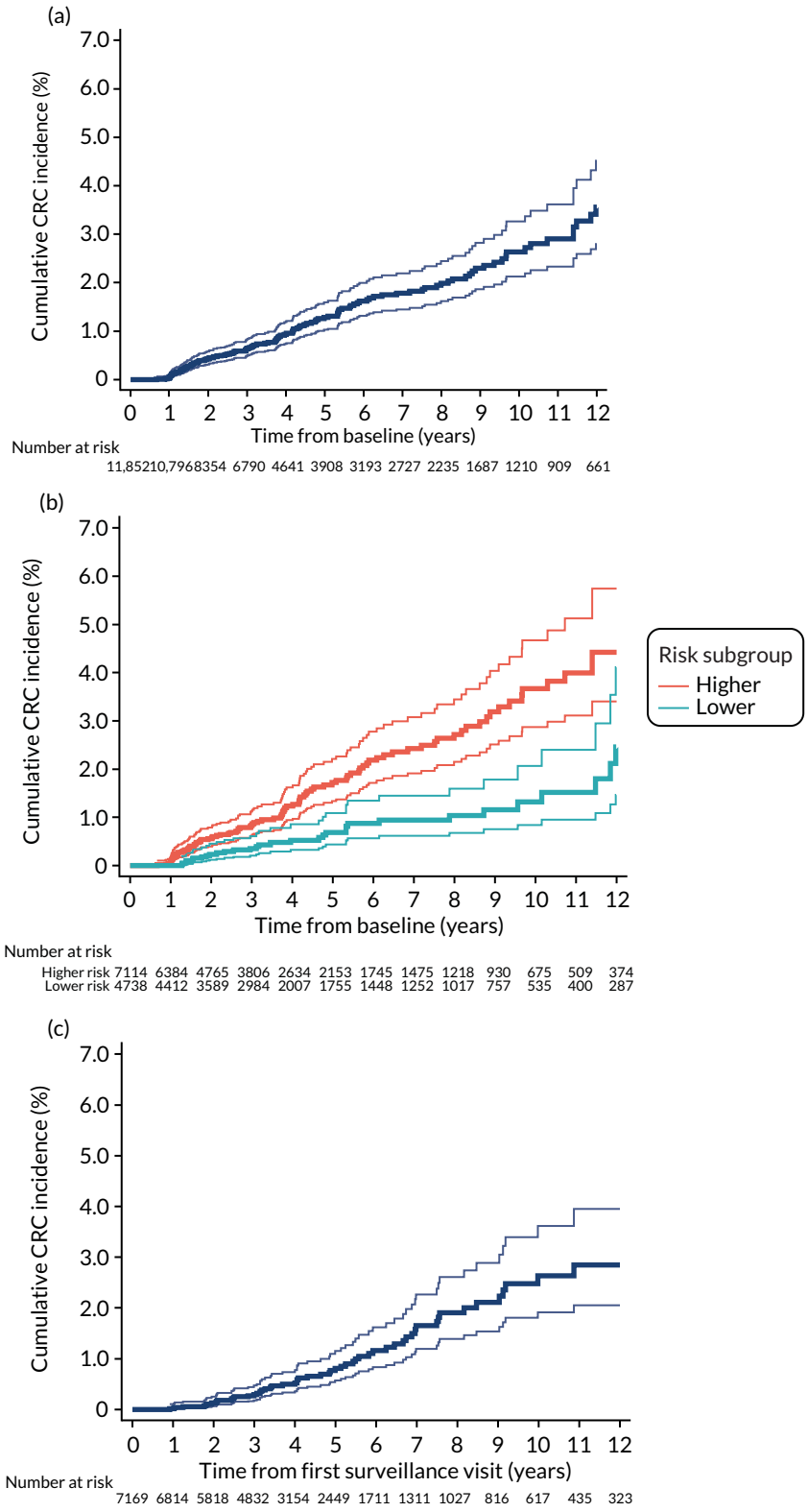

FIGURE 3 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the intermediate-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole intermediate-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole intermediate-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole intermediate-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups. (*continued*)

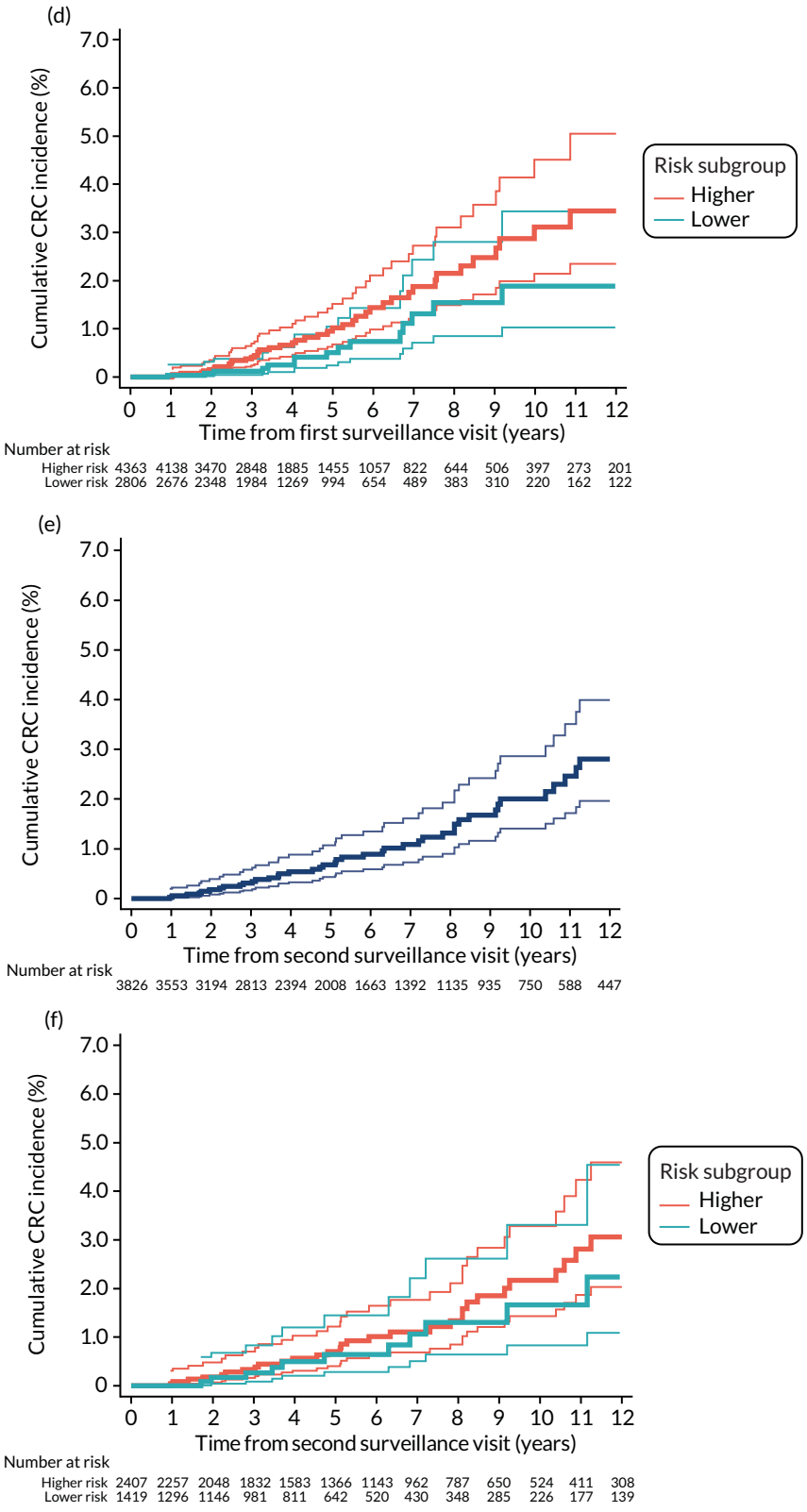

FIGURE 3 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the intermediate-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole intermediate-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole intermediate-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole intermediate-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups.

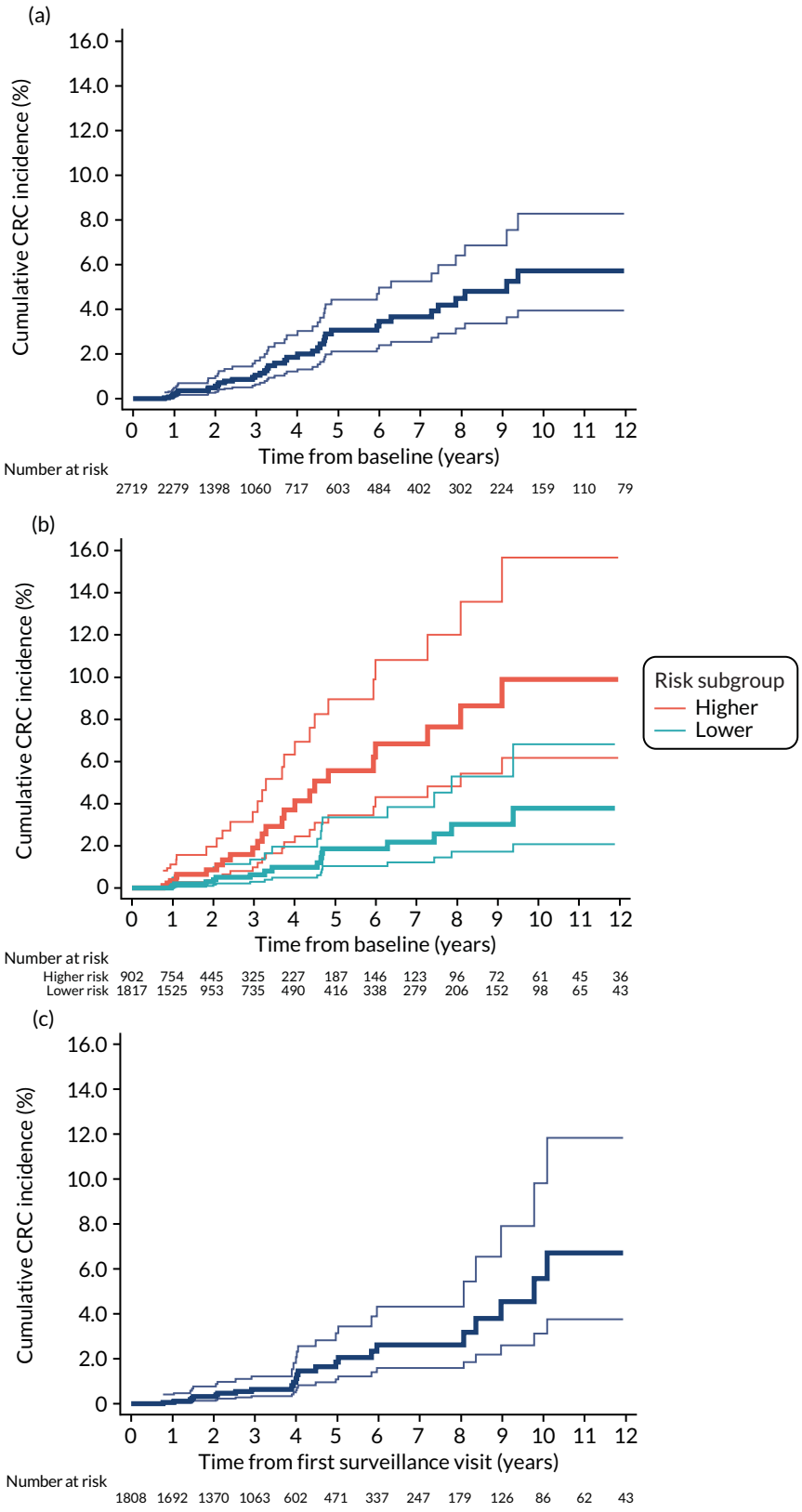

FIGURE 4 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the high-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole high-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole high-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole high-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups. (*continued*)

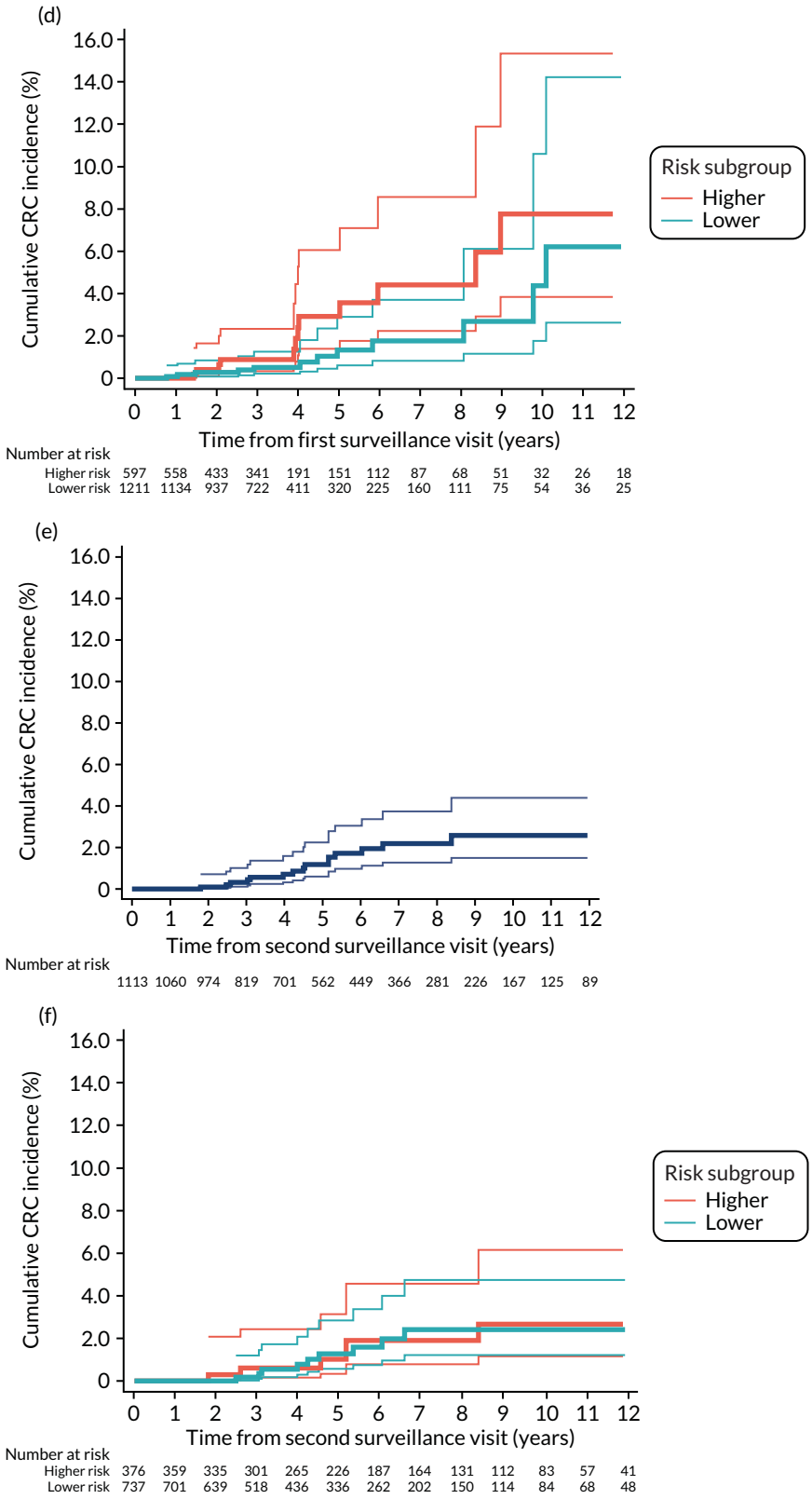

FIGURE 4 Kaplan–Meier estimates of cumulative CRC incidence after baseline in the high-risk group. (a) Cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the whole high-risk group; (b) cumulative CRC incidence after baseline with no surveillance (censoring at first surveillance) in the higher- and lower-risk subgroups; (c) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the whole high-risk group; (d) cumulative CRC incidence with a single surveillance visit (censoring at second surveillance) in the higher- and lower-risk subgroups; (e) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the whole high-risk group; and (f) cumulative CRC incidence with two or more surveillance visits (censoring at end of follow-up) in the higher- and lower-risk subgroups.

Comparison of colorectal cancer incidence in the presence of one surveillance visit compared with two or more visits

The low-risk group

In the whole low-risk group, CRC incidence was lower with attendance at two or more surveillance visits than with one visit (HR 0.31, 95% CI 0.15 to 0.63). This pattern was also observed in the higher-risk subgroup (HR 0.25, 95% CI 0.11 to 0.57). In the lower-risk subgroup, attendance at two or more surveillance visits was not associated with a reduction in CRC incidence compared with attendance at one visit (HR 0.74, 95% CI 0.14 to 3.81). However, the HR estimate for the lower-risk subgroup has a wide 95% CI, as there were only 11 CRC cases (*Table 9*).

TABLE 9 Incidence of CRC after first surveillance by risk subgroup and number of surveillance visits

Risk group	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence of two or more vs. one surveillance visit[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
Low-risk group						
Whole risk group						0.0007
One visit	3959 (55.0)	34,507	41	119 (87 to 161)	1	
Two or more visits	3235 (45.0)	19,805	11	56 (31 to 100)	0.31 (0.15 to 0.63)	
Total	7194 (100)	54,312	52	96 (73 to 126)		
Higher-risk subgroup[c]						0.0003
One visit	2527 (53.1)	23,097	33	143 (102 to 201)	1	
Two or more visits	2236 (47.0)	14,332	8	56 (28 to 112)	0.25 (0.11 to 0.57)	
Total	4763 (66.2)	37,429	41	110 (81 to 149)		
Lower-risk subgroup[c]						0.72
One visit	1432 (58.9)	11,410	8	70 (35 to 140)	1	
Two or more visits	999 (41.1)	5472	3	55 (18 to 170)	0.74 (0.14 to 3.81)	
Total	2431 (33.8)	16,882	11	65 (36 to 118)		
Intermediate-risk group						
Whole risk group						0.016
One visit	3343 (46.6)	33,284	62	186 (145 to 239)	1	
Two or more visits	3826 (53.4)	24,059	49	204 (154 to 269)	0.60 (0.40 to 0.91)	
Total	7169 (100)	57,343	111	194 (161 to 233)		
Higher-risk subgroup[d]						0.019
One visit	1956 (44.8)	20,133	46	228 (171 to 305)	1	
Two or more visits	2407 (55.2)	15,977	36	225 (163 to 312)	0.56 (0.34 to 0.91)	
Total	4363 (60.9)	36,110	82	227 (183 to 282)		

continued

TABLE 9 Incidence of CRC after first surveillance by risk subgroup and number of surveillance visits (*continued*)

Risk group	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence of two or more vs. one surveillance visit[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
Lower-risk subgroup[d]						0.31
One visit	1387 (49.4)	13,151	16	122 (75 to 199)	1	
Two or more visits	1419 (50.6)	8082	13	161 (93 to 277)	0.66 (0.30 to 1.46)	
Total	2806 (39.1)	21,233	29	137 (95 to 197)		
High-risk group						
Whole risk group						0.017
One visit	695 (38.4)	7144	24	336 (225 to 501)	1	
Two or more visits	1113 (61.6)	6574	16	243 (149 to 397)	0.43 (0.21 to 0.86)	
Total	1808 (100)	13,718	40	292 (214 to 397)		
Higher-risk subgroup[e]						0.046
One visit	221 (37.0)	2378	12	505 (287 to 889)	1	
Two or more visits	376 (63.0)	2535	7	276 (132 to 579)	0.36 (0.13 to 0.99)	
Total	597 (33.0)	4913	19	387 (247 to 606)		
Lower-risk subgroup[e]						0.16
One visit	474 (39.1)	4766	12	252 (143 to 443)	1	
Two or more visits	737 (60.9)	4039	9	223 (116 to 428)	0.50 (0.19 to 1.30)	
Total	1211 (67.0)	8805	21	238 (155 to 366)		

a The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
b *p*-values were calculated with the LRT.
c The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
d The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
e The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.

The intermediate-risk group

In the whole intermediate-risk group, attending two or more surveillance visits was associated with a reduction in CRC incidence compared with a single visit (HR 0.60, 95% CI 0.40 to 0.91). This was also observed in the higher-risk subgroup (HR 0.56, 95% CI 0.34 to 0.91), but not in the lower-risk subgroup (HR 0.66, 95% CI 0.30 to 1.46). However, as before, the HR estimate for the lower-risk subgroup is imprecise as there were few CRC cases (see *Table 9*).

The high-risk group

In the whole high-risk group, CRC incidence was lower with attendance at two or more surveillance visits than with one visit (HR 0.43, 95% CI 0.21 to 0.86). This was also observed in the higher-risk subgroup (HR 0.36, 95% CI 0.13 to 0.99). In the lower-risk subgroup, CRC incidence was not significantly lower with two or more surveillance visits than with one (HR 0.50, 95% CI 0.19 to 1.30), although the HR estimate lacks precision (see *Table 9*).

Findings at the first surveillance visit

We first examined detection rates of AAs and CRC at the first surveillance visit by interval length, considering all possible intervals from baseline to first surveillance. The results are shown in *Table 10*.

TABLE 10 Detection rates of AAs and CRC at first surveillance by interval length

	AAs[a]			CRC		
Interval length to first surveillance	**Number of patients (%)**	**Number of AAs (%)**	**Unadjusted OR (95% CI)**	**Number of patients (%)**	**Number of CRCs (%)**	**Unadjusted OR (95% CI)**
Low-risk group						
Total	7264 (100)	546 (7.5)		7407 (100)	143 (1.9)	
< 18 months	1128 (15.5)	65 (5.8)	1	1142 (15.4)	14 (1.2)	1
2 years[b]	1094 (15.1)	63 (5.8)	1.00 (0.70 to 1.43)	1115 (15.1)	21 (1.9)	1.55 (0.78 to 3.06)
3 years[b]	1870 (25.7)	113 (6.0)	1.05 (0.77 to 1.44)	1893 (25.6)	23 (1.2)	0.99 (0.51 to 1.93)
4 years[b]	925 (12.7)	75 (8.1)	1.44 (1.02 to 2.04)	940 (12.7)	15 (1.6)	1.31 (0.63 to 2.72)
5 years[b]	1097 (15.1)	96 (8.8)	1.57 (1.13 to 2.17)	1110 (15.0)	13 (1.2)	0.95 (0.45 to 2.04)
6 years[b]	441 (6.1)	37 (8.4)	1.50 (0.98 to 2.28)	448 (6.0)	7 (1.6)	1.28 (0.51 to 3.19)
7 years[b]	229 (3.2)	29 (12.7)	2.37 (1.49 to 3.77)	236 (3.2)	7 (3.0)	2.46 (0.98 to 6.17)
8 years[b]	161 (2.2)	18 (11.2)	2.06 (1.19 to 3.57)	178 (2.4)	17 (9.6)	8.51 (4.11 to 17.59)
9 years[b]	118 (1.6)	22 (18.6)	3.75 (2.21 to 6.35)	124 (1.7)	6 (4.8)	4.10 (1.55 to 10.86)
≥ 9.5 years	201 (2.8)	28 (13.9)	2.65 (1.65 to 4.24)	221 (3.0)	20 (9.0)	8.02 (3.98 to 16.13)
Intermediate-risk group						
Total	7273 (100)	720 (9.9)		7408 (100)	135 (1.8)	
< 18 months	1950 (26.8)	153 (7.8)	1	1975 (26.7)	25 (1.3)	1
2 years[b]	1211 (16.7)	106 (8.8)	1.13 (0.87 to 1.46)	1234 (16.7)	23 (1.9)	1.48 (0.84 to 2.62)
3 years[b]	2216 (30.5)	204 (9.2)	1.19 (0.96 to 1.48)	2232 (30.1)	16 (0.7)	0.56 (0.30 to 1.06)
4 years[b]	680 (9.3)	72 (10.6)	1.39 (1.04 to 1.87)	698 (9.4)	18 (2.6)	2.06 (1.12 to 3.81)
5 years[b]	554 (7.6)	75 (13.5)	1.84 (1.37 to 2.47)	567 (7.7)	13 (2.3)	1.83 (0.93 to 3.60)
6 years[b]	285 (3.9)	38 (13.3)	1.81 (1.24 to 2.64)	294 (4.0)	9 (3.1)	2.46 (1.14 to 5.33)
7 years[b]	123 (1.7)	25 (20.3)	3.00 (1.87 to 4.79)	125 (1.7)	2 (1.6)	1.27 (0.30 to 5.42)
8 years[b]	100 (1.4)	19 (19.0)	2.76 (1.63 to 4.66)	106 (1.4)	6 (5.7)	4.68 (1.88 to 11.67)
9 years[b]	62 (0.9)	7 (11.3)	1.49 (0.67 to 3.34)	68 (0.9)	6 (8.8)	7.55 (2.99 to 19.06)
≥ 9.5 years	92 (1.3)	21 (22.8)	3.47 (2.08 to 5.81)	109 (1.5)	17 (15.6)	14.41 (7.52 to 27.63)

continued

TABLE 10 Detection rates of AAs and CRC at first surveillance by interval length (*continued*)

Interval length to first surveillance	AAs[a]			CRC		
	Number of patients (%)	Number of AAs (%)	Unadjusted OR (95% CI)	Number of patients (%)	Number of CRCs (%)	Unadjusted OR (95% CI)
High-risk group						
Total	1842 (100)	286 (15.5)		1886 (100)	44 (2.3)	
< 15 months	735 (39.9)	110 (15.0)	1	742 (39.3)	7 (0.9)	1
1.5 years[c]	287 (15.6)	35 (12.2)	0.79 (0.53 to 1.19)	288 (15.3)	1 (0.3)	0.37 (0.04 to 2.99)
2 years[c]	170 (9.2)	19 (11.2)	0.71 (0.43 to 1.20)	176 (9.3)	6 (3.4)	3.71 (1.23 to 11.17)
2.5 years[c]	85 (4.6)	17 (20.0)	1.42 (0.80 to 2.51)	87 (4.6)	2 (2.3)	2.47 (0.51 to 12.08)
3 years[c]	246 (13.4)	45 (18.3)	1.27 (0.87 to 1.86)	250 (13.3)	4 (1.6)	1.71 (0.50 to 5.88)
3.5 years[c]	100 (5.4)	14 (14.0)	0.92 (0.51 to 1.69)	103 (5.5)	3 (2.9)	3.15 (0.80 to 12.38)
4 years[c]	47 (2.6)	11 (23.4)	1.74 (0.86 to 3.51)	50 (2.7)	3 (6.0)	6.70 (1.68 to 26.75)
4.5 years[c]	27 (1.5)	6 (22.2)	1.62 (0.64 to 4.11)	32 (1.7)	5 (15.6)	19.44 (5.80 to 65.22)
5 years[c]	47 (2.6)	8 (17.0)	1.17 (0.53 to 2.56)	48 (2.5)	1 (2.1)	2.23 (0.27 to 18.54)
≥ 5.25 years	98 (5.3)	21 (21.4)	1.55 (0.92 to 2.62)	110 (5.8)	12 (10.9)	12.86 (4.94 to 33.43)

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b Interval length ± 6 months.
c Interval length ± 3 months.

The numbers of patients with a surveillance visit in *Table 10* are larger than the numbers of patients counted as having surveillance in our analyses of long-term CRC incidence (shown in *Tables 1–9*). This is because of the censoring of follow-up after first surveillance in some patients (reasons for which are outlined below).

In the low-risk group, 143 patients were diagnosed with CRC at first surveillance, 69 patients were diagnosed with colitis, IBD, hyperplastic polyposis, proctitis or volvulus, or had a bowel resection performed at first surveillance, and one patient's last examination in first surveillance occurred after the date of final censoring.

Among intermediate-risk patients, 163 patients were diagnosed with CRC at first surveillance (28 CRCs were excluded from analysis as they were assumed to have developed from incompletely resected baseline lesions), 74 patients were diagnosed with colitis, IBD, hyperplastic polyposis, proctitis or volvulus, or had a bowel resection performed at first surveillance, one patient's last examination in first surveillance occurred after the date of final censoring, and one patient had no further surveillance and could not be traced in national data sources.

In the high-risk group, 54 patients were diagnosed with CRC at first surveillance (10 CRCs were excluded from analysis as they were assumed to have developed from incompletely resected baseline lesions), 23 patients were diagnosed with colitis, IBD, hyperplastic polyposis, proctitis or volvulus, or had a bowel resection performed at first surveillance, and one patient had no further surveillance and could not be traced in national data sources.

For our analyses of long-term CRC incidence we compared baseline characteristics among patients with and without surveillance (see *Tables 1–3*). We repeated this comparison for patients included in our analyses of findings at first surveillance and found very similar results (data not shown).

Detection rates of advanced adenomas and colorectal cancer at first surveillance, considering all possible surveillance intervals

The low-risk group

In the low-risk group, AA detection rates were approximately 6% with intervals of < 18 months, 2 and 3 years, increasing to 8–9% with intervals of 4, 5 and 6 years. There was a jump in AA detection rates to 13% with an interval of 7 years and then again to 19% with an interval of 9 years. Detection rates of CRC fell between 1% and 2% with intervals of < 18 months through to 6 years, increasing to 3% with an interval of 7 years and to 10% with an interval of 8 years. When we applied our chosen cut-off point for interval length (i.e. 8.5 years), we captured 117 of 143 (82%) CRCs diagnosed among low-risk patients recorded as having had a 'surveillance examination' (see *Table 10*).

The intermediate-risk group

In the intermediate-risk group, AA detection rates were 8–9% with intervals of < 18 months through to 3 years, increasing to 11% with an interval of 4 years and to approximately 13% with intervals of 5 and 6 years. There was a jump in AA detection rates to 20% with an interval of 7 years. For CRC, detection rates were approximately 1–2% with intervals of < 18 months, 2 and 3 years, increasing to 3% with an interval of 4 years. There was a jump in CRC detection rates to 6% with an interval of 8 years. When we applied our selected interval length cut-off point (i.e. 6.5 years), we captured 104 of 135 (77%) CRCs diagnosed among intermediate-risk patients recorded as having had a 'surveillance examination' (see *Table 10*).

The high-risk group

In the high-risk group, AA detection rates varied between 11% and 23% at all interval lengths, with no discernible pattern. Detection rates of CRC increased from < 0.5% with an interval of 18 months to approximately 3% with an interval of 2 years. There was a jump in CRC detection rates to 6% with an interval of 4 years and a further jump to 16% with an interval of 4.5 years. When we applied our selected interval length cut-off point (i.e. 3.75 years), we captured 23 of 44 (52%) CRCs diagnosed among high-risk patients recorded as having had a 'surveillance examination' (see *Table 10*).

Detection rates of advanced adenomas and colorectal cancer at first surveillance, applying our surveillance interval length cut-off points

For our main analyses of findings at first surveillance we excluded patients whose first surveillance examination was performed after our selected interval length cut-off points (i.e. 8.5 years for the low-risk group, 6.5 years for the intermediate-risk group and 3.75 years for the high-risk group). We examined the effect of interval length on AA and CRC detection rates at first surveillance in the risk groups overall and by risk subgroup.

The low-risk group

Among low-risk patients, AAs were detected in 496 (7.1%) individuals at the first surveillance visit. There was a significant increasing trend in the detection rate of AAs at first surveillance with increasing interval length. Compared with an interval of < 18 months, detection rates of AAs at first surveillance were similar with an interval of 2 and 3 years (i.e. 6%), but increased with an interval of ≥ 4 years (i.e. ≥ 8%). AA detection rates remained similar with intervals of 5 and 6 years, but increased again with an interval of 7 years to approximately twice that of the three shortest intervals (*Table 11*).

Among low-risk patients, 117 (1.7%) had CRC detected at first surveillance. There was a significant trend of increasing rates of detection of CRC at first surveillance with increasing interval length. The CRC detection rate was similar with interval lengths of < 18 months (1.2%) through to 6 years (1.6%), but increased with an interval of 7 years (3.0%) and was substantially higher with an interval of 8 years (9.6%) (see *Table 11*).

TABLE 11 Detection rate of AAs and CRC at first surveillance among low-risk patients by interval length

Interval length to first surveillance	AAs[a]				CRC			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%
< 18 months	1128	16.2	65	5.8	1142	16.2	14	1.2
2 years[b]	1094	15.8	63	5.8	1115	15.8	21	1.9
3 years[b]	1870	26.9	113	6.0	1893	26.8	23	1.2
4 years[b]	925	13.3	75	8.1	940	13.3	15	1.6
5 years[b]	1097	15.8	96	8.8	1110	15.7	13	1.2
6 years[b]	441	6.3	37	8.4	448	6.3	7	1.6
7 years[b]	229	3.3	29	12.7	236	3.3	7	3.0
8 years[b]	161	2.3	18	11.2	178	2.5	17	9.6
Total	6945	100	496	7.1	7062	100	117	1.7
p-value[c]			< 0.0001				< 0.0001	

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b Interval length ± 6 months.
c *p*-values were from a test for trend.

Findings at first surveillance by risk subgroup

We then examined findings at first surveillance by interval length in the lower- and higher-risk subgroups of low-risk patients. There was a significant trend of increased AA and CRC detection at first surveillance with longer interval lengths in both risk subgroups. In the lower-risk subgroup, AA detection rates increased from 3% with an interval of < 18 months through to 7% with intervals of 4 and 5 years and jumping to 11% with an interval of 6 years. In the higher-risk subgroup, AA detection rates started at a higher rate of 7% with an interval of < 18 months, increasing to approximately 9–10% with intervals of 4 and 5 years and jumping to 15% with an interval of 7 years. Comparing the detection rates of AAs in the higher- and lower-risk subgroups, the OR was 1.47 (95% CI 1.20 to 1.81) (*Table 12*).

In the lower-risk subgroup, CRC detection rates were approximately 1% with intervals of < 18 months through to 5 years, increasing to 2% with an interval of 6 years and jumping to 12% with an interval of 8 years. In the higher-risk subgroup, CRC detection rates varied between 1% and 2% with intervals of < 18 months through to 6 years, increasing to 5% with an interval of 7 years and 8% with an interval of 8 years. The OR for the comparison of CRC detection rates in the higher- and lower-risk subgroups was 1.68 (95% CI 1.09 to 2.59) (see *Table 12*).

The intermediate-risk group

Among intermediate-risk patients, AAs were detected in 648 (9.4%) patients at first surveillance. A significant trend of increasing AA detection rate at first surveillance was seen with increasing interval length. Compared with an interval of < 18 months, the detection rates of AAs at first surveillance were similar with intervals of 2 and 3 years (9%), but increased to 11% with an interval of 4 years and to > 13% for an interval of 5 or 6 years (*Table 13*).

Among intermediate-risk patients, 104 (1.5%) patients had CRC detected at first surveillance. A significant trend of increasing detection rate of CRC at first surveillance was seen with increasing interval length. Compared with an interval of < 18 months, detection rates of CRC at first surveillance were similar with an interval of 2 or 3 years, but were two times greater with an interval of 4 years (see *Table 13*).

TABLE 12 Detection rate of AAs and CRC at first surveillance among low-risk patients by interval length and risk subgroup

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
< 18 months	326	14.0	9	2.8	802	17.4	56	7.0	328	13.9	2	0.6	814	17.3	12	1.5
2 years[c]	369	15.9	13	3.5	725	15.7	50	6.9	372	15.8	3	0.8	743	15.8	18	2.4
3 years[c]	588	25.3	28	4.8	1282	27.8	85	6.6	590	25.1	2	0.3	1303	27.7	21	1.6
4 years[c]	309	13.3	22	7.1	616	13.3	53	8.6	313	13.3	4	1.3	627	13.3	11	1.8
5 years[c]	430	18.5	28	6.5	667	14.4	68	10.2	435	18.5	5	1.1	675	14.3	8	1.2
6 years[c]	162	7.0	17	10.5	279	6.0	20	7.2	165	7.0	3	1.8	283	6.0	4	1.4
7 years[c]	86	3.7	8	9.3	143	3.1	21	14.7	86	3.7	0	0.0	150	3.2	7	4.7
8 years[c]	57	2.4	4	7.0	104	2.3	14	13.5	65	2.8	8	12.3	113	2.4	9	8.0
Total	2327	100	129	5.5	4618	100	367	7.9	2354	100	27	1.1	4708	100	90	1.9
p-value[d]			< 0.0001				0.0002				< 0.0001				0.0181	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.47 (1.20 to 1.81); 0.0002								1.68 (1.09 to 2.59); 0.014							

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.

TABLE 13 Detection rate of AAs and CRC at first surveillance among intermediate-risk patients by interval length

Interval length to first surveillance	AAs[a]				CRC			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%
< 18 months	1950	28.3	153	7.8	1975	28.2	25	1.3
2 years[b]	1211	17.6	106	8.8	1234	17.6	23	1.9
3 years[b]	2216	32.1	204	9.2	2232	31.9	16	0.7
4 years[b]	680	9.9	72	10.6	698	10.0	18	2.6
5 years[b]	554	8.0	75	13.5	567	8.1	13	2.3
6 years[b]	285	4.1	38	13.3	294	4.2	9	3.1
Total	6896	100	648	9.4	7000	100	104	1.5
p-value[c]			< 0.0001				0.015	

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b Interval length ± 6 months.
c *p*-values were from a test for trend.

Findings at first surveillance by risk subgroup

We observed a significant trend of increased AA detection at first surveillance with increasing interval length within the lower-risk and higher-risk subgroups of intermediate-risk patients. Among lower-risk patients, AA detection rates were approximately 6–7% with intervals of < 18 months through to 3 years, increasing to 11% with an interval of 4 years. Among higher-risk patients, AA detection rates varied between 9% and 11% with intervals of < 18 months through to 4 years, increasing to approximately 18% with an interval of 5 years. The OR for the comparison of AA detection rates in the higher- and lower-risk subgroups was 1.58 (95% CI 1.33 to 1.89) (*Table 14*).

In the lower-risk subgroup, we did not observe a significant trend in CRC detection rates at first surveillance by interval length. The detection rates were between 0.5% and 2.4%. By comparison, in the higher-risk subgroup there was a significant increasing trend in CRC detection rates at first surveillance with increasing interval length. Detection rates were approximately 1–2% with intervals of < 18 months through to 3 years, increasing to 4% with an interval of 4 years. The OR for the comparison of CRC detection rates in the higher- and lower-risk subgroups was 2.12 (95% CI 1.34 to 3.35) (see *Table 14*).

The high-risk group

Among high-risk patients, AAs were detected at first surveillance in 240 (14.8%) and CRC was detected in 23 (1.4%). We did not detect a significant trend in AA detection rates at first surveillance with changing interval length. The AA detection rates were > 11% for all intervals. There was a significant trend in CRC detection rates with increasing interval length, with an increased detection of CRC with an interval of 2 years compared with an interval of < 15 months (*Table 15*). However, there were fewer than 10 CRC cases in each interval length category.

Findings at first surveillance by risk subgroup

In both risk subgroups of high-risk patients, AA detection rates at first surveillance varied between 10% and 21%, although there was no discernible trend with interval length. For CRC, detection rates at first surveillance in the lower-risk subgroup were between 0% and 3% and we did not detect a trend with interval length. In the higher-risk subgroup there was a significant trend in CRC detection

TABLE 14 Detection rate of AAs and CRC at first surveillance among intermediate-risk patients by interval length and risk subgroup

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
< 18 months	642	24.0	35	5.5	1308	31.0	118	9.0	645	23.9	3	0.5	1330	30.9	22	1.7
2 years[c]	399	14.9	24	6.0	812	19.3	82	10.1	407	15.1	8	2.0	827	19.2	15	1.8
3 years[c]	1024	38.2	68	6.6	1192	28.3	136	11.4	1029	38.1	5	0.5	1203	28.0	11	0.9
4 years[c]	255	9.5	29	11.4	425	10.1	43	10.1	256	9.5	1	0.4	442	10.3	17	3.8
5 years[c]	241	9.0	20	8.3	313	7.4	55	17.6	247	9.1	6	2.4	320	7.4	7	2.2
6 years[c]	117	4.4	15	12.8	168	4.0	23	13.7	118	4.4	1	0.8	176	4.1	8	4.5
Total	2678	100	191	7.1	4218	100	457	10.8	2702	100	24	0.9	4298	100	80	1.9
p-value[d]			0.0007				0.0002				0.28				0.014	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.58 (1.33 to 1.89); < 0.0001								2.12 (1.34 to 3.35); 0.0007							

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.

TABLE 15 Detection rate of AAs and CRC at first surveillance among high-risk patients by interval length

Interval length to first surveillance	AAs[a]				CRC			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%
< 15 months	735	45.3	110	15.0	742	45.1	7	0.9
1.5 years[b]	287	17.7	35	12.2	288	17.5	1	0.3
2 years[b]	170	10.5	19	11.2	176	10.7	6	3.4
2.5 years[b]	85	5.2	17	20.0	87	5.3	2	2.3
3 years[b]	246	15.2	45	18.3	250	15.2	4	1.6
3.5 years[b]	100	6.2	14	14.0	103	6.3	3	2.9
Total	1623	100	240	14.8	1646	100	23	1.4
p-value[c]			0.32				0.0460	

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b Interval length ± 3 months.
c *p*-values were from a test for trend.

rates with interval length, although the pattern was not linear as CRC detection rates increased from 2% with an interval of < 15 months to 4% with an interval of 2 years and 5% with an interval of 3 years (*Table 16*). Although statistical power was limited, the OR for the comparison of CRC detection rates in the higher- and lower-risk subgroups was 3.09 (95% CI 1.33 to 7.19).

Sensitivity analyses

Patients without a complete baseline colonoscopy

Our first sensitivity analysis involved the exclusion of patients who did not have a complete baseline colonoscopy (low-risk group, $n = 2682$; intermediate-risk group, $n = 2885$; high-risk group, $n = 365$). This had little effect on the results for the long-term CRC incidence analyses (see *Appendix 2*, *Tables 28–32*), although adenoma histology, adenoma dysplasia and age were no longer independently associated with CRC incidence in the low-, intermediate- and high-risk groups, respectively (see *Appendix 2*, *Tables 28–30*).

We also performed this sensitivity analysis for the detection rates of AAs and CRC at first surveillance by interval length and risk subgroup (see *Appendix 2*, *Table 33*) and the results were similar to those of the main analysis. A minor difference was that in the high-risk group there was no longer a significant trend of increasing CRC detection with increasing interval in the higher-risk subgroup, nor a significant difference in the odds of CRC detection between the two risk subgroups. However, the number of CRC cases in the high-risk group was low in this analysis.

Incompletely resected baseline lesions

We also performed a sensitivity analysis of the criteria used to decide whether or not a CRC had arisen from an incompletely resected baseline lesion, which we excluded from analyses. In the main analysis we excluded cancers that were found in the same or adjacent colonic segment to a baseline adenoma that was ≥ 15 mm in size and seen on two or more occasions within 5 years before cancer diagnosis (low-risk group, $n = 0$; intermediate-risk group, $n = 38$; high-risk group, $n = 12$). In the sensitivity analysis we excluded some additional cancers that met some but not all the criteria above, but that we thought were likely to have arisen from an incompletely resected baseline lesion (low-risk group, $n = 6$; intermediate-risk group, $n = 29$; high-risk group, $n = 7$).

TABLE 16 Detection rate of AAs and CRC at first surveillance among high-risk patients by interval length and risk subgroup

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
< 15 months	513	47.5	76	14.8	222	40.9	34	15.3	516	47.4	3	0.6	226	40.6	4	1.8
1.5 years[c]	161	14.9	23	14.3	126	23.2	12	9.5	161	14.8	0	0.0	127	22.8	1	0.8
2 years[c]	104	9.6	11	10.6	66	12.2	8	12.1	107	9.8	3	2.8	69	12.4	3	4.3
2.5 years[c]	47	4.4	9	19.1	38	7.0	8	21.1	48	4.4	1	2.1	39	7.0	1	2.6
3 years[c]	184	17.0	35	19.0	62	11.4	10	16.1	185	17.0	1	0.5	65	11.7	3	4.6
3.5 years[c]	71	6.6	9	12.7	29	5.3	5	17.2	72	6.6	1	1.4	31	5.6	2	6.5
Total	1080	100	163	15.1	543	100	77	14.2	1089	100	9	0.8	557	100	14	2.5
p-value[d]			0.46				0.51				0.38				0.043	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	0.93 (0.69 to 1.25); 0.62								3.09 (1.33 to 7.19); 0.0077							

a Patients in whom CRC was detected at first surveillance were excluded from the analyses of AA detection rates.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c Interval ± 3 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.

These additional exclusions did not materially alter the results (see *Appendix 2*, *Tables 34–37*). In the analyses of long-term CRC incidence by baseline characteristics there were slight changes to the associated *p*-values for some variables, such that they crossed to the opposite side of the 0.05 significance threshold, although the HR point estimates did not change substantially (see *Appendix 2*, *Tables 34–36*). In the intermediate-risk group there were changes in significance for sex, year of baseline visit and length of baseline visit, although no such changes were seen for any of the variables used to classify the risk subgroups.

In addition, in all three risk groups the estimates for the comparison of CRC incidence in the presence and absence of surveillance were similar in the sensitivity analysis and the main analysis (see *Appendix 2*, *Tables 34–36*). We also observed little change in results when we performed this sensitivity analysis for the detection rates of AAs and CRC at first surveillance by interval and risk subgroup (see *Appendix 2*, *Table 37*).

Higher-risk classification criteria for the intermediate-risk group

In our sensitivity analysis of the risk classification criteria for intermediate-risk patients we additionally included poor bowel preparation and adenomas $\geq$ 20 mm in size in the classification of higher risk. As a result, the proportion of patients classified as higher risk increased from 60% to 74% in our analyses of long-term CRC incidence. This did not have much impact on CRC incidence rates, estimates for the comparison of CRC incidence in the presence and absence of surveillance or SIRs (see *Appendix 2*, *Tables 38* and *39*). In our analyses of findings at first surveillance the proportion of patients classified as higher risk increased from 61% to 76% and results by interval length within each risk subgroup were not materially altered (see *Appendix 2*, *Table 40*).

Surveillance interval length cut-off point for the low-risk group

In a fourth sensitivity analysis we changed our interval length cut-off point for the low-risk group from 8.5 years to 6.5 years. With this change in cut-off point there was still a significant trend of increasing detection of AAs at first surveillance with increasing interval length in both risk subgroups. Detection rates of AAs and CRC were also still significantly higher in the higher-risk subgroup than in the lower-risk subgroup. However, there was no longer a significant trend in CRC detection rates with interval length in either risk subgroup (see *Appendix 2*, *Table 41*).

Hospital attended

For our final sensitivity analysis we also considered the hospital that patients attended as a potential confounding variable. In the analyses of long-term CRC incidence the hospital attended was independently associated with incidence rates in the low- and intermediate-risk groups, but not in the high-risk group. When we additionally adjusted for hospital the multivariable HRs for the other variables changed very little, although adenoma histology was no longer significant in the low-risk group (see *Appendix 2*, *Table 42*).

Chapter 4 Economic evaluation assessing the cost-effectiveness of surveillance

Background and aims

Colorectal cancer costs the NHS > £1B each year.[41] Preventing or diagnosing this cancer earlier will reduce the costs associated with treatment and complications. Since the introduction of the national BCSP in 2006 there has been a marked increase in demand for NHS endoscopy services. Surveillance colonoscopies constitute a sizeable proportion of all colonoscopies carried out in the NHS. A national colonoscopy audit from 2011 estimated that surveillance colonoscopies accounted for approximately 20% of all colonoscopies performed in the UK over a 2-week period.[21] Therefore, the implications of changing surveillance for NHS resource use and costs are likely to be substantial.

The aim of this economic evaluation was to undertake a costing and cost-effectiveness analysis, comparing costs and outcomes of patients who underwent surveillance colonoscopy following baseline colonoscopy with those who did not. We follow the clinical analysis presented in this report by comparing a strategy of surveillance with no surveillance within the three main risk groups defined in the 2002 UK-ASG,[7] each of which we additionally stratified into lower- and higher-risk subgroups on the basis of baseline CRC risk factors (as described in *Chapter 3*). However, unlike the clinical analysis, we make no comparison with the general population. (For an economic analysis this would require detailed information on resource use, as well as incidence rates of CRC.)

Methods

Form of evaluation

The economic analysis consists of both a within-study analysis using individual patient-level data recorded on the study database and a lifetime analysis using a Markov model. The study database provided resource use information on the number and type of colonic examinations. Both analyses included all 28,972 patients included in the clinical analysis (i.e. 14,401 low-risk patients, 11,852 intermediate-risk patients and 2719 high-risk patients).

For the within-study analysis an annual rate of total cost per person-year was calculated for each risk subgroup across a median follow-up of 9.3 years. As the study database did not include any information on QoL, it was not possible to estimate QALYs directly from the study data. The within-study analysis used the diagnosis of CRC as the main outcome measure, with cost-effectiveness expressed in terms of the incremental cost per CRC prevented.

An extrapolation model was then used to estimate the cost-effectiveness of each surveillance strategy over the lifetime of the cohort. Surveillance costs and transition probabilities for each risk subgroup were estimated using patient-level data on the study database. For this analysis to measure outcomes using QALYs, QoL data were obtained from the PHE PROMs survey of CRC patients known to the National Cancer Registration and Analysis Service[37] and combined with survival data from the Northern and Yorkshire Cancer Registry and Information Service.[42]

Estimation of costs

Table 17 shows the unit costs used in our analyses and the sources of these costs. Costs were applied to the resource use associated with both adenoma surveillance and cancer treatment. The analysis was undertaken from the perspective of the NHS, with costs reported in GBP using 2017/18 prices. Unit costs for surveillance procedures were taken from the NHS national schedule of reference costs for 2017–18.[33] Estimates for the lifetime cost of CRC treatment were taken from published estimates from a whole disease model of CRC.[44] These costs were inflated from 2012/13 prices to 2017/18 prices using the gross domestic product deflator.

TABLE 17 Unit costs

Resource category	Unit cost (2017/18 GBP/£)	Source
Diagnostic colonoscopy	525	NHS reference costs 2017/18[33]
Colonoscopy with polypectomy	641	NHS reference costs 2017/18[33]
Diagnostic flexible sigmoidoscopy	402	NHS reference costs 2017/18[33]
Flexible sigmoidoscopy with polypectomy	512	NHS reference costs 2017/18[33]
Rigid sigmoidoscopy (diagnostic or therapeutic)	730	NHS reference costs 2017/18[33]
Pathology cost for adenoma	84	Murphy *et al.*[43] Inflated to 2017/18 prices using GDP deflator
Pathology cost for CRC	84	Murphy *et al.*[43] Inflated to 2017/18 prices using GDP deflator
CRC treatment		
Lifetime cost by age (years) (Dukes' stage A)		Whyte *et al.*[44] Estimated using a whole disease model of CRC. Inflated to 2017/18 prices using GDP deflator
40–49	9085	
50–59	5928	
60–69	4798	
70–79	3298	
80–100	1432	
Lifetime cost by age (years) (Dukes' stage B)		
40–49	9071	
50–59	7281	
60–69	5554	
70–79	3585	
80–100	1604	
Lifetime cost by age (years) (Dukes' stage C)		
40–49	15,038	
50–59	10,058	
60–69	7534	
70–79	4655	
80–100	1620	

TABLE 17 Unit costs (*continued*)

Resource category	Unit cost (2017/18 GBP/£)	Source
Lifetime cost by age (years) (Dukes' stage D)		
40–49	12,148	
50–59	8763	
60–69	6755	
70–79	4530	
80–100	837	

GDP, gross domestic product.

The definition of surveillance visits used in previous chapters is maintained in this chapter. Visits were costed by applying unit costs to each colonic examination. Costs were different for colonoscopies, flexible sigmoidoscopies and rigid sigmoidoscopies, and varied depending on whether the examination was diagnostic or therapeutic. The distinction between a diagnostic and a therapeutic examination was made using data on whether or not a polyp was removed or whether there was an associated biopsy or pathology report.

Within-study analysis

The within-study analysis compared patients who underwent surveillance with those who did not for each of the six risk subgroups (i.e. for the lower- and higher-risk subgroups within each of the low-, intermediate- and high-risk groups). Cost-effectiveness was measured in terms of the incremental cost per CRC prevented by adopting surveillance compared with no surveillance. This follows the approach of a recent cost-effectiveness study of post-polypectomy surveillance.[45]

Total annual costs and CRC incidence rates were calculated for each of the three main risk groups and for the lower- and higher-risk subgroups within each risk group. Poisson models were used to estimate annual CRC incidence rates for each risk group across varying exposure time. Differences in CRC incidence rates were compared using the Wald test, with SEs being combined using the delta method. We calculated ICERs as the ratio between the difference in costs and the difference in CRC incidence rates.

Missing data were infrequent in the data set, with the exception of CRC staging information, which was missing for 32% of CRC cases. Logit models indicated that these missing data were significantly positively associated with age at baseline and negatively associated with the date of the surveillance visit (data not shown). Missing CRC staging data were handled by means of multiple imputation using an ordered logit model. The procedure was repeated to produce 40 imputed data sets, with Rubin's rule used to summarise across imputations.[46] In the main analysis, total costs were then estimated based on the imputed data. Ten patients in the data were untraceable. These patients were treated as having had no surveillance visits and having not developed CRC. Both costs and number of CRC cases were discounted at a rate of 3.5% per year. The analysis was conducted in Stata®/SE 14 (StataCorp LP, College Station, TX, USA).

Extrapolation model

We designed a multistate Markov model to extrapolate the results from the within-study analysis over a lifetime horizon. *Figure 5* shows the structure of the model. The model consisted of eight states: (1) no surveillance visits, (2) a positive count of surveillance visits, (3) Dukes' stage A CRC, (4) Dukes' stage B CRC, (5) Dukes' stage C CRC, (6) Dukes' stage D CRC, (7) death from CRC and (8) death from other

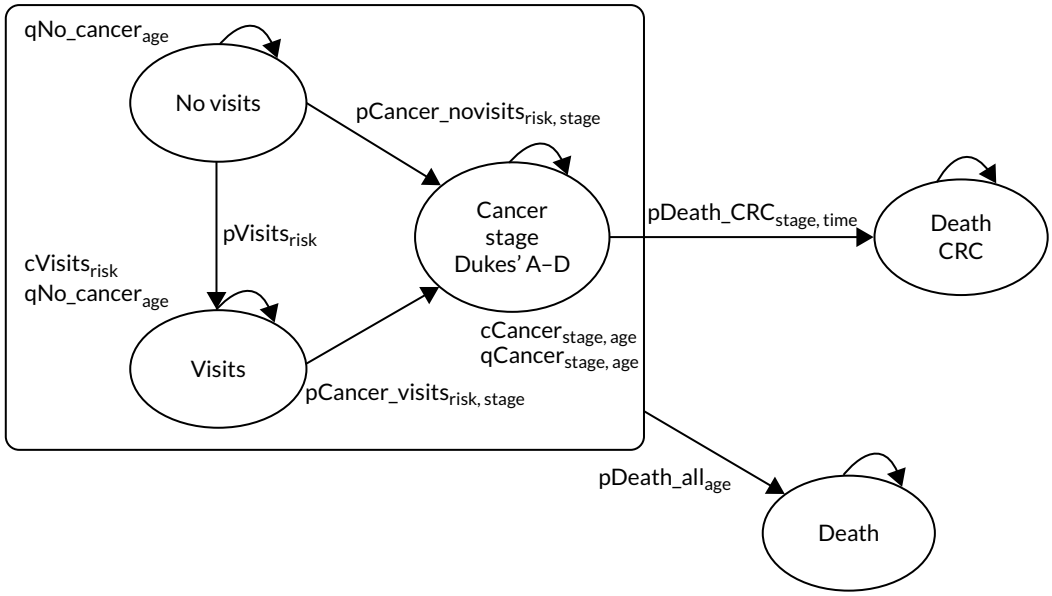

FIGURE 5 Markov model for our lifetime economic analysis.

causes. Time-homogeneous transition probabilities were estimated for each of the three main risk groups using state and time data from the main study database and using the msm package in R (The R Foundation for Statistical Computing, Vienna, Austria). SEs for each set of transition probabilities were calculated using an assumed multivariate normal distribution of the maximum likelihood estimates and covariance matrix.

All patients begin the model in the 'no visits' state, having attended a baseline colonoscopy but having had no surveillance visits. In each cycle patients have a probability of attending a surveillance visit that is dependent on which risk group they are in. The patients also face a probability of developing CRC and having it diagnosed at Dukes' stage A, B, C or D. A transition to the 'visits' state reduces the patient's risk of CRC and this benefit is assumed to last for the remaining length of the model. The transition probabilities between the 'no visits' state and the 'visits' state, as well as the transitions to each of the cancer states, were estimated separately for each risk group.

The numbers of surveillance visits and intervals between them as observed within each risk subgroup in the study data were used to estimate a constant annual probability for each subgroup. The model does not explicitly model the impact of the number of surveillance visits as the surveillance strategies being compared are defined in terms of whether or not surveillance occurred. However, the impact of the number of surveillance visits on CRC cases diagnosed is captured in the probability of transitioning from the 'visits' state to each of the four cancer states.

Missing CRC staging data were handled using the imputed data from the within-study analysis. Transition probabilities were calculated for each of the 40 imputed data sets, with SEs estimated by combining the estimates using Rubin's rule.[46] The sensitivity of the results to the use of the imputed CRC data were assessed by collapsing the model to a single cancer state for each of the risk subgroups.

A full set of transition probabilities and SEs could not be estimated for the higher-risk subgroup of the high-risk group because of a failure of model convergence. Therefore, a simplified version of the model was used for this group, in which the four cancer states were collapsed to a single state. QoL estimates, CRC treatment costs and CRC survival rates, which are separately estimated for each cancer state, were collapsed to mean values for this subgroup.

The probability of death from any cause, QoL estimates and costs associated with CRC are dependent on the age of the cohort. These parameters required an initial age to be specified for the model. The initial age used for the base-case analysis was 60 years, as this was the mean age of patients in the hospital cohort.

The main clinical study was not powered to identify differences in CRC-related mortality by stage and there were relatively few CRC deaths in each category when stratifying by stage, which would make extrapolation based on these data unreliable. Therefore, the probabilities of survival of CRC were sourced from the 2013 *National Bowel Cancer Audit Annual Report*.[35] The probability of death from any cause was taken from national lifetables published by the Office for National Statistics.[36]

Resource use and costs

The extrapolation model includes costs for colonoscopy and lifetime costs associated with the diagnosis and treatment of CRC. A separate cost for adenoma surveillance was entered into the model for each risk subgroup. This cost was derived by estimating the mean annual cost of surveillance per patient during the within-study period and then applying that cost over the modelled duration of surveillance, from a starting age of 60 years through to 75 years, the upper age limit in the 2002 UK-ASG.[7] The lifetime cost of CRC was applied only to the first cycle in which CRC was diagnosed.

Quality of life

Quality-of-life data were not collected in the main clinical study. Therefore, the primary outcome measure in the within-study analysis was the incidence of CRC. The extrapolation model used estimated mean EQ-5D scores from a one-off study of CRC patients by a PHE PROMs survey.[37] This study collected QoL data from 21,802 patients who were diagnosed with CRC in England from 2010 to 2011 and were alive between 12 and 36 months after diagnosis, when they were sent a questionnaire including the EuroQol-5 Dimensions, five-level version. Responses were then scored using the 'crosswalk' mapping function developed by van Hout *et al.*[47] This allowed for comparison with the utility estimates derived from the EuroQol-5 Dimensions, three-level version (EQ-5D-3L), which was used for the non-cancer health states. The EQ-5D-3L scores for the non-cancer health states came from Ara and Brazier,[38] who reported EQ-5D-3L scores from pooled responses in the Health Survey for England from people without cancer.

The Ara and Brazier[38] scores and the estimates from the PROMs survey[37] were combined with estimated survival from the lifetime model to calculate QALYs. The use of the PROMs survey for QoL data differs from recent studies examining the cost-effectiveness of CRC screening or surveillance strategies,[23,43] which have mainly used estimates reported in Ara and Brazier.[38] The estimates from the PROMs survey[37] were preferred over those from Ara and Brazier[38] as the former is the largest UK survey of QoL for CRC patients currently available, and provides estimates by both CRC stage and age. Whyte *et al.*[48] estimated EQ-5D-3L scores by age and estimated CRC stage; however, these estimates are based on all cancer patients included in the Health Survey for England rather than only CRC patients. Therefore, the PROMs data were deemed more representative of the patients in our study cohort. The effect of using the estimates from Whyte *et al.*[48] on our model results was assessed in a sensitivity analysis.[48]

Future QALYs and costs were discounted to present values at an annual rate of 3.5%. ICERs were then calculated as the ratio between the mean difference in QALYs and the mean difference in costs. Cost-effectiveness was evaluated assuming a willingness-to-pay threshold of £20,000 per QALY.[49]

Sensitivity analyses

Uncertainty in the model estimates was characterised using a deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA). The DSA assessed the sensitivity of the model estimates to variation in individual parameters, whereas the PSA aimed to estimate the joint effect of uncertainty in all the parameters. For the DSA each parameter was both increased and decreased by 25% of its baseline value. The impact of these changes was measured in terms of the effect on the estimated

ICER for each surveillance strategy. A sensitivity analysis was also used to assess the impact of using different strategies to handle the missing CRC staging data.

In the PSA all transition probabilities, costs and QoL estimates were varied, except for the survival probabilities. The PSA was carried out by sampling 2000 sets of the model parameters drawn at random from appropriate statistical distributions. Uncertainty around each cost estimate was characterised using a gamma distribution, whereas beta distributions were fitted to both the transition probabilities and QoL estimates. These replications were used to plot the cost-effectiveness plane[50] and to construct cost-effectiveness acceptability curves that show the likelihood that the intervention is cost-effective as the willingness-to-pay changes.[51]

Table 18 shows the estimated transition probabilities, costs and QoL estimates used in the model. The transition probabilities between the 'no visit' and 'visit' states differ between risk groups, with the lowest probability estimated for the lower-risk subgroup of the low-risk group and the highest probability estimated for the higher-risk subgroup of the high-risk group. For the whole low-risk group and the higher-risk subgroup of intermediate-risk patients the transition probabilities to the different CRC states were mostly lower with surveillance than without. In contrast, for the lower-risk subgroup of intermediate-risk patients and the lower-risk subgroup of high-risk patients the transition probabilities to CRC were mostly higher with surveillance than without. Mean EQ-5D scores were higher for patients with CRC than for people in the same age group without cancer.

TABLE 18 Transition probabilities, costs and QoL estimates used in our extrapolation model

		Risk group					
		Low risk		Intermediate risk		High risk	
Parameter	Distribution for PSA	Lower-risk subgroup	Higher-risk subgroup	Lower-risk subgroup	Higher-risk subgroup	Lower-risk subgroup	Higher-risk subgroup
Annual transition probabilities							
No visits: visits	Beta	8.44×10^{-2}	1.08×10^{-1}	1.43×10^{-1}	1.72×10^{-1}	2.30×10^{-1}	2.36×10^{-1}
No visits: Dukes' stage A	Beta	3.82×10^{-4}	6.01×10^{-4}	5.14×10^{-4}	7.73×10^{-4}	1.21×10^{-3}	
Visits: Dukes' stage A	Beta	2.75×10^{-4}	3.00×10^{-4}	5.30×10^{-4}	5.66×10^{-4}	5.87×10^{-4}	
No visits: Dukes' stage B	Beta	2.18×10^{-4}	7.09×10^{-4}	2.75×10^{-4}	1.22×10^{-3}	7.69×10^{-4}	
Visits: Dukes' stage B	Beta	1.49×10^{-4}	3.07×10^{-4}	3.11×10^{-4}	6.48×10^{-4}	9.23×10^{-4}	
No visits: Dukes' stage C	Beta	1.93×10^{-4}	6.09×10^{-4}	4.47×10^{-4}	8.90×10^{-4}	5.33×10^{-4}	
Visits: Dukes' stage C	Beta	2.18×10^{-4}	3.86×10^{-4}	2.83×10^{-4}	9.09×10^{-4}	6.29×10^{-4}	
No visits: Dukes' stage D	Beta	1.42×10^{-4}	3.82×10^{-4}	1.65×10^{-4}	5.00×10^{-4}	3.14×10^{-4}	
Visits: Dukes' stage D	Beta	5.90×10^{-5}	1.39×10^{-4}	3.38×10^{-4}	2.87×10^{-4}	3.45×10^{-4}	
No visits: CRC	Beta						8.86×10^{-3}
Visits: CRC	Beta						4.50×10^{-3}
Surveillance cost							
Visits state	Gamma	1049	1238	1193	1434	1573	1691
Perforation treatment	Gamma	5748	5748	5748	5748	5748	5748
Cost of bleed	Gamma	474	474	474	474	474	474

TABLE 18 Transition probabilities, costs and QoL estimates used in our extrapolation model (*continued*)

Cost of CRC	Distribution for PSA	Dukes' stage A	B	C	D
Age 40–49 years	Gamma	£9085	£9071	£15,038	£12,148
Age 50–59 years	Gamma	£5928	£7281	£10,058	£8763
Age 60–69 years	Gamma	£4798	£5554	£7534	£6755
Age 70–79 years	Gamma	£3298	£3585	£4655	£4530
Age 80–100 years	Gamma	£1432	£1604	£1620	£837
Mean EQ-5D-5L score[a]	**Distribution for PSA**				
Non-cancer states	Beta	0.80	0.80	0.80	0.80
		Dukes' stage			
CRC states		***A***	***B***	***C***	***D***
Age < 55 years	Beta	0.81	0.81	0.76	0.71
Age 55–64 years	Beta	0.85	0.83	0.79	0.72
Age 65–74 years	Beta	0.85	0.83	0.81	0.77
Age 75–84 years	Beta	0.80	0.79	0.78	0.72
Age ≥ 85 years	Beta	0.75	0.72	0.73	0.63

EQ-5D-5L, EuroQol-5 Dimensions, five-level version.
a Mean EQ-5D-5L scores by CRC stage and age group were kindly provided by Amy Downing (Dr Amy Downing, University of Leeds, 2019, personal communication).

Note
Costs are reported in GBP.

The below list summarises the main modelling assumptions made in the lifetime analysis:

- The level of surveillance recorded in the study data set reflects practice under the 2002 UK-ASG.[7]
- The level of surveillance offered to each risk group is independent of the level of surveillance offered to the other risk groups.
- Transition probabilities are time homogeneous.
- Patients who did not attend surveillance are representative of patients who attended surveillance if their surveillance was withdrawn.
- There is no age cut-off point for surveillance in either of the considered surveillance strategies.
- There were no changes to the BCSP during the modelled period.
- The probability of a bleed occurring during a surveillance procedure is independent of polypectomy being performed.
- The probability of a bleed or bowel perforation occurring during a surveillance procedure is independent of risk group.
- The costs and QoL estimates associated with surveillance can be captured by explicitly modelling the growth of polyps.

Although we assumed that the probability of a bleed occurring during a surveillance procedure is independent of polypectomy being performed, polypectomy does in fact increase the risk of a bleed.[52] However, a simplification of the model is that it does not distinguish between a polypectomy being performed or not. Therefore, when applying the probability of a bleed it was necessary that the probability was independent of a polypectomy being performed. To achieve this we used an average across all colonoscopies performed sourced from Rutter *et al.*[52]

Results

Within-study analysis

Of the 525 CRCs in the study, 167 (32%) were missing CRC staging data. The proportion of missing CRC staging data varied between the risk groups. The highest proportion was 35% in the higher-risk subgroup of low-risk patients, whereas the lowest proportion was 24% in the lower-risk subgroup of intermediate-risk patients. However, the risk group was not a significant predictor of missing CRC staging data (data not shown).

The low-risk group

Table 19 shows the mean surveillance resources used and their associated cost in the lower- and higher-risk subgroups of the low-risk group over the full follow-up period.

TABLE 19 Surveillance resource use and costs in the low-risk group

Surveillance resource use and costs	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
	No visits ($n = 2804$)	Visits ($n = 2431$)	No visits ($n = 4403$)	Visits ($n = 4763$)
Surveillance resource use per patient				
Therapeutic colonoscopy	0	0.63 (0.87)	0	0.90 (1.13)
Diagnostic colonoscopy	0	0.91 (0.85)	0	0.92 (0.92)
Therapeutic flexible sigmoidoscopy	0	0.05 (0.22)	0	0.05 (0.29)
Diagnostic flexible sigmoidoscopy	0	0.19 (0.48)	0	0.18 (0.50)
Rigid sigmoidoscopy	0	0	0	0
Total	0	1.78 (1.09)	0	2.04 (1.45)
CRC cases[a]				
Dukes' stage A	12 (0.104)	5 (0.166)	29 (0.051)	11 (0.084)
Dukes' stage B	7 (0.096)	3 (0.144)	34 (0.049)	11 (0.080)
Dukes' stage C	7 (0.089)	3 (0.154)	30 (0.050)	14 (0.088)
Dukes' stage D	5 (0.072)	0	19 (0.041)	5 (0.062)
Total	31	11	112	41
Person-years	32,903	16,882	51,688	37,429
Incidence per 1000 person-years	0.94	0.65	2.17	1.10
	Mean (SD/SE)	*Mean (SD/SE)*	*Mean (SD/SE)*	*Mean (SD/SE)*
Surveillance costs (£)				
Therapeutic colonoscopy	0 (0)	457 (632)	0 (0)	649 (816)
Diagnostic colonoscopy	0 (0)	479 (445)	0 (0)	481 (484)
Therapeutic flexible sigmoidoscopy	0 (0)	28 (134)	0 (0)	28 (175)
Diagnostic flexible sigmoidoscopy	0 (0)	77 (192)	0 (0)	73 (201)
Rigid sigmoidoscopy	0 (0)	0 (0)	0 (0)	0 (0)
Total	0 (0)	1041 (682)	0 (0)	1231 (921)

TABLE 19 Surveillance resource use and costs in the low-risk group (*continued*)

Surveillance resource use and costs	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
	No visits ($n = 2804$)	Visits ($n = 2431$)	No visits ($n = 4403$)	Visits ($n = 4763$)
CRC costs (£)				
Dukes' stage A	10 (3.96)	5 (3.74)	18 (4.86)	3 (1.57)
Dukes' stage B	6 (3.34)	5 (3.66)	20 (4.99)	7 (2.49)
Dukes' stage C	6 (3.90)	3 (4.43)	17 (5.45)	13 (4.57)
Dukes' stage D	5 (3.24)	0 (0)	14 (4.53)	4 (2.25)
Total and discounted costs (£)				
Total CRC cost	27 (6.19)	13 (6.10)	69 (8.84)	26 (5.51)
Total cost per patient	27 (6.19)	1054 (15.14)	69 (8.84)	1258 (14.60)
Discounted total cost per patient	22 (5.17)	928 (13.79)	58 (7.55)	1116 (13.30)
Discounted total cost per 1000 person-years	1906 (43.56)	133,612 (168.87)	4942 (66.94)	142,023 (73.19)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	131,706 (127,543 to 135,868); < 0.001		137,081 (133,552 to 140,609); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.29 (−0.80 to 0.22); 0.262		−1.07 (−1.59 to −0.55); < 0.001	
Incremental cost per CRC prevented	453,221		127,945	

SD, standard deviation.
a Including cases with missing staging data. Handled using multiple imputation.

Notes
Costs are reported in GBP.
p-values are from the Wald test.

Among those attending surveillance, the mean total number of surveillance examinations performed in the lower- and higher-risk subgroups was 1.78 and 2.04, respectively. The mean total cost of surveillance was £1041 in the lower-risk subgroup and £1231 in the higher-risk subgroup (see *Table 19*).

In the lower-risk subgroup of low-risk patients, the mean discounted total cost for patients attending surveillance was £133,612 per 1000 person-years, whereas the equivalent figure for patients not attending surveillance was £1906 per 1000 person-years. Therefore, in this subgroup, the total incremental cost for those with surveillance compared with those with no surveillance was £131,706 (see *Table 19*).

In the lower-risk subgroup of low-risk patients, more CRCs were diagnosed among those with no surveillance than among those with surveillance, at 0.94 and 0.65 per 1000 person-years, respectively. When we combined the difference in costs and CRC cases, the incremental cost per CRC prevented was £453,221 (see *Table 19*).

In the higher-risk subgroup of low-risk patients, the total incremental cost for those with surveillance compared with those with no surveillance was £137,081 per 1000 person-years, similar to that in the lower-risk subgroup. However, the difference in the CRC incidence rate among those with no

surveillance and those with surveillance was greater than in the lower-risk subgroup, at 2.17 and 1.10 per 1000 person-years, respectively. Therefore, when we combined the difference in costs and CRC cases the incremental cost per CRC prevented was £127,945, which is far lower than in the lower-risk subgroup (see *Table 19*).

The intermediate-risk group

In the intermediate-risk group surveillance resource use was similar in the lower- and higher-risk subgroups (*Table 20*). The total incremental cost of surveillance per 1000 person years was £140,780 in the lower-risk subgroup and £153,409 in the higher-risk subgroup. As the incidence of CRC was lower in the lower- than higher-risk subgroup, the incremental cost per CRC prevented was higher in the lower-risk subgroup (i.e. £2,587,860) than in the higher-risk subgroup (i.e. £145,729) (see *Table 20*).

TABLE 20 Surveillance resource use and costs in the intermediate-risk group

	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
Surveillance resource use and costs	No visits ($n = 1932$)	Visits ($n = 2806$)	No visits ($n = 2751$)	Visits ($n = 4363$)
Surveillance resource use per patient				
Therapeutic colonoscopy	0	0.81 (1.01)	0	1.11 (1.24)
Diagnostic colonoscopy	0	0.97 (0.89)	0	0.93 (0.96)
Therapeutic flexible sigmoidoscopy	0	0.06 (0.29)	0	0.09 (0.43)
Diagnostic flexible sigmoidoscopy	0	0.15 (0.44)	0	0.20 (0.60)
Rigid sigmoidoscopy	0	0.00 (0.00)	0	0.00 (0.03)
Total	0	1.98 (1.32)	0	2.33 (1.76)
CRC cases[a]				
Dukes' stage A	12 (0.090)	10 (0.101)	22 (0.051)	20 (0.052)
Dukes' stage B	6 (0.077)	7 (0.092)	36 (0.056)	22 (0.155)
Dukes' stage C	10 (0.088)	5 (0.082)	29 (0.052)	30 (0.244)
Dukes' stage D	5 (0.063)	6 (0.085)	15 (0.041)	10 (0.042)
Total	33	29	102	82
Person-years	23,237	21,233	30,690	36,110
Incidence per 1000 person-years	1.42	1.37	3.32	2.27
	Mean (SD/SE)	*Mean (SD/SE)*	*Mean (SD/SE)*	*Mean (SD/SE)*
Surveillance costs (£), mean (SD/SE)				
Therapeutic colonoscopy	0 (0)	586 (729)	0 (0)	801 (901)
Diagnostic colonoscopy	0 (0)	507 (468)	0 (0)	490 (505)
Therapeutic flexible sigmoidoscopy	0 (0)	35 (172)	0 (0)	55 (256)
Diagnostic flexible sigmoidoscopy	0 (0)	59 (177)	0 (0)	80 (240)
Rigid sigmoidoscopy	0 (0)	0 (0)	0 (0)	1 (19)
Total surveillance cost	0 (0)	1187 (826)	0 (0)	1427 (1095)

TABLE 20 Surveillance resource use and costs in the intermediate-risk group (*continued*)

	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
Surveillance resource use and costs	No visits ($n = 1932$)	Visits ($n = 2806$)	No visits ($n = 2751$)	Visits ($n = 4363$)
CRC costs (£)				
Dukes' stage A	13 (5.29)	6 (3.13)	12 (4.83)	6 (2.34)
Dukes' stage B	5 (4.13)	5 (2.62)	24 (6.55)	14 (3.90)
Dukes' stage C	20 (10.13)	8 (4.02)	38 (10.35)	21 (5.54)
Dukes' stage D	5 (3.50)	10 (5.50)	18 (6.87)	5 (2.58)
Total and discounted costs (£)				
Total CRC cost	44 (11.75)	29 (7.59)	92 (13.57)	47 (7.14)
Total cost per patient	44 (11.75)	1216 (17.73)	92 (13.57)	1473 (18.09)
Discounted total cost per patient	35 (8.91)	1087 (15.84)	79 (11.83)	1328 (16.52)
Discounted total cost per 1000 person-years	2891 (76.13)	143,672 (100.16)	7078 (104.23)	160,488 (80.89)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	140,780 (136,315 to 145,244); < 0.001		153,409 (149,822 to 157,996); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.05 (−0.75 to 0.64); 0.878		−1.05 (−1.86 to −0.24); 0.011	
Incremental cost per CRC prevented	2,587,860		145,729	

SD, standard deviation.
a Including cases with missing staging data. Handled using multiple imputation.

Notes
Costs are reported in GBP.
p-values are from the Wald test.

The high-risk group

The high-risk group had the greatest level of surveillance resource use and associated costs of any of the three risk groups (*Table 21*). The total incremental cost of surveillance per 1000 person-years was similar in the lower- and higher-risk subgroups of high-risk patients, at £196,436 and £186,212, respectively. However, because the subgroups had different CRC incidence rates, the incremental costs per CRC prevented differed significantly, being £568,719 in the lower-risk subgroup and £36,636 in the higher-risk subgroup (see *Table 21*).

Appendix 3, *Tables 43–45*, report total costs for each baseline risk group when using only complete CRC staging data. These tables apply mean costs by age group to known CRC cases with unknown staging data. This change did not alter the main results to a large degree, as the lifetime cost of CRC care made up a relatively small proportion of the total cost.

Lifetime analysis

A comparison of observed and predicted percentage in each state from a single imputed data set showed that the model fitted the data reasonably well (see *Appendix 3*, *Figures 9–14*). The results from our lifetime model are shown in *Table 22*. For each of the three main risk groups ICERs were lower in the higher- than in the lower-risk subgroup.

TABLE 21 Surveillance resource use and costs in the high-risk group

Surveillance resource use and costs	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
	No visits ($n = 606$)	Visits ($n = 1211$)	No visits ($n = 305$)	Visits ($n = 597$)
Surveillance resource use per patient				
Therapeutic colonoscopy	0	1.55 (1.39)	0	1.59 (1.54)
Diagnostic colonoscopy	0	0.68 (0.84)	0	0.77 (0.83)
Therapeutic flexible sigmoidoscopy	0	0.08 (0.36)	0	0.11 (0.51)
Diagnostic flexible sigmoidoscopy	0	0.11 (0.37)	0	0.15 (0.44)
Rigid sigmoidoscopy	0	0.00 (0.00)	0	0.00 (0.00)
Total	0	2.41 (1.63)	0	2.62 (1.88)
CRC cases[a]				
Dukes' stage A	7 (0.142)	5 (0.104)	7 (0.103)	3 (0.085)
Dukes' stage B	5 (0.130)	8 (0.114)	12 (0.107)	8 (0.123)
Dukes' stage C	3 (0.187)	5 (0.105)	7 (0.102)	4 (0.214)
Dukes' stage D	2 (0.092)	3 (0.087)	2 (.)[b]	5 (0.242)
Total	17	21	27	19
Person-years	6226	8805	3017	4913
Incidence per 100,000 person-years	273	239	895	387
	Mean (SD/SE)	*Mean (SD/SE)*	*Mean (SD/SE)*	*Mean (SD/SE)*
Surveillance costs (£)				
Therapeutic colonoscopy	0 (0)	1120 (1006)	0 (0)	1149 (1115)
Diagnostic colonoscopy	0 (0)	357 (440)	0 (0)	405 (437)
Therapeutic flexible sigmoidoscopy	0 (0)	45 (213)	0 (0)	67 (302)
Diagnostic flexible sigmoidoscopy	0 (0)	43 (148)	0 (0)	61 (180)
Rigid sigmoidoscopy	0 (0)	0 (0)	0 (0)	0 (0)
Total surveillance cost	0 (0)	1565 (1087)	0 (0)	1682 (1248)
CRC costs (£)				
Dukes' stage A	28 (14.11)	13 (6.66)	59 (29.34)	4 (6.81)
Dukes' stage B	18 (12.00)	12 (6.07)	72 (26.85)	52 (21.35)
Dukes' stage C	17 (14.24)	13 (7.24)	48 (24.78)	39 (22.86)
Dukes' stage D	15 (13.99)	10 (6.57)	0 (0)	40 (22.58)
Total and discounted costs (£)				
Total CRC cost	79 (23.80)	48 (12.29)	184 (45.00)	135 (36.48)
Total cost per patient	79 (23.80)	1613 (33.89)	184 (45.00)	1817 (63.83)
Discounted total cost per patient	69 (20.77)	1477 (31.26)	154 (37.87)	1660 (57.90)
Discounted total cost per 1000 person-years	6706 (175.33)	203,144 (181.67)	15,518 (229.97)	201,731 (339.67)

TABLE 21 Surveillance resource use and costs in the high-risk group (*continued*)

Surveillance resource use and costs	Risk subgroup, mean (SD)/count (SE)			
	Lower risk		Higher risk	
	No visits ($n = 606$)	Visits ($n = 1211$)	No visits ($n = 305$)	Visits ($n = 597$)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	196,436, (187,027 to 205,845); < 0.001		186,212 (169,741 to 202,682); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.35 (−1.99 to 1.30); 0.681		−5.08 (−8.84 to −1.32); 0.008	
Incremental cost per CRC prevented	568,719		36,636	

SD, standard deviation.
a Including cases with missing staging data. Handled using multiple imputation.
b It was not possible to calculate the SE for this estimate using Rubin's rule.

Notes
Costs are reported in GBP.
p-values are from the Wald test.

TABLE 22 Estimates of cost-effectiveness from our extrapolation model

Estimates of cost-effectiveness	Risk subgroup			
	Lower risk		Higher risk	
	No visits	Visits	No visits	Visits
Low-risk group				
Cost of surveillance (£)	0	897	0	1091
Total CRC cost (£)	125	110	312	220
Discounted total cost (£)	83	742	207	971
Life-years	23	23	22	23
Discounted QALYs	12	12	12	12
Incremental cost (£)	660		764	
Incremental QALYs	0.005		0.028	
ICER (£)	136,496		27,341	
Probability of cost-effectiveness (%)[a]	11		58	
Intermediate-risk group				
Cost of surveillance (£)	0	1281	0	1522
Total CRC cost (£)	188	200	448	371
Discounted total cost (£)	124	1098	298	1406
Life-years	23	23	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	974		1108	
Incremental QALYs	−0.008		0.024	
ICER (£)	Dominated[a]		46,990	
Probability of cost-effectiveness (%)[a]	4		34	

continued

TABLE 22 Estimates of cost-effectiveness from our extrapolation model (*continued*)

Estimates of cost-effectiveness	Risk subgroup			
	Lower risk		Higher risk	
	No visits	Visits	No visits	Visits
High-risk group				
Cost of surveillance (£)	0	2144	0	2000
Total CRC cost (£)	343	358	1,077	694
Discounted total cost (£)	228	1877	726	2019
Life-years	22	22	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	1649		1293	
Incremental QALYs	−0.018		0.165	
ICER (£)	Dominated[a]		7821	
Probability of cost-effectiveness (%)[b]	10		86	

a More costly and less effective.
b At a threshold of £20,000 per QALY.

Note
Costs are reported in GBP.

In the case of the low-risk group, the incremental cost of surveillance per patient was only slightly higher in the higher-risk subgroup than in the lower-risk subgroup. However, as the QALY benefit from surveillance was much larger in the higher-risk subgroup than in the lower-risk subgroup, the ICER was approximately five times lower in the higher- than in the lower-risk subgroup (see *Table 22*).

A similar pattern was found in the intermediate-risk group. In both the higher- and lower-risk subgroups of intermediate-risk patients, the incremental cost of surveillance was approximately £1000 per patient. However, as the higher-risk subgroup had a higher QALY gain from surveillance than the lower-risk subgroup, the ICER in the higher-risk subgroup was approximately £47,000, whereas surveillance in the lower-risk subgroup was dominated (i.e. more costly and less effective) (see *Table 22*).

The same pattern was observed in the high-risk group. Surveillance was dominated in the lower-risk subgroup, whereas the ICER in the higher-risk subgroup was £7821. This shows that surveillance was cost-effective in the higher-risk subgroup of high-risk patients when using a cost-effectiveness threshold of £20,000 per QALY gained (see *Table 22*).

Sensitivity analyses

The results of the DSA for the low-risk group are shown in *Appendix 3*, *Figure 15*. In both the lower- and higher-risk subgroups the results were most sensitive to variation in the cost of surveillance. In the case of the higher-risk subgroup, a 25% reduction in the cost of surveillance reduced the estimated ICER to below the £20,000 per QALY threshold. ICERs in the lower-risk subgroup did not fall below this threshold. Estimated ICERs for both subgroups were insensitive to changes in costs associated with CRC treatment.

The results of the DSA for the intermediate-risk group are shown in *Appendix 3*, *Figure 16*. The ICER for the lower-risk subgroup was most sensitive to variation in the transition probabilities between the 'visits' state and the Dukes' stage D state, and between the 'no visits' state and the Dukes' stage C state. The ICER in the higher-risk subgroup was most sensitive to variation in the QoL estimates for the non-cancer states. Variation in the cost of surveillance produced the largest increase in the ICER in the lower-risk subgroup and the largest decrease in the ICER in the higher-risk subgroup. In the case of the higher-risk subgroup, a 25% reduction in the cost of surveillance reduced the ICER to < £30,000 per QALY.

The results of the DSA for the high-risk group are shown in *Appendix 3*, *Figure 17*. For the lower-risk subgroup changes in the transition probability between the 'visits' state and the Dukes' stage D state resulted in large changes in the ICER. In the case of the higher-risk subgroup, no variation in the analysis resulted in an ICER above the £20,000 per QALY threshold. The results for each risk group were relatively insensitive to changes in the estimates of CRC incidence.

The results from the PSA are shown in *Figures 6* and *7*. *Figure 6* shows the cost-effectiveness plane for each of the three risk groups. The plane shows a similar spread of costs for each risk group and a great variability in QALYs. *Figure 7* shows the cost-effectiveness acceptability curves for each risk group. In each risk group surveillance had a higher probability of being cost-effective in the higher-risk subgroup than in the lower-risk subgroup. For example, in the low-risk group the probabilities of surveillance being cost-effective were 11% and 58% in the lower- and higher-risk subgroups, respectively. In the intermediate-risk group the equivalent probabilities were 4% and 34% in the lower- and higher-risk subgroups, respectively. In the high-risk group surveillance had a 10% probability of being cost-effective in the lower-risk subgroup compared with an 86% probability in the higher-risk subgroup (see *Figure 7*).

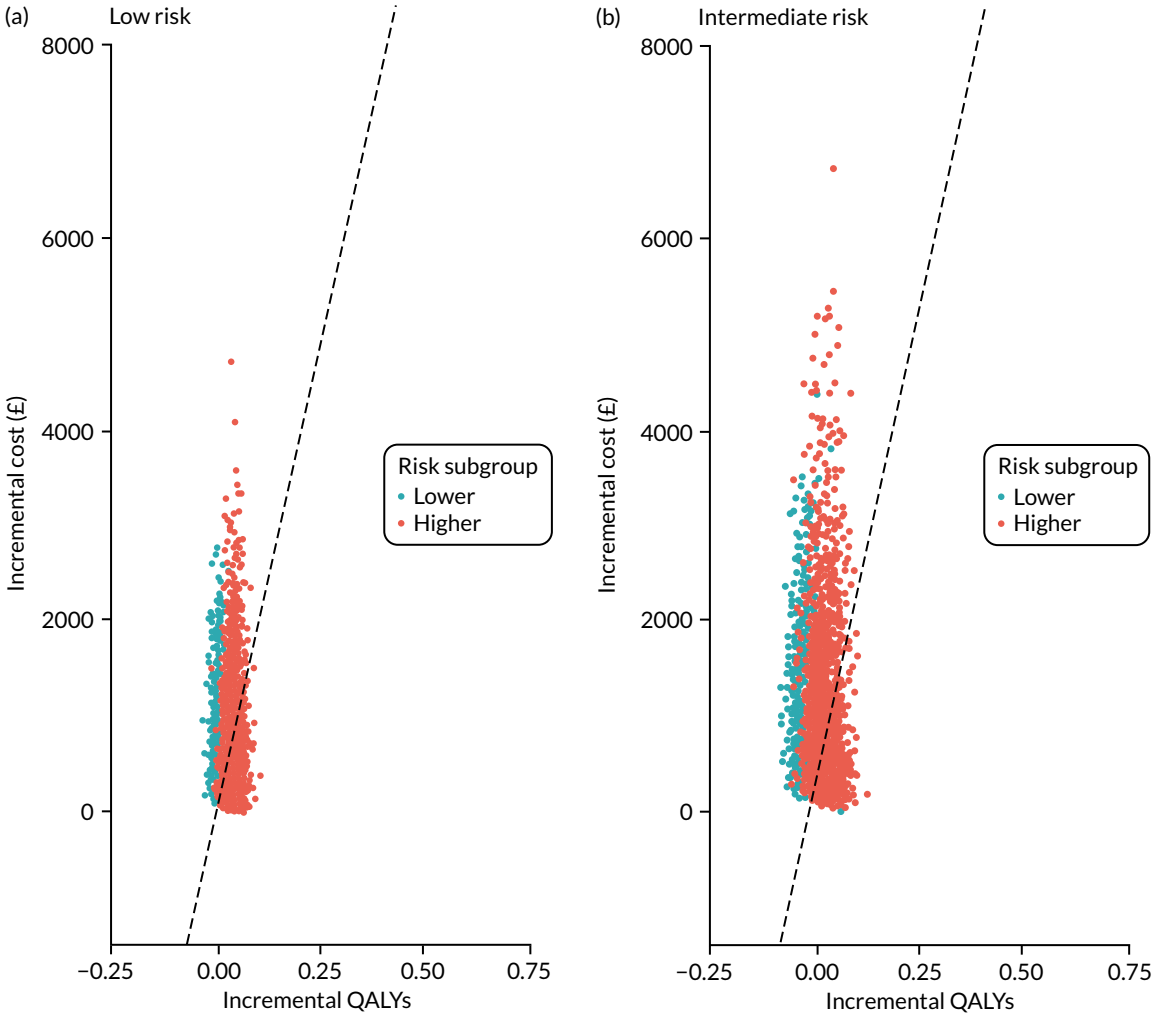

FIGURE 6 Cost-effectiveness plane showing the incremental costs and QALYs for surveillance compared with no surveillance from our PSA. (a) Low-risk group; (b) intermediate-risk group; and (c) high-risk group. The dashed line indicates a cost-effectiveness threshold of £20,000 per QALY. Points falling below the threshold are considered cost-effective. (*continued*)

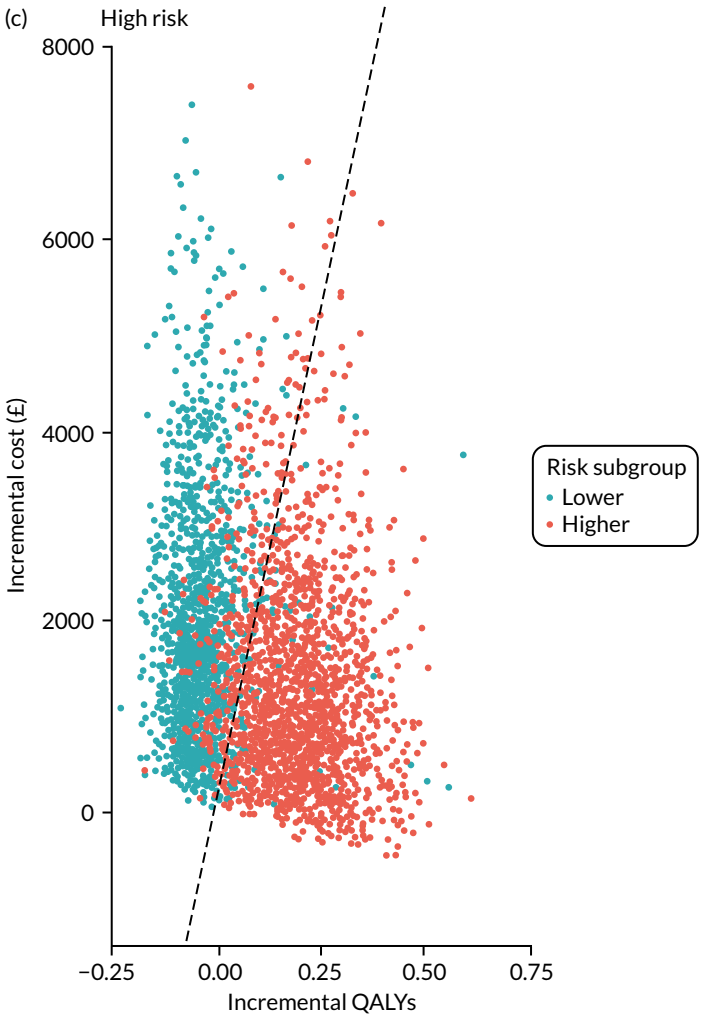

FIGURE 6 Cost-effectiveness plane showing the incremental costs and QALYs for surveillance compared with no surveillance from our PSA. (a) Low-risk group; (b) intermediate-risk group; and (c) high-risk group. The dashed line indicates a cost-effectiveness threshold of £20,000 per QALY. Points falling below the threshold are considered cost-effective.

Figure 8 shows the expected value of perfect information (EVPI) for each risk group. The greatest value was attached to eliminating uncertainty around the estimates for the higher-risk subgroup of the low-risk group. The EVPI for this subgroup was £2,451,967 at a threshold of £20,000 per QALY, compared with an EVPI of just £18 in the lower-risk subgroup of the low-risk group.

In additional sensitivity analyses we found that the results from the extrapolation model were robust to the use of different QoL estimates, from Whyte *et al.*[48] (see *Appendix 3*, *Table 46*), and to the use of a simplified model structure with the four cancer states collapsed to a single state (see *Appendix 3*, *Table 47*).

Discussion

The economic analysis presented in this chapter examined the cost-effectiveness of surveillance compared with no surveillance in patients in whom adenomas were detected and removed at baseline colonoscopy, considering the three risk groups defined in the 2002 UK-ASG.[7] To our knowledge, this is the first analysis of its kind.

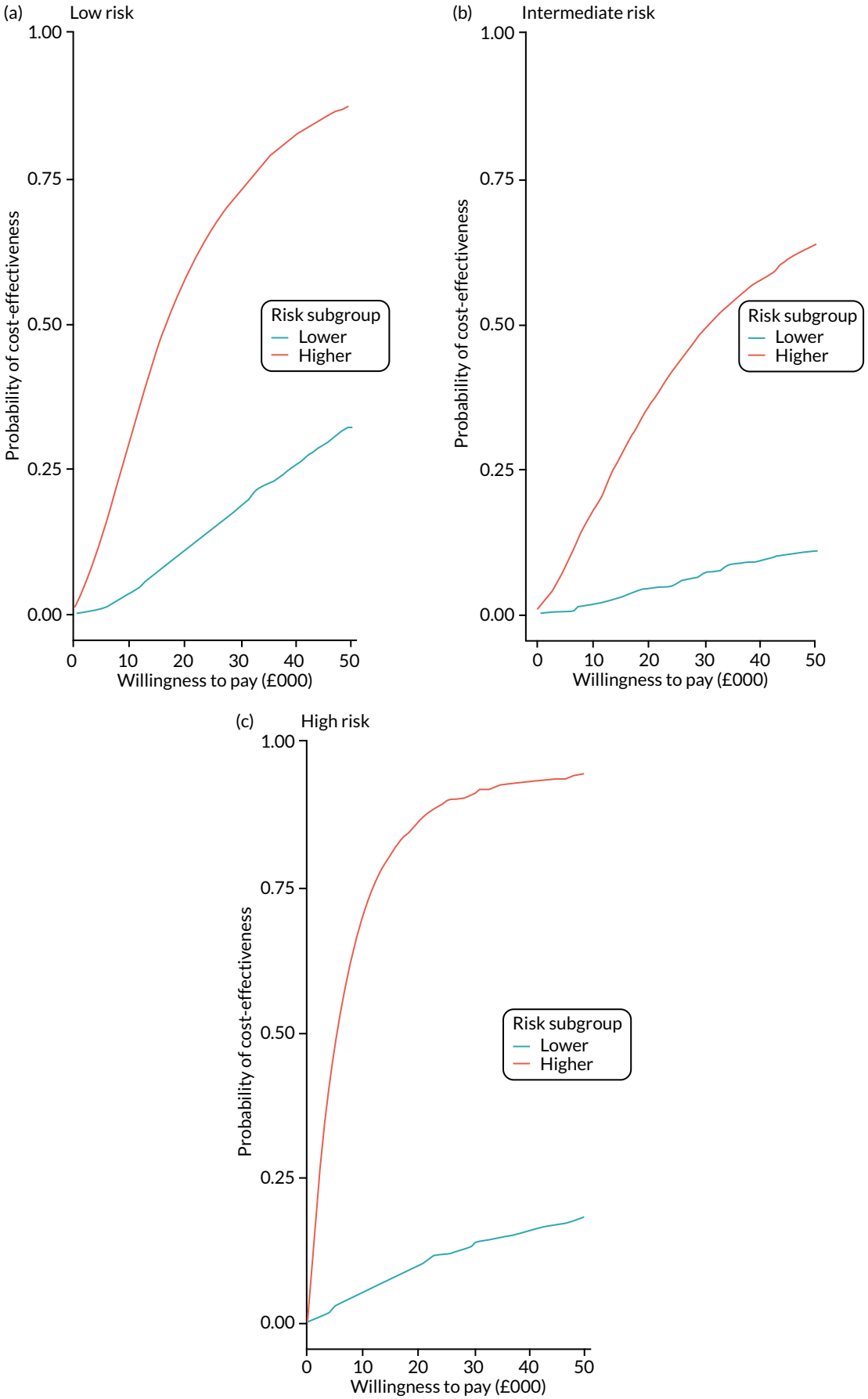

FIGURE 7 Cost-effectiveness acceptability curves showing the probabilities of surveillance being cost-effective at different willingness-to-pay thresholds. (a) Low-risk group; (b) intermediate-risk group; and (c) high-risk group.

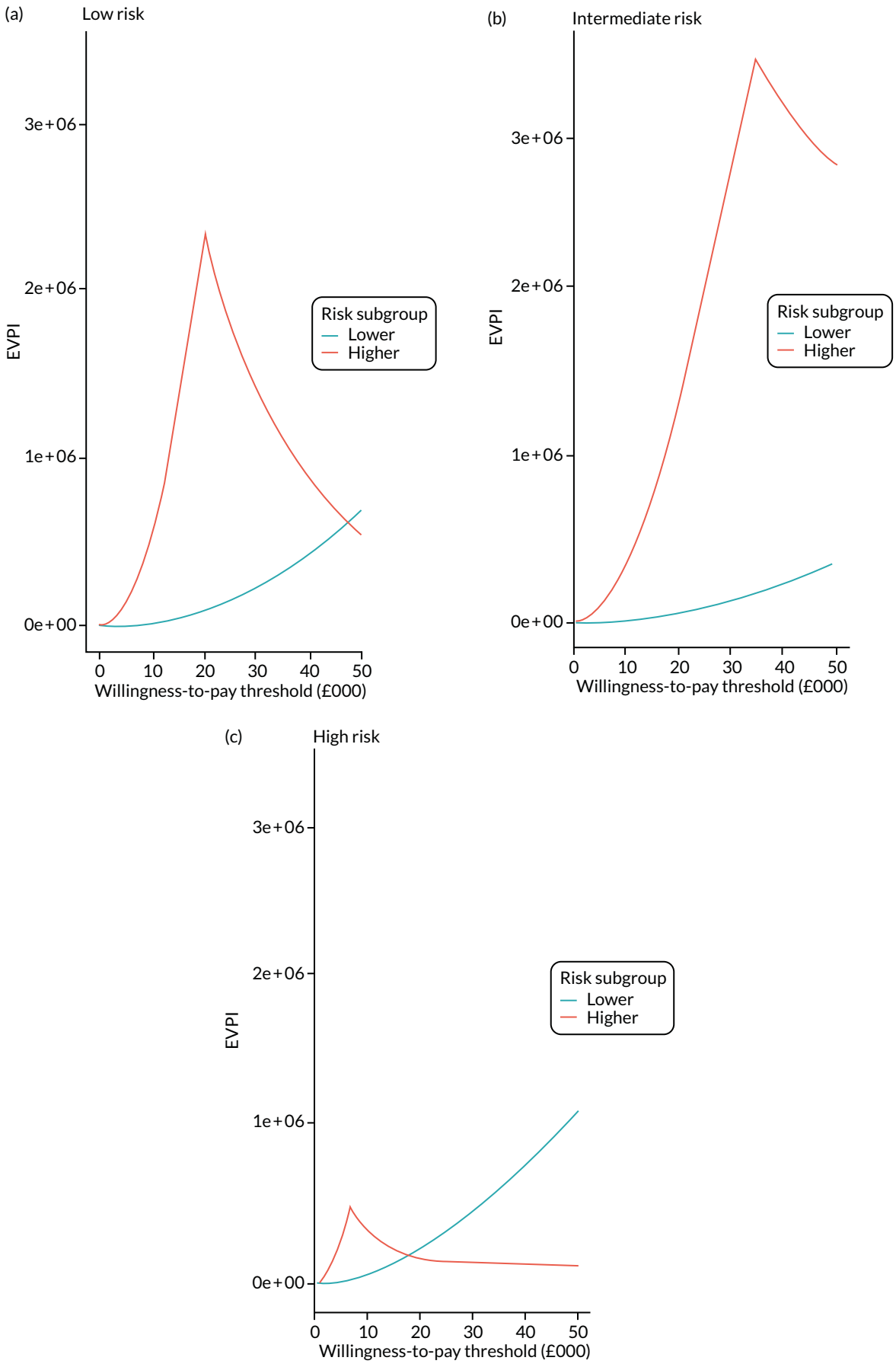

FIGURE 8 The EVPI for different willingness-to-pay thresholds. (a) Low-risk group; (b) intermediate-risk group; and (c) high-risk group.

The within-study analysis found a high degree of heterogeneity between the three risk groups. In each risk group costs per CRC diagnosis were lower in the higher-risk subgroup than in the lower-risk subgroup. The lack of QoL data for patients in the study meant that a full within-study cost–utility analysis was not feasible. We therefore developed an extrapolation model to estimate the cost-effectiveness of surveillance over a lifetime horizon. The model results showed that for each risk group surveillance was more cost-effective for patients in the higher-risk subgroup than for those in the lower-risk subgroup. However, the higher-risk subgroup of high-risk patients was the only subgroup to have an ICER below the cost-effectiveness threshold of £20,000 per QALY. The ICER in this subgroup was £7821.

The PSA found a relatively high degree of uncertainty at a willingness-to-pay threshold of £20,000 per QALY. This resulted in an EVPI of close to £2.5M over the length of the model. This high figure suggests that future research aimed at reducing this uncertainty is likely to be cost-effective. However, the DSA indicated that much of this variation results from the high degree of variability in the estimated costs of surveillance, which reflects heterogeneity in the treatment of individual patients rather than sampling uncertainty.

To our knowledge, this is the first study to estimate the cost-effectiveness of the surveillance recommendations in the 2002 UK-ASG.[7] The previous NIHR *Health Technology Assessment* report[23] using this study database found 3-yearly surveillance with no age cut-off point to be highly cost-effective and the most cost-effective strategy for the intermediate-risk group. However, the results from this previous study address a different research question and are not directly comparable to the results reported here. The results are likely to differ because of differences in model structure. The previous report did not model CRC treatment by stage, whereas the model in this chapter applied EQ-5D scores and costs to CRC states by both stage and age. The analysis in this chapter also used a different source for the EQ-5D scores for the different CRC stages. These scores were higher than those used in the previous report.

The present analysis benefited from the high-quality data of the study database, drawn from 17 UK hospitals. There were few missing data and the follow-up period was long. The estimated transition probabilities for the lifetime model were therefore based on high-quality data.

The study data also allowed model parameters to be estimated separately for each baseline risk subgroup. This allowed the model to capture the heterogeneity between these groups, which have been collapsed in previous studies.[23,43,48] However, the model does not account for heterogeneity within these subgroups. For example, the cost of surveillance may be lower for a patient attending a single surveillance visit than for one attending five or more visits, but both patients may experience a similar reduction in CRC risk. The difficulty in modelling this is simultaneously estimating the probability of attending surveillance and the reduction in CRC risk, together with the uncertainty around these estimates. The lifetime analysis stratified patients by baseline risk subgroup and by CRC stage within each subgroup. Stratifying by further covariates, such as age, resulted in the model failing to converge. Even without stratifying further, there were insufficient data to estimate all model parameters for the higher-risk subgroup of high-risk patients. Instead, we estimated a simplified model for this subgroup. There is clear evidence from the clinical data and the simplified extrapolation model that surveillance in this subgroup is both highly clinically effective and cost-effective.

The analysis in this chapter has several limitations. First, both the within-study analysis and the lifetime model assumed that patients who did not attend surveillance were representative in terms of characteristics and outcomes of patients who attended surveillance if their surveillance was withdrawn. However, the findings from the main clinical study show that these groups are not well matched on several baseline characteristics. For example, non-attenders tended to be older than attenders. Age is a positive predictor of CRC risk and, therefore, unadjusted estimates of the difference between the groups may be upwardly biased. Adjusting estimates for this source of bias is not straightforward because the number of surveillance visits attended is a time-variant covariate. For the within-study analysis we examined this

source of bias by estimating ICERs for a representative patient at the mean age for each risk subgroup (see *Appendix 3*, *Table 48*). These estimates show the results for the higher-risk subgroups to be relatively robust whereas the ICER for the lower-risk subgroups increased. For the lifetime model it is possible to estimate the effect of explanatory variables in a multistate model using a proportional intensities model. However, attempts at estimating age-dependent transition probabilities resulted in the model failing to converge.

Second, the PROMs survey is known to have a relatively high degree of non-response, which varies by both age group and cancer stage. However, the DSA found the results of the extrapolation model to be relatively insensitive to changes in the mean EQ-5D scores associated with the different cancer stages.

An additional limitation is that CRC staging data were missing for 32% of patients. We addressed this using multiple imputation in the main analysis and by using a simplified model structure in a sensitivity analysis, collapsing the four cancer states to a single state. The sensitivity analysis showed that the model results were robust to the use of the simplified model.

Further limitations include the fact that estimated costs of lifetime CRC treatment came from a source that is nearly 10 years old.[44] Other studies examining the cost-effectiveness of CRC screening and surveillance strategies have also used this source;[23,43,48] however, given the age of the estimates, there is a need for more recent high-quality data on the cost of CRC treatment. This analysis could be extended by considering how a change in the UK surveillance guidelines could affect the BCSP, as it is likely that patients who are no longer offered surveillance would instead be offered a faecal immunochemical test (FIT) as part of routine screening.

Conclusion

In conclusion, the within-study analysis found that surveillance offered the greatest benefit to patients in the higher-risk subgroups of each of the three main risk groups. We found that the cost per CRC diagnosis by surveillance was surprisingly low in the higher-risk subgroup of low-risk patients. This suggests that surveillance might be cost-effective in this subgroup.

The extrapolation model found surveillance in the higher-risk subgroup of each risk group to be either cost-effective or have a high probability of being cost-effective at a threshold of £20,000 per QALY. However, missing CRC staging data and uncertainty around QoL estimates for both non-cancer and CRC states placed a high degree of uncertainty on our cost-effectiveness estimates. Further research is needed to provide greater evidence on the QoL benefits of adenoma surveillance. The results from both the within-study analysis and the extrapolation model suggest that the 2002 UK-ASG risk groups do not clearly differentiate patients by risk from a clinical effectiveness or cost-effectiveness perspective.

Chapter 5 Patient and public involvement

Patient and public involvement (PPI) for this study was integrated from the research proposal development stage through to the dissemination stage, with the aim of contributing to all aspects of the study from the perspective of patients and the public.

Formation of the patient and public involvement group

The PPI group included three endoscopy service users, with varying backgrounds and experiences of CRC and health services in the UK. Although the research idea and plan originated from the research team, we discussed the project with one of our patient representatives prior to the submission of the research proposal. Feedback helped shape the expression of interest application. This patient representative was on the Trial Steering Committee for our original study of the intermediate-risk group.[23]

We recruited a further three PPI representatives for the study. Two members were recruited from the University of the Third Age (London, UK) and had no previous experience or involvement in research. One service user was already an active member of another study run by the research team.

To be able to contribute as a PPI representative each member of the group had to be aged within the current screening age range (i.e. 55–74 years) and have had a previous colonoscopy. Individuals who were interested in participating contacted the PPI lead (BP) by e-mail and were then sent an information sheet summarising the study and describing what participation as a representative would entail. Representatives were informed that they could choose to withdraw their involvement at any time. Reimbursement for time and travel to meetings, as well as electronic reviews of various study documents, were offered in line with the NIHR INVOLVE payment policy.[53] The members of the PPI group were contacted and kept up to date about the study by e-mail throughout their involvement.

Introduction to the study

The PPI group began meeting in March 2018. We conducted a total of two formal meetings and two workshops for this study, all held at the St Mary's Hospital Medical School (London, UK). The first meeting involved an introduction to the study, as well as carefully planned 'icebreaker' activities to help facilitate members getting to know each other and the research team. The agenda for each meeting was set by the research team, and all materials and presentations were provided in advance. The PPI lead asked representatives for their evaluation at the end of each meeting. The feedback collected from representatives included comments on how useful and positive the meetings were and the different perspectives shared among the group were very informative, as outlined in this chapter.

Feedback on study results

Three representatives met to share their views on the results and findings in the data analysis phase of the study. One member of the group expressed concern about cost-cutting versus health benefit and risk and asked if the drive for our research was mostly about cutting NHS costs. There were longer discussions on the management of surveillance for each risk group. One member said that they would be happy for the lower-risk subgroup of the intermediate-risk patients to forgo surveillance if they were managed by the screening programme. Another member indicated that they would also be happy for the lower-risk subgroup of the intermediate-risk patients to be reclassified as low risk and not be referred for surveillance if these patients were picked up by the screening programme. Another member said that, personally, they would want surveillance if they fell into the lower-risk subgroup of

the intermediate-risk patients; however, their views could be slightly biased given a personal history of CRC. Overall, the PPI group did reach a consensus that the focus of surveillance should be on the high-risk group and the higher-risk subgroup of the intermediate-risk patients, and that the lower-risk subgroup of the intermediate-risk patients could be reclassified as no longer requiring surveillance and could instead be managed by screening, together with the low-risk group.

For the final workshop the study representatives were joined by five more patients and members of the public to interpret the study results and to advise on appropriate methods for dissemination. The research team provided the new group members with a one-page information sheet summarising in lay English what had happened on the study so far. The group identified that a talk at the Maggie's Centre at Charing Cross Hospital (London, UK) would be an appropriate place to present the study. Following this workshop, group members commented that the workshop was valuable, very interesting and enjoyable, and the new members felt that they had learnt a lot.

The PPI group were actively involved in electronic reviews of a number of important study documents, including a study summary for the research team's website and drafts of the final manuscript.

Overall, the outcome of involving patients and the public has proved to be highly successful and a strength for members of the PPI group, the research team and the study. The research team were able to form links with people who had previous experience of working with researchers (experience which the team were able to gain useful information from) and people who were getting involved in PPI for the first time. On the whole, the group worked well together and felt that their contribution was mutually respected by the research team.

Chapter 6 Discussion

The aim of this study was to examine the need for, and clinical effectiveness and cost-effectiveness of, colonoscopy surveillance for patients who have adenomas detected and removed at baseline colonoscopy. We examined the surveillance recommendations given in the 2002 UK-ASG,[7] which stratify patients with adenomas into three risk groups according to baseline adenoma characteristics. In low-risk patients [i.e. those with one or two small (< 10 mm in size) adenomas] no surveillance or surveillance at 5 years is recommended. In the case of intermediate-risk patients (i.e. those with three or four small adenomas or one or two adenomas of which at least one is ≥ 10 mm in size) 3-yearly surveillance is recommended. In high-risk patients (i.e. those with five or more small adenomas, or three or more adenomas of which at least one is ≥ 10 mm in size) surveillance is recommended at 1 year and then usually every 3 years.

We hypothesised that this recommended level of surveillance might no longer be necessary. This is because the 2002 UK-ASG[7] were largely based on studies that predated improvements in colonoscopy quality and used detection rates of AAs at follow-up colonoscopy as a proxy for CRC risk.[11–14] Considering the enormous pressure placed on endoscopy resources by adenoma surveillance and the burden of invasive surveillance procedures on patients, it was seen as a priority to revise the 2002 UK-ASG[7] to minimise the number of unnecessary colonoscopies being performed.

We developed a retrospective cohort study by obtaining data on 28,972 patients who underwent baseline colonoscopy and polypectomy at 17 UK hospitals and were followed up for a median of 9.3 years. Among this cohort, 50% were classed as low risk, 41% as intermediate risk and 9% as high risk. Our analyses revealed heterogeneity both between and within the risk groups in terms of long-term CRC risk, estimated effects of surveillance on CRC risk and cost-effectiveness of surveillance.

Need for and benefit of post-polypectomy surveillance

The low-risk group

We demonstrated that patients classed as low risk did indeed have a low risk of developing CRC following adenoma removal. Although we identified heterogeneity in CRC risk among low-risk patients, namely that two-thirds of patients had a higher CRC risk than the remaining one-third, the 'higher-risk' subgroup had a CRC risk no higher than the general population, even without surveillance. This subgroup included patients who had an incomplete colonoscopy, colonoscopy of unknown completeness, tubulovillous or villous adenoma, or proximal polyps at baseline. Among patients without these baseline characteristics, CRC risk without surveillance was lower than in the general population.

Interestingly, even though the low-risk group had a low CRC risk following baseline colonoscopy and polypectomy, colonoscopy surveillance suppressed this risk even further. Attendance at a single surveillance visit was associated with a 44% reduction in CRC risk compared with no surveillance. Although this demonstrates that low-risk patients can derive benefit from surveillance, it is important to remember that colonoscopy carries a risk of serious complications and that endoscopy resources are extremely overstretched. Considering these two factors, it is reasonable to suggest that surveillance should be directed towards patients who following adenoma removal remain at increased CRC risk compared with the general population. On this basis, surveillance may not be warranted for patients classed as low risk in the 2002 UK-ASG.[7]

The intermediate-risk group

Our analyses of the intermediate-risk group supported the findings from our previous study,[20,23] showing that intermediate-risk patients may be stratified into higher- and lower-risk subgroups. The higher-risk subgroup included patients whose baseline colonoscopy was incomplete or of unknown

completeness, and those with an adenoma with high-grade dysplasia or proximal polyps at baseline, who together accounted for 60% of the whole risk group. In this subgroup, CRC risk without surveillance was higher than in the general population and a single surveillance visit substantially reduced this risk. By contrast, the remaining 40% of intermediate-risk patients (with none of these baseline risk factors) had a lower CRC risk than the general population before any surveillance. This finding suggests that surveillance may not be necessary for the lower-risk subgroup of intermediate-risk patients. The association between attendance at surveillance and CRC risk in this subgroup was not clear because the HR estimates had wide 95% CIs because of small numbers of CRC cases.

The high-risk group

We found that patients classed as high risk were indeed at high risk of CRC following baseline colonoscopy and polypectomy. Compared with the general population, CRC risk was two times higher among high-risk patients in the absence of surveillance, remaining higher in the presence of one surveillance visit. Only with two surveillance visits did CRC risk in this group fall to the level of risk in the general population. In addition, we found that cumulative incidence of CRC at 10 years was 6% without surveillance and with one surveillance visit, dropping to 3% with two surveillance visits. From these findings it seems likely that high-risk patients would benefit from attending two surveillance visits.

When we divided the high-risk group into higher- and lower-risk subgroups using the baseline characteristics identified as CRC risk factors (i.e. incomplete colonoscopies, colonoscopies of unknown completeness, adenomas with high-grade dysplasia), there were few CRC cases in each subgroup. As a result, our estimates from the subgroup analyses lacked precision, preventing clear conclusions from being drawn. Our findings suggest that all high-risk patients require surveillance to reduce their post-polypectomy CRC risk to that of the general population.

Our results suggest that surveillance is likely required for the whole high-risk group ($n = 2719$) and the higher-risk subgroup of the intermediate-risk group ($n = 7114$), who comprised 34% of our study cohort. By contrast, we have shown that surveillance might not be necessary for the low-risk group ($n = 14{,}401$) or the lower-risk subgroup of the intermediate-risk group ($n = 4738$), who accounted for 66% of our cohort. Patients who are not deemed to require surveillance could return to the BCSP when invited, which involves biennial stool-based screening with the FIT.

Surveillance intervals

Our results shed light on what surveillance intervals might be appropriate for each risk group. It is interesting to note that in the study the median time from baseline to first surveillance in the low-risk group was 3.2 years. This surveillance interval is shorter than the 5-year interval recommended in the 2002 UK-ASG.[7] This is consistent with other studies reporting inappropriately short surveillance intervals in low-risk patients.[54,55] Possible reasons for this include physician or patient concern about missed or recurring adenomas developing into CRC. The median surveillance intervals in the intermediate-risk group (i.e. 3 years) and high-risk group (i.e. 1.5 years) more closely aligned with the UK-ASG[7] recommendations (i.e. 3 years and 1 year, respectively).[7]

In the low-risk group, AA detection rates were < 9% and CRC detection rates were < 2% with intervals of < 18 months through to 6 years. Detection rates increased to 13% for AAs and 3% for CRC with an interval of 7 years. These results suggest that if surveillance is performed in low-risk patients it could be delayed until 7 years after baseline because detection rates of AAs and CRC are low during the first 6 years.

In the intermediate-risk group, detection rates of AAs and CRC remained relatively constant with intervals of < 18 months through to 3 years, at around 8–9% for AAs and 1–2% for CRC. Detection

rates increased to 11% and 3% for AAs and CRC, respectively, with an interval of 4 years. These data suggest that for the intermediate-risk patients in our study surveillance at 4 years would have been worthwhile, as the yield of AAs was sufficient to justify performing colonoscopy.

Detection rates of AAs and CRC were approximately one and a half to two times greater in the higher- than in the lower-risk subgroup of intermediate-risk patients when we examined findings at first surveillance by risk subgroup. In the higher-risk subgroup, the detection rate of AAs was 11% with an interval of 3 years and CRC detection rates increased from approximately 1–2% to 4% when the interval extended beyond 3 years. This suggests that a 3-year interval might be appropriate for the higher-risk subgroup of intermediate-risk patients to avoid delays in the diagnosis of CRC.

In the high-risk group, AA detection rates at first surveillance were $\geq$ 11% for all intervals. Detection rates of CRC were < 1% with intervals of < 1.5 years, increasing to 3% with an interval of 2 years, with no further increases as the interval extended up to 3.5 years. The small numbers of CRCs in this analysis make it difficult to draw clear conclusions about an appropriate interval for high-risk patients.

Important baseline risk factors

When examining all three risk groups we identified several common important risk factors for CRC, including older age and having an incomplete colonoscopy, adenoma with high-grade dysplasia or proximal polyps at baseline. This is consistent with the findings from our previous study[20] of the intermediate-risk group. These characteristics have also been identified as risk factors for advanced colorectal neoplasia at follow-up colonoscopy in other studies.[56,57]

The increased CRC risk among patients with an adenoma with high-grade dysplasia or proximal polyps at baseline might have been due, at least in part, to incomplete resection. Support for this comes from a study[58] that found advanced polyps and proximal polyps to be risk factors for incomplete resection. However, this study[58] defined advanced polyps as adenomas with high-grade dysplasia, serrated adenomas or cancer, making it difficult to interpret the risk associated with high-grade dysplasia alone. It is possible that some proximal polyps in our study were serrated lesions, another important class of CRC precursors.[59] Serrated lesions are usually located in the proximal colon and are often flat and covered with mucus, making them difficult to detect and remove.[59] Unfortunately, we could not investigate the significance of these lesions as they were not recorded consistently in our data.

Overall, these findings highlight the importance of having a high-quality baseline colonoscopy (i.e. a complete examination with careful mucosal inspection and complete resection of detected lesions). In the UK, a national colonoscopy audit in 1999 revealed poor standards of practice, including low colonoscopy completion rates.[60] This led to the implementation of a national colonoscopy quality improvement programme that proved to be extremely effective.[61] More recent studies of colonoscopy in the UK have reported completion rates of 92–95%.[21,62,63] In our study, 80% of patients had a complete baseline colonoscopy. When we excluded the 20% without a complete baseline colonoscopy in a sensitivity analysis we saw little change in the results. We are therefore confident that our results are applicable in the current era of high-quality colonoscopy.

Attendance at surveillance

In the low-, intermediate- and high-risk groups, 50%, 60% and 66% of patients attended surveillance, respectively. Compared with patients who attended surveillance, non-attenders were older, and a higher proportion had an incomplete colonoscopy or poor bowel preparation at baseline. In the intermediate-risk group, the proportion of women was higher among non-attenders than among attenders. Similarly, in our previous study of the intermediate-risk group we found that surveillance

attendance was lower among older patients, women and patients with an incomplete baseline colonoscopy or poor bowel preparation.[20,23] Another study[64] has also reported that older age and female sex are associated with poor compliance with adenoma surveillance.

Our finding that 40% of the intermediate-risk group and 34% of the high-risk group did not attend surveillance is at odds with the UK-ASG,[7] which recommends surveillance for both of these groups (at 3 years and 1 year for intermediate- and high-risk patients, respectively).[7] This suggests some underuse of surveillance colonoscopy in these patients. A study conducted in the USA found that surveillance colonoscopy was underused in patients classed as 'high risk' because of the presence of AAs or multiple adenomas at baseline.[65] Reasons for the underuse of surveillance in this previous study were not given, although the authors noted that 'physician preference and patient request' influence surveillance utilisation. In our study, we unfortunately did not have any information on why some patients failed to attend surveillance. It is possible that various factors played a role, including scheduling errors, patient objections to colonoscopy and patient comorbidities.

Comparison with previous studies of post-polypectomy colorectal cancer risk

Few high-quality data exist on the long-term risk of CRC among post-polypectomy patients. Apart from the present study and our previous study of the intermediate-risk group,[20,23] to the best of our knowledge only two other studies[6,66] have compared CRC risk following adenoma removal with that in the general population.

The first of these, by Atkin *et al.*,[6] included 1618 people who had adenomas removed during rigid sigmoidoscopy between 1957 and 1980 and were followed for a mean of 13.8 years.[6] Compared with the general population, CRC risk without surveillance was nearly four times greater among patients who had an adenoma $\geq$ 10 mm in size or with tubulovillous or villous histology at baseline, and seven times greater among patients who had more than one adenoma with such features. By contrast, CRC risk without surveillance was not significantly different among patients who had small (i.e. $<$ 10 mm in size) tubular adenomas at baseline. The age of these data and the fact that rigid sigmoidoscopy rather than colonoscopy was performed at baseline limits the applicability of these findings in current practice.

The second study by Cottet *et al.*[66] examined 5779 patients who underwent baseline colonoscopy and polypectomy between 1990 and 1999 and were followed for a median of 7.7 years. Among patients who had an AA at baseline, CRC risk was four times higher than in the general population in the absence of surveillance and colonoscopy surveillance was associated with significant reductions in CRC risk. In comparison, among those with only non-AAs at baseline, CRC risk without surveillance was similar to that in the general population and surveillance did not have a significant effect on CRC risk. We cannot draw clear conclusions from these analyses, however, because the numbers of CRC cases were low and estimates imprecise. Furthermore, the study predated improvements in colonoscopy quality.

Cost-effectiveness of surveillance

The results from our economic evaluation indicate that for each risk group surveillance was more cost-effective for the higher-risk subgroup than for the lower-risk subgroup. In the within-study analysis, incremental costs per CRC prevented by adopting surveillance compared with no surveillance were lower in the higher-risk subgroups of each risk group. The lowest incremental cost per CRC prevented by adopting surveillance was seen for the higher-risk subgroup of the high-risk group (i.e. £36,636). This suggests that surveillance in the higher-risk subgroup of high-risk patients is more cost-effective than surveillance in any of the other risk subgroups.

We also performed a lifetime economic analysis in which we assessed cost-effectiveness in terms of the incremental cost per QALY gained. This is a more useful and comparable metric that is widely used to assess the cost-effectiveness of health interventions, including by the National Institute for Health and Care Excellence.[49] Our analyses revealed that the incremental cost per QALY gained by adopting surveillance was lower in the higher-risk subgroup of each risk group compared with the lower-risk subgroup. Similar to the within-study analysis, the lowest incremental cost per QALY gained with surveillance was seen for the higher-risk subgroup of the high-risk group (i.e. £7821). We deemed this to be highly cost-effective as we assumed a cost-effectiveness threshold of £20,000 per QALY, which is commonly used by National Institute for Health and Care Excellence.[49]

Interestingly, surveillance was not found to be cost-effective for the lower-risk subgroup of high-risk patients or for either risk subgroup of intermediate-risk patients. This is worth noting because the results from our clinical analysis suggest that these patients likely require surveillance, given that they remain at an increased risk of CRC following adenoma removal, as compared with the general population. However, in a sensitivity analysis of our economic model we showed that the ICERs for these risk subgroups were sensitive to variation in the baseline parameter estimates, including the state transition probabilities and QoL estimates. When we varied our estimated parameters by $\pm$ 25%, large decreases were seen in some ICERs, with some approaching the £20,000 per QALY threshold. The results also suggest considerable heterogeneity within the 2002 UK-ASG[7] risk groups. Future research aimed at improving the discrimination of risk grouping and reducing the uncertainty surrounding these estimates would be worthwhile.

Strengths and limitations

Our study has several strengths. To the best of our knowledge, it is the largest study to date to have examined the long-term risk of CRC following adenoma removal and the clinical effectiveness and cost-effectiveness of post-polypectomy surveillance. We created our data set by obtaining data from 17 NHS hospitals on approximately 30,000 patients who underwent baseline colonoscopy and polypectomy. The hospitals were located throughout the UK, providing a wide geographic coverage, and included both general and teaching hospitals. We obtained detailed data on baseline patient, procedural and polyp characteristics, and surveillance colonoscopies, and carried out extensive data cleaning. There were very few missing data. We were able to obtain complete follow-up data on CRC diagnoses and deaths for almost all patients (98%), as we used multiple national data sources and could follow up patients even if they migrated within the UK. Importantly, the vast majority (87%) of baseline colonoscopies were performed from 2000 to 2010, after the introduction of the national colonoscopy quality improvement programme following the 1999 UK colonoscopy audit.[61]

In addition, we had the statistical power to perform multiple sensitivity analyses to assess the impact of various methodological choices on our results. In our first sensitivity analysis we excluded patients without a complete baseline colonoscopy (i.e. one-fifth of the cohort), finding that this had little impact on the results from our analyses of long-term CRC incidence and findings at first surveillance. This indicates that our results are likely to apply in the modern era of high-quality colonoscopy. Our second sensitivity analysis concerned the criteria used to decide whether or not a CRC had arisen from an incompletely resected baseline lesion and should therefore be excluded from analyses. When we relaxed the criteria, resulting in the exclusion of some additional cancers, we observed no material changes in the results.

In our third sensitivity analysis we showed that our results for the higher- and lower-risk subgroups of intermediate-risk patients were robust to changes in the risk classification criteria (i.e. when we applied the slightly different criteria from our previous study of the intermediate-risk group).[20,23] Similarly, for the low-risk group, results from our analyses of findings at first surveillance were robust when we changed the cut-off point for interval length from 8.5 to 6.5 years. For our final sensitivity

analysis we also adjusted for hospital in our multivariable models for long-term CRC incidence and findings at first surveillance and noted little change in the results. Together, these sensitivity analyses demonstrate the robustness of our results in the presence of methodological and parameter uncertainty.

A limitation of this study is that it is observational and so we cannot assume a causal relationship between surveillance and the observed reductions in CRC incidence among patients attending surveillance. However, we made adjustments for several potential confounders and still observed a substantial reduction in CRC incidence with attendance at surveillance. A second limitation is that there is likely some misclassification in our data set because of our use of routinely collected data. In addition, it is possible that we incorrectly classed some examinations in our data set as surveillance examinations when they actually were being performed to investigate symptoms; however, we were unable to differentiate the purpose of the examination. Some patients in our study might also have undergone surveillance at other hospitals from which we did not collect data. Missing data were more common among patients who attended surveillance than among those who did not attend surveillance. This was particularly true for data on baseline examination quality, including colonoscopy completeness and bowel preparation quality. It is possible that this introduced bias into our data set. Finally, as we excluded CRCs deemed likely to have arisen from incompletely resected baseline lesions, it is possible that some of our estimates of CRC risk are underestimations because, even with current practice, not all lesions are detected and completely resected during colonoscopy.

Our economic evaluation had a number of limitations. Staging data were missing for 32% of patients with CRC, which placed uncertainty around our estimates of cost-effectiveness. Further uncertainty surrounded our QoL estimates for both non-cancer and CRC states. In addition, our estimated costs of lifetime CRC treatment came from a source that is nearly 10 years old.[44]

Conclusions

Implications for health care

Our results suggest that a large proportion of patients in whom adenomas are detected and removed at baseline colonoscopy might not need to undergo surveillance colonoscopy. We found that, following a complete baseline colonoscopy, the long-term risk of CRC in the whole low-risk group and lower-risk subgroup of intermediate-risk patients (i.e. those without high-grade dysplasia or proximal polyps at baseline) was similar to or lower than that in the general population who undergo no surveillance. It is possible that routine screening with the FIT might be sufficient for these patients who, together, accounted for 66% of our cohort. Revision of the 2002 UK-ASG[7] in the light of these findings could help to minimise the exposure of patients to unnecessary invasive surveillance procedures and alleviate pressures on endoscopy services.

In comparison, we showed that surveillance is probably warranted for the remaining 34% of patients, including the higher-risk subgroup of intermediate-risk patients (i.e. those without a complete colonoscopy or with high-grade dysplasia or proximal polyps at baseline) and the whole high-risk group. In our study, post-polypectomy CRC risk was higher among these patients than in the general population in the absence of surveillance, and surveillance was associated with substantial reductions in CRC risk. We showed that a 3-year surveillance interval is likely to be appropriate for the higher-risk subgroup of intermediate-risk patients, although further research is needed to confirm this and to define an optimal interval for high-risk patients.

In our economic evaluation we showed that surveillance is more cost-effective for the higher-risk subgroup than for the lower-risk subgroup of each risk group. We demonstrated that surveillance is highly cost-effective for the higher-risk subgroup of high-risk patients.

Recommendations for research

- Randomised controlled trials of post-polypectomy patients and additional economic evaluations are needed to generate greater evidence about the requirements for, and clinical effectiveness and cost-effectiveness of, surveillance. Studies with large sample sizes and long-term follow-up would help determine the optimal number of, and interval between, surveillance visits for patients remaining at increased CRC risk post polypectomy.
- Future studies should repeat the analyses performed in the present study without prior classification of patients into risk groups, according to baseline adenoma number and size. This would help elucidate the effects of individual baseline adenoma characteristics on findings at surveillance colonoscopy and long-term CRC incidence.
- Further research is needed on the long-term CRC incidence and effects of surveillance on CRC incidence among patients who have serrated polyps detected and removed at baseline colonoscopy.
- Additional research is needed to generate high-quality data on the QoL of patients with CRC.
- Qualitative studies should assess patients' attitudes towards, and experiences of, surveillance to help understand barriers to and facilitators of compliance with surveillance.
- Future studies should examine alternative surveillance strategies based on FIT and other technologies, such as a multitarget stool deoxyribonucleic acid test.[67]

Acknowledgements

The authors would like to acknowledge Professor Wendy Atkin who was the original chief investigator of the study, who sadly passed away in 2018. We would like to thank all of the people listed below for their involvement in the study. A special thank you to the patients who contributed data to the study.

Infrastructure support for this work was provided by the NIHR Imperial Biomedical Research Centre.

Trial Steering Committee

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Patient and public representatives

We are grateful to Helen Watson, Lindy Berkman and John Sharkey for reviewing the study proposal and results, in addition to helping us run a workshop with other patients and members of the public to develop plans for wider dissemination of the results. We would also like to thank Karen Ma, Irene Fuchs, Paul Ewart, Angela Quilley and Lynne Wright who attended the workshop.

National Institute for Health and Care Research Health Technology Assessment grant co-applicants

Amanda J Cross (chief investigator), Alastair Gray (Health Economist), Kate Wooldrage (Statistician) and Stephen W Duffy (Statistician).

Participating hospitals

We would like to thank the principal investigators, consultant gastroenterologists, surgeons, endoscopists, nurses, pathologists, administrative staff, and information and communications technology staff at each of the participating hospitals named below. In addition, we would like to thank everyone who helped us collect endoscopy and pathology data for the study. A full list of those involved is given in the NIHR final report[23] for our previous study of the intermediate-risk group:

Royal Sussex County Hospital, Brighton; Cumberland Infirmary, Carlisle; Imperial College Healthcare NHS Trust, Charing Cross Hospital, Hammersmith Hospital and St Mary's Hospital, London; Glasgow Royal Infirmary, Glasgow; Leicester General Hospital, Leicester; Royal Liverpool University Hospital, Liverpool; New Cross Hospital, Wolverhampton; University Hospital of North Tees, Stockton-on-Tees; Queen Elizabeth Hospital, Woolwich; Queen Mary's Hospital, Sidcup; Royal Shrewsbury Hospital, Shropshire; St George's Hospital, Tooting; St Mark's Hospital, Harrow; Royal Surrey County Hospital, Surrey; Torbay District General Hospital, Devon; and Yeovil District Hospital, Yeovil.

Data providers

NHS Digital, formerly the Health and Social Care Information Centre England: Copyright © 2019, data re-used with the permission of NHS Digital. All rights reserved.

NHS Central Register and NSS: we would like to acknowledge the support of the electronic Data Research and Innovation Service Team (NSS) for their involvement in obtaining approvals and provisioning and linking data.

This project involves data derived from patient-level information collected by the NHS as part of the care and support of cancer patients. The data are collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of PHE. Access to the data was facilitated by the PHE Office for Data Release.

Contributions of authors

Amanda J Cross (https://orcid.org/0000-0002-0893-2377) (Professor of Cancer Epidemiology) was the chief investigator for the study and was responsible for the design of the study and obtaining funding, had oversight of data analysis and interpretation, and contributed to the drafting and revision of the report.

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Publications

Cafferty FH, Wong JM, Yen AM, Duffy S, Atkin WS, Chen TH. Findings at follow-up endoscopies in subjects with suspected colorectal abnormalities: effects of baseline findings and time to follow-up. *Cancer J* 2007;**13**:263–70.

Atkin W, Brenner A, Martin J, Wooldrage K, Shah U, Lucas F, *et al.* The clinical effectiveness of different surveillance strategies to prevent colorectal cancer in people with intermediate-grade colorectal adenomas: a retrospective cohort analysis, and psychological and economic evaluations. *Health Technol Assess* 2017;**21**(25).

Atkin W, Wooldrage K, Brenner A, Martin J, Shah U, Perera S, *et al.* Adenoma surveillance and colorectal cancer incidence: a retrospective, multicentre, cohort study. *Lancet Oncol* 2017;**18**:823–34.

Cross AJ, Robbins EC, Pack K, Stenson I, Kirby PL, Patel B, *et al.* Long-term colorectal cancer incidence after adenoma removal and the effects of surveillance on incidence: a multicentre, retrospective, cohort study. *Gut* 2020;**69**:1645–58.

Cross AJ, Robbins EC, Pack K, Stenson I, Rutter MD, Veitch AM, *et al.* Post-polypectomy surveillance interval and advanced neoplasia detection rates: a multicenter, retrospective cohort study [published online ahead of print April 12 2022]. *Endoscopy* 2022.

Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to available anonymised data may be granted following review and appropriate agreements being in place.

Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation.

References

1. Atkin WS, Edwards R, Kralj-Hans I, Wooldrage K, Hart AR, Northover JM, *et al.* Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet* 2010;**375**:1624–33. https://doi.org/10.1016/S0140-6736(10)60551-X
2. Segnan N, Armaroli P, Bonelli L, Risio M, Sciallero S, Zappa M, *et al.* Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian randomized controlled trial – SCORE. *J Natl Cancer Inst* 2011;**103**:1310–22. https://doi.org/10.1093/jnci/djr284
3. Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Church T, Laiyemo AO, *et al.* Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. *N Engl J Med* 2012;**366**:2345–57. https://doi.org/10.1056/NEJMoa1114635
4. Holme Ø, Løberg M, Kalager M, Bretthauer M, Hernán MA, Aas E, *et al.* Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. *JAMA* 2014;**312**:606–15. https://doi.org/10.1001/jama.2014.8266
5. Atkin W, Wooldrage K, Parkin DM, Kralj-Hans I, MacRae E, Shah U, *et al.* Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial. *Lancet* 2017;**389**:1299–311. https://doi.org/10.1016/S0140-6736(17)30396-3
6. Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas. *N Engl J Med* 1992;**326**:658–62. https://doi.org/10.1056/NEJM199203053261002
7. Atkin WS, Saunders BP, British Society for Gastroenterology. Surveillance guidelines after removal of colorectal adenomatous polyps. *Gut* 2002;**51**:V6–9. https://doi.org/10.1136/gut.51.suppl_5.v6
8. Atkin WS, Valori R, Kuipers EJ, Hoff G, Senore C, Segnan N, *et al.* European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition – colonoscopic surveillance following adenoma removal. *Endoscopy* 2012;**44**:E151–63. https://doi.org/10.1055/s-0032-1309821
9. Lieberman DA, Rex DK, Winawer SJ, Giardiello FM, Johnson DA, Levin TR. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2012;**143**:844–57. https://doi.org/10.1053/j.gastro.2012.06.001
10. Hassan C, Quintero E, Dumonceau JM, Regula J, Brandão C, Chaussade S, *et al.* Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2013;**45**:842–51. https://doi.org/10.1055/s-0033-1344548
11. van Stolk RU, Beck GJ, Baron JA, Haile R, Summers R. Adenoma characteristics at first colonoscopy as predictors of adenoma recurrence and characteristics at follow-up. *Gastroenterology* 1998;**115**:13–18. https://doi.org/10.1016/S0016-5085(98)70359-2
12. Noshirwani KC, van Stolk RU, Rybicki LA, Beck GJ. Adenoma size and number are predictive of adenoma recurrence: implications for surveillance colonoscopy. *Gastrointest Endosc* 2000;**51**:433–7. https://doi.org/10.1016/S0016-5107(00)70444-5
13. Martínez ME, Sampliner R, Marshall JR, Bhattacharyya AK, Reid ME, Alberts DS. Adenoma characteristics as risk factors for recurrence of advanced adenomas. *Gastroenterology* 2001;**120**:1077–83. https://doi.org/10.1053/gast.2001.23247

14. Winawer SJ, Zauber AG, O'Brien MJ, Ho MN, Gottlieb L, Sternberg SS, *et al.* Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. *New Engl J Med* 1993;**328**:901–6. https://doi.org/10.1056/NEJM199304013281301

15. Jørgensen OD, Kronborg O, Fenger C. A randomized surveillance study of patients with pedunculated and small sessile tubular and tubulovillous adenomas. The Funen Adenoma Follow-up Study. *Scand J Gastroenterol* 1995;**30**:686–92. https://doi.org/10.3109/00365529509096314

16. Veitch A, Rutter M. Improving quality in endoscopy: are we nearly there yet? *Frontline Gastroenterol* 2015;**6**:127–31. https://doi.org/10.1136/flgastro-2015-100564

17. Valori R. Quality improvements in endoscopy in England. *Tech Gastrointest Endosc* 2012;**14**:63–72. https://doi.org/10.1016/j.tgie.2011.11.001

18. Morris EJ, Rutter MD, Finan PJ, Thomas JD, Valori R. Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service. *Gut* 2015;**64**:1248–56. https://doi.org/10.1136/gutjnl-2014-308362

19. National Institute for Health and Care Research. *Frequency of Follow-Up for Patients with Intermediate Grade Colorectal Adenomas*. URL: https://fundingawards.nihr.ac.uk/award/04/33/01 (accessed 11 March 2020).

20. Atkin W, Wooldrage K, Brenner A, Martin J, Shah U, Perera S, *et al.* Adenoma surveillance and colorectal cancer incidence: a retrospective, multicentre, cohort study. *Lancet Oncol* 2017;**18**:823–34. https://doi.org/10.1016/S1470-2045(17)30187-0

21. Gavin DR, Valori RM, Anderson JT, Donnelly MT, Williams JG, Swarbrick ET. The national colonoscopy audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. *Gut* 2013;**62**:242–9. https://doi.org/10.1136/gutjnl-2011-301848

22. Ko CW. Colonoscopy risks: what is known and what are the next steps? *Gastroenterology* 2018;**154**:473–5. https://doi.org/10.1053/j.gastro.2018.01.010

23. Atkin W, Brenner A, Martin J, Wooldrage K, Shah U, Lucas F, *et al.* The clinical effectiveness of different surveillance strategies to prevent colorectal cancer in people with intermediate-grade colorectal adenomas: a retrospective cohort analysis, and psychological and economic evaluations. *Health Technol Assess* 2017;**21**(25). https://doi.org/10.3310/hta21250

24. World Health Organization (WHO). *International Classification of Diseases, Eighth Edition*. Geneva: WHO; 1968.

25. World Health Organization (WHO). *International Classification of Diseases, Ninth Edition*. Geneva: WHO; 1979.

26. World Health Organization (WHO). *International Classification of Diseases, Tenth Edition*. Geneva: WHO; 1990.

27. American Cancer Society. *Manual of Tumor Nomenclature and Coding*. New York, NY: American Cancer Society; 1952.

28. World Health Organization (WHO). *International Classification of Diseases for Oncology Revision 1*. Geneva: WHO; 1976.

29. World Health Organization (WHO). *International Classification of Diseases for Oncology Revision 2*. Geneva: WHO; 1990.

30. Lin OS. Performing colonoscopy in elderly and very elderly patients: risks, costs and benefits. *World J Gastrointest Endosc* 2014;**6**:220–6. https://doi.org/10.4253/wjge.v6.i6.220

31. Office for National Statistics. *Cancer Registration Statistics, England*. 2007. URL: www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland (accessed 11 March 2020).
32. Shenbagaraj L, Thomas-Gibson S, Stebbing J, Broughton R, Dron M, Johnston D, *et al.* Endoscopy in 2017: a national survey of practice in the UK. *Frontline Gastroenterol* 2019;**10**:7–15. https://doi.org/10.1136/flgastro-2018-100970
33. NHS Improvement. *Archived Reference Costs. 2017/18 Reference Costs and Guidance*. URL: https://improvement.nhs.uk/resources/reference-costs/ (accessed 11 March 2020).
34. Whyte S, Chilcott J, Halloran S. Reappraisal of the options for colorectal cancer screening in England. *Colorectal Dis* 2012;**14**:e547–61. https://doi.org/10.1111/j.1463-1318.2012.03014.x
35. Scott N, Hill J, Smith J, Walker K, Kuryba A, van der Meulen J, *et al. National Bowel Cancer Audit – 2013*. URL: https://digital.nhs.uk/data-and-information/publications/statistical/national-bowel-cancer-audit/national-bowel-cancer-audit-2013 (accessed 11 March 2020).
36. Office for National Statistics. *National Life Tables: UK*. 2019. URL: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesunitedkingdomreferencetables (accessed 11 June 2020).
37. Downing A, Morris EJ, Richards M, Corner J, Wright P, Sebag-Montefiore D, *et al.* Health-related quality of life after colorectal cancer in England: a patient-reported outcomes study of individuals 12 to 36 months after diagnosis. *J Clin Oncol* 2015;**33**:616–24. https://doi.org/10.1200/JCO.2014.56.6539
38. Ara R, Brazier JE. Using health state utility values from the general population to approximate baselines in decision analytic models when condition-specific data are not available. *Value Health* 2011;**14**:539–45. https://doi.org/10.1016/j.jval.2010.10.029
39. Great Britain. *Health and Social Care Act 2001*. London: The Stationery Office; 2001.
40. Great Britain. *NHS Act 2006*. London: The Stationery Office; 2006.
41. Cancer Research UK. *Bowel Cancer Statistics*. London: Cancer Research UK; 2017.
42. Aravani A, Thomas J, Day M, Forman D, Morris E, Tatarek-Gintowt R. *Survival by Stage of Colorectal Cancer in England: Northern and Yorkshire Cancer Registry and Information Service*. Leeds: Northern and Yorkshire Cancer Registry and Information Service; 2009.
43. Murphy J, Halloran S, Gray A. Cost-effectiveness of the faecal immunochemical test at a range of positivity thresholds compared with the guaiac faecal occult blood test in the NHS Bowel Cancer Screening Programme in England. *BMJ Open* 2017;**7**:e017186. https://doi.org/10.1136/bmjopen-2017-017186
44. Whyte S, Harnan S, Scope A, Simpson E, Tappenden P, Duffy S, *et al. Early Awareness Interventions for Cancer: Colorectal Cancer*. Sheffield: Policy Research Unit in Economic Evaluation of Health and Care Interventions; 2012.
45. Cross AJ, Wooldrage K, Robbins EC, Kralj-Hans I, MacRae E, Piggott C, *et al.* Faecal immunochemical tests (FIT) versus colonoscopy for surveillance after screening and polypectomy: a diagnostic accuracy and cost-effectiveness study. *Gut* 2019;**68**:1642–52. https://doi.org/10.1136/gutjnl-2018-317297
46. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York, NY: John Wiley & Sons; 2004.
47. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, *et al.* Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health* 2012;**15**:708–15. https://doi.org/10.1016/j.jval.2012.02.008

48. Whyte S, Thomas C, Kearns B, Webster M, Chilcott J. *Optimising Bowel Cancer Screening. Phase 1: Optimising the Cost Effectiveness of Repeated FIT Screening and Screening Strategies Combining Bowel Scope and FIT Screening*. Sheffield: The University of Sheffield; 2017.

49. National Institute for Health and Care Excellence (NICE). *Developing NICE Guidelines: The Manual*. 2014. URL: www.nice.org.uk/process/pmg20/chapter/incorporating-economic-evaluation (accessed 11 March 2020).

50. Black WC. The CE plane: a graphic representation of cost-effectiveness. *Med Decis Making* 1990;**10**:212–14. https://doi.org/10.1177/0272989X9001000308

51. Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves – facts, fallacies and frequently asked questions. *Health Econ* 2004;**13**:405–15. https://doi.org/10.1002/hec.903

52. Rutter MD, Nickerson C, Rees CJ, Patnick J, Blanks RG. Risk factors for adverse events related to polypectomy in the English Bowel Cancer Screening Programme. *Endoscopy* 2014;**46**:90–7. https://doi.org/10.1055/s-0033-1344987

53. National Institute for Health and Care Research (NIHR) INVOLVE. *National Institute for Health Research Programmes: Payment Rates for Public Involvement*. 2009. URL: www.invo.org.uk/posttypepublication/national-institute-for-health-research-payment-rates-for-public-involvement/ (accessed 17 December 2020).

54. Schreuders E, Sint Nicolaas J, de Jonge V, van Kooten H, Soo I, Sadowski D, *et al.* The appropriateness of surveillance colonoscopy intervals after polypectomy. *Can J Gastroenterol* 2013;**27**:33–8. https://doi.org/10.1155/2013/279897

55. Thomas RC, Selinger C, Rutter MD. Adherence to BSG adenoma surveillance guidelines will reduce colonoscopic workload. *Gut* 2005;**54**:173. https://doi.org/10.1136/gut.2004.049924

56. Saini SD, Kim HM, Schoenfeld P. Incidence of advanced adenomas at surveillance colonoscopy in patients with a personal history of colon adenomas: a meta-analysis and systematic review. *Gastrointest Endosc* 2006;**64**:614–26. https://doi.org/10.1016/j.gie.2006.06.057

57. Martínez ME, Baron JA, Lieberman DA, Schatzkin A, Lanza E, Winawer SJ, *et al.* A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. *Gastroenterology* 2009;**136**:832–41. https://doi.org/10.1053/j.gastro.2008.12.007

58. Lee SP, Sung IK, Kim JH, Lee SY, Park HS, Shim CS. Risk factors for incomplete polyp resection during colonoscopic polypectomy. *Gut Liver* 2015;**9**:66–72. https://doi.org/10.5009/gnl13330

59. East JE, Vieth M, Rex DK. Serrated lesions in colorectal cancer screening: detection, resection, pathology and surveillance. *Gut* 2015;**64**:991–1000. https://doi.org/10.1136/gutjnl-2014-309041

60. Bowles CJ, Leicester R, Romaya C, Swarbrick E, Williamd CB, Epstein O. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? *Gut* 2004;**53**:277–83. https://doi.org/10.1136/gut.2003.016436

61. Rees CJ, Koo S, Anderson J, McAlindon M, Veitch AM, Morris AJ, *et al.* British society of gastroenterology Endoscopy Quality Improvement Programme (EQIP): overview and progress. *Frontline Gastroenterol* 2019;**10**:148–53. https://doi.org/10.1136/flgastro-2018-101073

62. Lee TJ, Rutter MD, Blanks RG, Moss SM, Goddard AF, Chilton A, *et al.* Colonoscopy quality measures: experience from the NHS Bowel Cancer Screening Programme. *Gut* 2012;**61**:1050–7. https://doi.org/10.1136/gutjnl-2011-300651

63. Rajasekhar PT, Rutter MD, Bramble MG, Wilson DW, East JE, Greenaway JR, *et al.* Achieving high quality colonoscopy: using graphical representation to measure performance and reset standards. *Colorectal Dis* 2012;**14**:1538–45. https://doi.org/10.1111/j.1463-1318.2012.03057.x

64. Brueckl WM, Fritsche B, Seifert B, Boxberger F, Albrecht H, Croner RS, *et al.* Non-compliance in surveillance for patients with previous resection of large (> or = 1 cm) colorectal adenomas. *World J Gastroenterol* 2006;**12**:7313–18. https://doi.org/10.3748/wjg.v12.i45.7313

65. Laiyemo AO, Pinsky PF, Marcus PM, Lanza E, Cross AJ, Schatzkin A, Schoen RE. Utilization and yield of surveillance colonoscopy in the continued follow-up study of the polyp prevention trial. *Clin Gastroenterol Hepatol* 2009;**7**:562–7. https://doi.org/10.1016/j.cgh.2008.12.009

66. Cottet V, Jooste V, Fournel I, Bouvier AM, Faivre J, Bonithon-Kopp C. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. *Gut* 2012;**61**:1180–6. https://doi.org/10.1136/gutjnl-2011-300295

67. Imperiale TF, Ransohoff DF, Itzkowitz SH, Levin TR, Lavin P, Lidgard GP, *et al.* Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med* 2014;**370**:1287–97. https://doi.org/10.1056/NEJMoa1311194

Appendix 1 Supplementary information on methods

TABLE 23 Hospitals excluded from the study

Hospital	Reason for exclusion
Blackpool Victoria Hospital, Blackpool	Difficulties with data extraction
Bradford Royal Infirmary, Bradford	Difficulties with data extraction
Birmingham City Hospital, Birmingham	Difficulties in obtaining R&D approval
George Eliot Hospital, Nuneaton	Difficulties with data extraction
King George Hospital, Ilford	Difficulties with data extraction
Norfolk and Norwich University Hospital, Norwich	Missing data
Pinderfields Hospital, Wakefield	Missing data
Queen Alexandra Hospital, Portsmouth	Missing data
The University Hospital of North Staffordshire NHS Trust (now known as the Royal Stoke University Hospital) Stoke-on-Trent	Difficulties with data extraction
Stafford Hospital (now known as County Hospital), Stafford	Difficulties with data extraction

R&D, research and development.

TABLE 24 Histopathological outcomes of interest

Category	Type
Benign lesion	Hyperplastic polyp
	Unicryptal adenoma
	Adenoma
	Serrated adenoma
	Mixed polyp (hyperplastic and adenomatous features)
	Sessile serrated lesion
Possible CRC	Possible cancer (suspicious features but might be non-adenomatous)
	Cancer of unknown primary
	Cancer or adenoma with high-grade dysplasia (in dispute)
CRC	Cancer
	Cancer with remnant of adenoma
	Cancer with remnant of serrated adenoma
	Cancer with remnant of mixed adenoma
	Cancer with remnant of mixed/serrated adenoma
	Cancer with remnant of sessile serrated lesion

TABLE 25 Position of segments in the colon and rectum

Colorectal segment	Position
Anus	1
Rectum	2
Rectosigmoid	3
Sigmoid colon	4
Descending colon	5
Splenic flexure	6
Transverse colon	7
Hepatic flexure	8
Ascending colon	9
Caecum	10
Ileum	11

Appendix 2 Supplementary tables for the main clinical study

TABLE 26 Incidence of CRC after baseline by number of surveillance visits, stratified by age and sex

Age/sex	Number of surveillance visits	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
						Multivariable adjusted HR (95% CI)[b]	*p*-value[c]
Low-risk group							
Age (years)							
< 55	Zero	1422 (39.8)	22,551	10	44 (24 to 82)	1	0.21
	One or more	2147 (60.2)	17,872	11	62 (34 to 111)	0.98 (0.41 to 2.32)	
55–64	Zero	1652 (41.4)	23,744	29	122 (85 to 176)	1	
	One or more	2339 (58.6)	18,377	17	93 (58 to 149)	0.51 (0.27 to 0.94)	
65–74	Zero	2251 (52.9)	24,518	59	241 (186 to 311)	1	
	One or more	2007 (47.1)	14,280	17	119 (74 to 191)	0.34 (0.19 to 0.58)	
≥ 75	Zero	1882 (72.9)	13,779	45	327 (244 to 437)	1	
	One or more	701 (27.1)	3782	7	185 (88 to 388)	0.40 (0.18 to 0.89)	
Sex							
Women	Zero	3164 (49.6)	38,894	66	170 (133 to 216)	1	0.49
	One or more	3218 (50.4)	24,443	26	106 (72 to 156)	0.51 (0.32 to 0.82)	
Men	Zero	4043 (50.4)	45,698	77	168 (135 to 211)	1	
	One or more	3976 (49.6)	29,869	26	87 (59 to 128)	0.41 (0.25 to 0.65)	
Intermediate-risk group							
Age (years)							
< 55	Zero	560 (26.7)	10,404	11	106 (59 to 191)	1	0.34
	One	583 (27.8)	7410	7	94 (45 to 198)	0.66 (0.26 to 1.72)	
	Two	451 (21.5)	4200	4	95 (36 to 254)	0.49 (0.15 to 1.55)	
	Three or more	503 (24.0)	2980	6	201 (90 to 448)	0.67 (0.24 to 1.89)	
55–64	Zero	880 (27.9)	14,242	22	154 (102 to 235)	1	
	One	905 (28.7)	10,529	17	161 (100 to 260)	0.75 (0.39 to 1.42)	
	Two	808 (25.6)	5457	11	202 (112 to 364)	0.73 (0.35 to 1.54)	
	Three or more	565 (17.9)	3303	2	61 (15 to 242)	0.15 (0.03 to 0.65)	

continued

TABLE 26 Incidence of CRC after baseline by number of surveillance visits, stratified by age and sex (*continued*)

Age/sex	Number of surveillance visits	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
						Multivariable adjusted HR (95% CI)[b]	*p*-value[c]
65–74	Zero	1455 (37.2)	17,031	55	323 (248 to 421)	1	
	One	1221 (31.2)	11,463	24	209 (140 to 312)	0.45 (0.28 to 0.73)	
	Two	825 (21.1)	4848	12	248 (141 to 436)	0.45 (0.23 to 0.85)	
	Three or more	414 (10.6)	2049	7	342 (163 to 717)	0.43 (0.19 to 0.97)	
≥ 75	Zero	1788 (66.7)	12,251	47	384 (288 to 511)	1	
	One	634 (23.6)	3881	14	361 (214 to 609)	0.69 (0.38 to 1.26)	
	Two	195 (7.3)	972	4	411 (154 to 1096)	0.63 (0.23 to 1.78)	
	Three or more	65 (2.4)	250	3	1202 (388 to 3727)	1.33 (0.41 to 4.36)	
Sex							
Women	Zero	2143 (40.7)	25,511	55	216 (166 to 281)	1	0.16
	One	1532 (29.1)	15,318	28	183 (126 to 265)	0.71 (0.44 to 1.13)	
	Two	962 (18.3)	6718	12	179 (101 to 315)	0.62 (0.33 to 1.19)	
	Three or more	634 (12.0)	3501	10	286 (154 to 531)	0.79 (0.38 to 1.62)	
Men	Zero	2540 (38.6)	28,415	80	282 (226 to 351)	1	
	One	1811 (27.5)	17,965	34	189 (135 to 265)	0.51 (0.33 to 0.77)	
	Two	1317 (20.0)	8759	19	217 (138 to 340)	0.50 (0.29 to 0.84)	
	Three or more	913 (13.9)	5081	8	157 (79 to 315)	0.26 (0.12 to 0.57)	
High-risk group							
Age (years)							
< 55	Zero	62 (21.9)	1158	1	86 (12 to 613)	1	0.48
	One	64 (22.6)	944	3	318 (102 to 985)	2.80 (0.29 to 27.02)	
	Two or more	157 (55.5)	1089	2	184 (46 to 734)	1.32 (0.12 to 14.77)	
55–64	Zero	148 (19.7)	2222	10	450 (242 to 836)	1	
	One	177 (23.6)	2286	6	263 (118 to 584)	0.38 (0.13 to 1.05)	
	Two or more	425 (56.7)	2574	4	155 (58 to 414)	0.17 (0.05 to 0.57)	
65–74	Zero	346 (32.5)	3516	16	455 (279 to 743)	1	
	One	275 (25.8)	2777	11	396 (219 to 715)	0.61 (0.28 to 1.32)	
	Two or more	444 (41.7)	2442	7	287 (137 to 601)	0.37 (0.15 to 0.92)	
≥ 75	Zero	355 (57.2)	2346	17	724 (450 to 1165)	1	
	One	179 (28.8)	1138	4	351 (132 to 936)	0.34 (0.11 to 1.01)	
	Two or more	87 (14.0)	469	3	640 (207 to 1985)	0.48 (0.14 to 1.69)	

TABLE 26 Incidence of CRC after baseline by number of surveillance visits, stratified by age and sex (*continued*)

Age/sex	Number of surveillance visits	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
						Multivariable adjusted HR (95% CI)[b]	*p*-value[c]
Sex							
Women	Zero	276 (34.5)	2880	15	521 (314 to 864)	1	0.72
	One	207 (25.9)	2174	10	460 (248 to 855)	0.62 (0.28 to 1.39)	
	Two or more	316 (39.6)	1943	5	257 (107 to 618)	0.29 (0.10 to 0.83)	
Men	Zero	635 (33.1)	6363	29	456 (317 to 656)	1	
	One	488 (25.4)	4970	14	282 (167 to 476)	0.43 (0.22 to 0.82)	
	Two or more	797 (41.5)	4630	11	238 (132 to 429)	0.30 (0.14 to 0.63)	

a The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
b The HRs are adjusted for the covariates included in the final multivariable model for each risk group. The models for the low-risk group included completeness of colonoscopy, adenoma histology and proximal polyps. The models for the intermediate-risk group included year of baseline visit, length of baseline visit, completeness of colonoscopy, adenoma dysplasia and proximal polyps. The models for the high-risk group included completeness of colonoscopy and adenoma dysplasia. In the low- and intermediate-risk groups, age was also selected for inclusion in the final multivariable models and so was included in the models containing an interaction with sex.
c *p*-values are from the test for interaction between the number of surveillance visits and the specified characteristic (age or sex).

TABLE 27 Number of surveillance visits, sex, age, year of baseline visit and median follow-up time, by risk subgroup

	Risk group														
	Low risk					Intermediate risk					High risk				
	Lower-risk subgroup[a]		Higher-risk subgroup[a]			Lower-risk subgroup[b]		Higher-risk subgroup[b]			Lower-risk subgroup[c]		Higher-risk subgroup[c]		
Variable	*n*	%	*n*	%	*p*-value	*n*	%	*n*	%	*p*-value	*n*	%	*n*	%	*p*-value
Total	5235	36.4	9166	63.6		4738	40.0	7114	60.0		1817	66.8	902	33.2	
Number of surveillance visits					< 0.0001					< 0.0001					0.24
Zero	2804	53.6	4403	48.0		1932	40.8	2751	38.7		606	33.4	305	33.8	
One	1432	27.4	2527	27.6		1387	29.3	1956	27.5		474	26.1	221	24.5	
Two	661	12.6	1282	14.0		930	19.6	1349	19.0		407	22.4	186	20.6	
Three or more	338	6.5	954	10.4		489	10.3	1058	14.9		330	18.2	190	21.1	
Sex					0.97					0.050					0.21
Women	2319	44.3	4063	44.3		2159	45.6	3112	43.7		520	28.6	279	30.9	
Men	2916	55.7	5103	55.7		2579	54.4	4002	56.3		1297	71.4	623	69.1	
Age (years)					< 0.0001					< 0.0001					0.079
< 55	1523	29.1	2046	22.3		984	20.8	1113	15.6		180	9.9	103	11.4	
55–64	1452	27.7	2539	27.7		1310	27.6	1848	26.0		514	28.3	236	26.2	
65–74	1442	27.5	2816	30.7		1513	31.9	2402	33.8		729	40.1	336	37.3	
≥ 75	818	15.6	1765	19.3		931	19.6	1751	24.6		394	21.7	227	25.2	
Year of baseline visit					< 0.0001					< 0.0001					< 0.0001
1984–99	441	8.4	1199	13.1		630	13.3	1240	17.4		175	9.6	154	17.1	
2000–4	1761	33.6	3407	37.2		1461	30.8	2761	38.8		520	28.6	354	39.2	
2005–10	3033	57.9	4560	49.7		2647	55.9	3113	43.8		1122	61.8	394	43.7	
Follow-up time (years), median (IQR)	9.5 (7.3–11.9)		9.6 (7.1–12.6)		0.023	9.1 (7.0–11.9)		9.2 (6.1–12.6)		0.98[d]	8.3 (6.0–10.6)		8.5 (4.9–12.2)		0.028[d]

a The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
d *p*-value calculated using the Wilcoxon rank-sum test to compare the lower- and higher-risk subgroups.

Note
p-values were calculated with the chi-squared test to compare the lower- and higher-risk subgroups, unless indicated otherwise.

TABLE 28 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	11,719 (100)	108,319	144	133 (113 to 157)				
Number of surveillance visits[c]						< 0.0001		0.0001
Zero	6149 (52.5)	69,666	108	155 (128 to 187)	1		1	
One	3222 (27.5)	25,706	29	113 (78 to 162)	0.54 (0.35 to 0.82)		0.56 (0.36 to 0.85)	
Two	1515 (12.9)	9055	5	55 (23 to 133)	0.22 (0.09 to 0.56)		0.24 (0.10 to 0.61)	
Three or more	833 (7.1)	3893	2	51 (13 to 205)	0.18 (0.04 to 0.77)		0.20 (0.05 to 0.83)	
Sex						1.00		0.70
Women	5128 (43.8)	48,698	65	133 (105 to 170)	1		1	
Men	6591 (56.2)	59,621	79	133 (106 to 165)	1.00 (0.72 to 1.39)		1.07 (0.77 to 1.48)	
Age (years)						< 0.0001		< 0.0001
< 55	2852 (24.3)	30,666	14	46 (27 to 77)	1		1	
55–64	3268 (27.9)	32,845	35	107 (77 to 148)	2.37 (1.28 to 4.41)		2.27 (1.22 to 4.22)	
65–74	3487 (29.8)	30,653	60	196 (152 to 252)	4.50 (2.51 to 8.07)		4.00 (2.23 to 7.17)	
≥ 75	2112 (18.0)	14,156	35	247 (178 to 344)	6.10 (3.27 to 1.39)		4.92 (2.62 to 9.22)	
Year of baseline visit						0.93		0.80
1984–99	941 (8.0)	12,859	17	132 (82 to 213)	1		1	
2000–4	3839 (32.8)	41,000	57	139 (107 to 180)	1.09 (0.61 to 1.95)		0.88 (0.49 to 1.57)	
2005–10	6939 (59.2)	54,460	70	129 (102 to 162)	1.12 (0.62 to 2.03)		0.81 (0.45 to 1.48)	

continued

TABLE 28 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Length of baseline visit						0.54		0.51
1 day	9214 (78.6)	85,093	112	132 (109 to 158)	1		1	
2 days to 3 months	1118 (9.5)	9808	16	163 (100 to 266)	1.26 (0.74 to 2.12)		1.33 (0.78 to 2.27)	
3–6 months	781 (6.7)	7455	11	148 (82 to 266)	1.11 (0.60 to 2.07)		1.27 (0.68 to 2.38)	
≥ 6 months	606 (5.2)	5963	5	84 (35 to 201)	0.63 (0.26 to 1.54)		0.71 (0.29 to 1.74)	
Bowel preparation quality						0.058		0.11
Excellent or good	3998 (34.1)	38,324	66	172 (135 to 219)	1		1	
Satisfactory	2294 (19.6)	19,860	26	131 (89 to 192)	0.77 (0.49 to 1.22)		0.74 (0.47 to 1.17)	
Poor	737 (6.3)	5958	7	117 (56 to 246)	0.70 (0.32 to 1.52)		0.69 (0.31 to 1.49)	
Unknown	4690 (40.0)	44,177	45	102 (76 to 136)	0.59 (0.41 to 0.87)		0.63 (0.43 to 0.92)	
Number of adenomas						0.21		0.55
One	9554 (81.5)	88,674	112	126 (105 to 152)	1		1	
Two	2165 (18.5)	19,646	32	163 (115 to 230)	1.30 (0.88 to 1.92)		1.13 (0.76 to 1.69)	
Adenoma histology						0.066		0.060
Tubular	9253 (79.0)	85,190	103	121 (100 to 147)	1		1	
Tubulovillous	1587 (13.5)	14,364	30	209 (146 to 299)	1.65 (1.10 to 2.46)[d]		1.67 (1.11 to 2.49)[d]	
Villous	124 (1.1)	1230	1	81 (11 to 577)	1.65 (1.10 to 2.46)[d]		1.67 (1.11 to 2.49)[d]	
Unknown	755 (6.4)	7536	10	133 (71 to 247)	1.07 (0.56 to 2.06)		1.15 (0.60 to 2.21)	
Adenoma dysplasia						0.36		0.38
Low grade	10,993 (93.8)	100,640	132	131 (111 to 156)	1		1	
High grade	262 (2.2)	2424	6	247 (111 to 551)	1.86 (0.82 to 4.21)		1.85 (0.81 to 4.25)	
Unknown	464 (4.0)	5255	6	114 (51 to 254)	0.84 (0.37 to 1.90)		0.87 (0.38 to 2.00)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Proximal polyps						0.0025		0.0050
No	6251 (53.3)	59,177	61	103 (80 to 132)	1		1	
Yes	5468 (46.7)	49,142	83	169 (136 to 209)	1.66 (1.19 to 2.31)		1.61 (1.15 to 2.24)	
Hyperplastic polyps						0.31		0.25
No	9318 (79.5)	85,790	109	127 (105 to 153)	1		1	
Yes	2401 (20.5)	22,530	35	155 (112 to 216)	1.22 (0.83 to 1.79)		1.26 (0.86 to 1.85)	
Hyperplastic polyp ≥ 10 mm in size						0.61		0.70
No	11,600 (99.0)	107,284	142	132 (112 to 156)	1		1	
Yes	119 (1.0)	1035	2	193 (48 to 772)	1.48 (0.37 to 5.96)		1.33 (0.33 to 5.39)	
Family history of cancer/CRC[e]						0.30		0.32
No	10,524 (89.8)	95,162	130	137 (115 to 162)	1		1	
Yes	1195 (10.2)	13,158	14	106 (63 to 180)	0.76 (0.43 to 1.31)		1.35 (0.76 to 2.38)	

a *p*-values were calculated with the LRT.
b The multivariable model contained number of surveillance visits, age, adenoma histology and proximal polyps. The variables that were selected for inclusion in the final multivariable model for all low-risk patients in the main analysis (apart from completeness of colonoscopy) are presented in *Table 4*. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the adenoma histology variable the HRs for the tubulovillous and villous categories are for these two categories combined.
e Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Over 70% of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 29 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	8967 (100)	80,572	150	186 (159 to 218)				
Number of surveillance visits[c]						0.0041		0.0080
Zero	3605 (40.2)	40,921	85	208 (168 to 257)	1		1	
One	2565 (28.6)	24,087	41	170 (125 to 231)	0.63 (0.43 to 0.93)		0.64 (0.43 to 0.95)	
Two	1755 (19.6)	10,462	16	153 (94 to 250)	0.47 (0.27 to 0.83)		0.50 (0.28 to 0.88)	
Three or more	1042 (11.6)	5103	8	157 (78 to 313)	0.36 (0.17 to 0.78)		0.36 (0.16 to 0.79)	
Sex						0.80		0.38
Women	3874 (43.2)	36,048	66	183 (144 to 233)	1		1	
Men	5093 (56.8)	44,524	84	189 (152 to 234)	1.04 (0.76 to 1.44)		1.16 (0.83 to 1.61)	
Age (years)						< 0.0001		< 0.0001
< 55	1573 (17.5)	17,584	18	102 (64 to 162)	1		1	
55–64	2416 (26.9)	24,093	25	104 (70 to 154)	1.06 (0.58 to 1.94)		1.04 (0.57 to 1.91)	
65–74	3013 (33.6)	26,134	63	241 (188 to 309)	2.64 (1.56 to 4.47)		2.52 (1.48 to 4.28)	
≥ 75	1965 (21.9)	12,761	44	345 (257 to 463)	4.13 (2.36 to 7.21)		3.49 (1.99 to 6.14)	
Year of baseline visit						0.061		0.020
1984–99	1044 (11.6)	13,531	41	303 (223 to 412)	1		1	
2000–4	2805 (31.3)	28,734	53	184 (141 to 241)	0.63 (0.41 to 0.96)		0.55 (0.36 to 0.86)	
2005–10	5118 (57.1)	38,307	56	146 (113 to 190)	0.59 (0.37 to 0.93)		0.54 (0.33 to 0.86)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Length of baseline visit						0.048		0.019
1 day	5040 (56.2)	44,805	67	150 (118 to 190)	1		1	
2 days to 3 months	1766 (19.7)	16,001	36	225 (162 to 312)	1.52 (1.01 to 2.27)		1.75 (1.16 to 2.64)	
3–6 months	1083 (12.1)	10,070	21	209 (136 to 320)	1.39 (0.85 to 2.27)		1.44 (0.88 to 2.37)	
≥ 6 months	1078 (12.0)	9695	26	268 (183 to 394)	1.77 (1.13 to 2.79)		1.79 (1.12 to 2.85)	
Bowel preparation quality						0.11		0.093
Excellent or good	3046 (34.0)	27,581	46	167 (125 to 223)	1		1	
Satisfactory	1664 (18.6)	13,640	28	205 (142 to 297)	1.27 (0.79 to 2.03)		1.34 (0.83 to 2.14)	
Poor	454 (5.1)	3320	12	361 (205 to 636)	2.24 (1.19 to 4.23)		2.00 (1.05 to 3.78)	
Unknown	3803 (42.4)	36,031	64	178 (139 to 227)	1.02 (0.70 to 1.50)		0.92 (0.62 to 1.37)	
Number of adenomas						0.24		0.40
One	5665 (63.2)	52,222	92	176 (144 to 216)	1		1	
Two	2461 (27.5)	21,306	48	225 (170 to 299)	1.31 (0.92 to 1.86)		1.05 (0.73 to 1.52)	
Three or more	841 (9.4)	7044	10	142 (76 to 264)	0.84 (0.44 to 1.62)		0.67 (0.33 to 1.32)	
Adenoma size (mm)						0.21		0.21
< 10	841 (9.4)	7044	10	142 (76 to 264)	1		1	
10–19	5160 (57.5)	46,777	80	171 (137 to 213)	1.16 (0.60 to 2.24)		1.43 (0.73 to 2.83)	
≥ 20	2966 (33.1)	26,751	60	224 (174 to 289)	1.52 (0.78 to 2.98)		1.77 (0.87 to 3.57)	
Adenoma histology						< 0.0001		0.0003
Tubular	3660 (40.8)	33,091	41	124 (91 to 168)	1		1	
Tubulovillous	4204 (46.9)	37,334	76	204 (163 to 255)	1.67 (1.14 to 2.44)		1.62 (1.10 to 2.38)	
Villous	768 (8.6)	6812	15	220 (133 to 365)	1.80 (1.00 to 3.25)		1.39 (0.75 to 2.56)	
Unknown	335 (3.7)	3334	18	540 (340 to 857)	4.17 (2.39 to 7.28)		4.28 (2.27 to 8.08)	

continued

TABLE 29 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.11		0.20
Low grade	7251 (80.9)	64,995	111	171 (142 to 206)	1		1	
High grade	1473 (16.4)	12,621	29	230 (160 to 331)	1.36 (0.90 to 2.05)		1.23 (0.81 to 1.87)	
Unknown	243 (2.7)	2956	10	338 (182 to 629)	1.82 (0.95 to 3.49)		1.80 (0.92 to 3.50)	
Proximal polyps						0.0009		0.0007
No	5781 (64.5)	53,627	81	151 (121 to 188)	1		1	
Yes	3186 (35.5)	26,945	69	256 (202 to 324)	1.74 (1.26 to 2.40)		1.77 (1.28 to 2.45)	
Hyperplastic polyps						0,74		0.66
No	7314 (81.6)	65,673	121	184 (154 to 220)	1		1	
Yes	1653 (18.4)	14,899	29	195 (135 to 280)	1.07 (0.71 to 1.61)		1.10 (0.72 to 1.67)	
Hyperplastic polyp ≥ 10 mm in size						0.63		0.50
No	8815 (98.3)	79,111	148	187 (159 to 220)	1		1	
Yes	152 (1.7)	1461	2	137 (34 to 547)	0.73 (0.18 to 2.93)		0.64 (0.16 to 2.59)	
Family history of cancer/CRC[d]						0.93		0.34
No	8564 (95.5)	76,306	142	186 (158 to 219)	1		1	
Yes	403 (4.5)	4266	8	188 (94 to 375)	0.97 (0.48 to 1.98)		1.45 (0.70 to 2.99)	

a *p*-values were calculated with the LRT.
b The multivariable model contained number of surveillance visits, age, adenoma dysplasia, proximal polyps, year of baseline visit and length of baseline visit. The variables that were selected for inclusion in the final multivariable model for all intermediate-risk patients in the main analysis (apart from completeness of colonoscopy) are presented in *Table 5*. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Over 70% of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 30 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	2354 (100)	19,266	64	332 (260 to 424)				
Number of surveillance visits[c]						0.012		0.0069
Zero	780 (33.1)	7847	33	421 (299 to 592)	1		1	
One	623 (26.5)	6181	19	307 (196 to 482)	0.51 (0.29 to 0.91)		0.50 (0.28 to 0.89)	
Two	518 (22.0)	3303	7	212 (101 to 445)	0.30 (0.13 to 0.70)		0.28 (0.12 to 0.66)	
Three or more	433 (18.4)	1935	5	258 (108 to 621)	0.40 (0.14 to 1.09)		0.37 (0.14 to 1.03)	
Sex						0.72		0.81
Women	669 (28.4)	5648	20	354 (228 to 549)	1		1	
Men	1685 (71.6)	13,618	44	323 (240 to 434)	0.91 (0.54 to 1.54)		0.94 (0.55 to 1.59)	
Age (years)						0.045		0.20
< 55	224 (9.5)	2445	4	164 (61 to 436)	1		1	
55–64	655 (27.8)	5915	15	254 (153 to 421)	1.56 (0.52 to 4.70)		1.59 (0.53 to 4.79)	
65–74	942 (40.0)	7580	27	356 (244 to 519)	2.21 (0.77 to 6.34)		2.13 (0.74 to 6.11)	
≥ 75	533 (22.6)	3325	18	541 (341 to 859)	3.45 (1.16 to 10.25)		2.70 (0.90 to 8.05)	
Year of baseline visit						0.56		0.69
1984–99	221 (9.4)	2610	5	192 (80 to 460)	1		1	
2000–4	685 (29.1)	6383	24	376 (252 to 561)	1.64 (0.63 to 4.31)		1.50 (0.57 to 3.94)	
2005–10	1448 (61.5)	10,273	35	341 (245 to 475)	1.54 (0.59 to 4.01)		1.41 (0.54 to 3.70)	
Length of baseline visit						0.79		0.96
1 day	1021 (43.4)	8406	25	297 (201 to 440)	1		1	
2 days to 3 months	471 (20.0)	3662	13	355 (206 to 611)	1.20 (0.61 to 2.35)		1.04 (0.53 to 2.04)	
3–6 months	389 (16.5)	3214	10	311 (167 to 578)	1.05 (0.50 to 2.18)		0.95 (0.45 to 2.00)	
≥ 6 months	473 (20.1)	3984	16	402 (246 to 656)	1.37 (0.73 to 2.57)		1.15 (0.60 to 2.20)	

continued

TABLE 30 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics, including only patients with a complete baseline colonoscopy (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Bowel preparation quality						0.64		0.68
Excellent or good	935 (39.7)	7922	24	303 (203 to 452)	1		1	
Satisfactory	385 (16.4)	2903	10	344 (185 to 640)	1.13 (0.54 to 2.37)		0.99 (0.47 to 2.07)	
Poor	129 (5.5)	852	5	587 (244 to 1410)	1.99 (0.76 to 5.21)		1.88 (0.71 to 4.95)	
Unknown	905 (38.5)	7588	25	329 (223 to 488)	1.11 (0.64 to 1.95)		1.09 (0.62 to 1.91)	
Number of adenomas						0.89		0.81
Three	1038 (44.1)	8736	27	309 (212 to 451)	1		1	
Four	496 (21.1)	4016	13	324 (188 to 557)	1.05 (0.54 to 2.04)		1.09 (0.56 to 2.12)	
Five	400 (17.0)	3180	13	409 (237 to 704)	1.31 (0.67 to 2.53)		1.39 (0.72 to 2.71)	
Six or more	420 (17.8)	3333	11	330 (183 to 596)	1.07 (0.53 to 2.16)		1.17 (0.57 to 2.37)	
Adenoma size (mm)						0.38		0.78
< 10	225 (9.6)	1893	5	264 (110 to 635)	1		1	
10–19	1168 (49.6)	9566	28	293 (202 to 424)	1.12 (0.43 to 2.90)		0.99 (0.38 to 2.57)	
≥ 20	947 (40.2)	7683	31	403 (284 to 574)	1.55 (0.60 to 3.98)		1.19 (0.45 to 3.14)	
Unknown	14 (0.6)	123	0	0	n/a		n/a	
Adenoma histology						0.24		0.49
Tubular	886 (37.6)	7379	22	298 (196 to 453)	1		1	
Tubulovillous	1151 (48.9)	9278	30	323 (226 to 462)	1.10 (0.63 to 1.91)		0.99 (0.57 to 1.73)	
Villous	277 (11.8)	2197	12	546 (310 to 962)	1.85 (0.92 to 3.74)		1.49 (0.72 to 3.07)	
Unknown	40 (1.7)	411	0	0	n/a		n/a	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.0010		0.0005
Low grade	1783 (75.7)	14,680	38	259 (188 to 356)	1		1	
High grade	537 (22.8)	4234	26	614 (418 to 902)	2.40 (1.46 to 3.95)		2.51 (1.52 to 4.14)	
Unknown	34 (1.4)	352	0	0	n/a		n/a	
Proximal polyps						0.29		0.18
No	465 (19.8)	3982	10	251 (135 to 467)	1		1	
Yes	1889 (80.3)	15,284	54	353 (271 to 461)	1.42 (0.72 to 2.79)		1.56 (0.79 to 3.07)	
Hyperplastic polyps						0.32		0.22
No	1670 (70.9)	13,503	41	304 (224 to 412)	1		1	
Yes	684 (29.1)	5763	23	399 (265 to 601)	1.30 (0.78 to 2.17)		1.38 (0.83 to 2.31)	
Hyperplastic polyp ≥ 10 mm in size						0.82		0.78
No	2290 (97.3)	18,752	62	331 (258 to 424)	1		1	
Yes	64 (2.7)	514	2	389 (97 to 1555)	1.18 (0.29 to 4.83)		1.23 (0.30 to 5.04)	
Family history of cancer/CRC[d]						0.18		0.29
No	2269 (96.4)	18,389	63	343 (268 to 439)	1		1	
Yes	85 (3.6)	876	1	114 (16 to 810)	1.33 (0.05 to 2.39)		0.40 (0.06 to 2.90)	

n/a, not applicable.

a *p*-values were calculated with the LRT.

b The multivariable model contained number of surveillance visits and adenoma dysplasia. The variables that were selected for inclusion in the final multivariable model for all high-risk patients in the main analysis (apart from completeness of colonoscopy) are presented in *Table 6*. Patients with unknown adenoma dysplasia were not included in the multivariable model because there were no CRC cases in these patients. For number of surveillance visits and adenoma dysplasia the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the multivariable model.

c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.

d Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Over 70% of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 31 Incidence of CRC after baseline by number of surveillance visits, including only patients with a complete baseline colonoscopy

Risk group/ subgroup	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
Low-risk group						
Whole risk group						< 0.0001
Zero visits	6149 (52.5)	69,666	108	155 (128 to 187)	1	
One visit	3222 (27.5)	25,706	29	113 (78 to 162)	0.54 (0.35 to 0.82)	
Two or more visits	2348 (20.0)	12,948	7	54 (26 to 113)	0.21 (0.10 to 0.47)	
Total	11,719 (100)	108,319	144	133 (113 to 157)		
Higher-risk subgroup[c]						< 0.0001
Zero visits	3345 (51.6)	36,763	77	209 (168 to 262)	1	
One visit	1790 (27.6)	14,296	21	147 (96 to 225)	0.50 (0.31 to 0.83)	
Two or more visits	1349 (20.8)	7475	4	54 (20 to 143)	0.14 (0.05 to 0.39)	
Total	6484 (55.3)	58,534	102	174 (144 to 212)		
Lower-risk subgroup[c]						0.15
Zero visits	2804 (53.6)	32,903	31	94 (66 to 134)	1	
One visit	1432 (27.4)	11,410	8	70 (35 to 140)	0.54 (0.25 to 1.20)	
Two or more visits	999 (19.1)	5472	3	55 (18 to 170)	0.42 (0.12 to 1.48)	
Total	5235 (44.7)	49,785	42	84 (62 to 114)		
Intermediate-risk group						
Whole risk group						0.0016
Zero visits	3605 (40.2)	40,921	85	208 (168 to 257)	1	
One visit	2565 (28.6)	24,087	41	170 (125 to 231)	0.63 (0.43 to 0.93)	
Two or more visits	2797 (31.2)	15,565	24	154 (103 to 230)	0.43 (0.26 to 0.71)	
Total	8967 (100)	80,572	150	186 (159 to 218)		
Higher-risk subgroup[d]						0.0006
Zero visits	1673 (39.6)	17,684	52	294 (224 to 386)	1	
One visit	1178 (27.9)	10,936	25	229 (154 to 338)	0.58 (0.35 to 0.96)	
Two or more visits	1378 (32.6)	7482	11	147 (81 to 265)	0.28 (0.14 to 0.56)	
Total	4229 (47.2)	36,102	88	244 (198 to 300)		
Lower-risk subgroup[d]						0.30
Zero visits	1932 (40.8)	23,237	33	142 (101 to 200)	1	
One visit	1387 (29.3)	13,151	16	122 (75 to 199)	0.66 (0.35 to 1.23)	
Two or more visits	1419 (30.0)	8082	13	161 (93 to 277)	0.63 (0.31 to 1.29)	
Total	4738 (52.8)	44,470	62	139 (109 to 179)		

TABLE 31 Incidence of CRC after baseline by number of surveillance visits, including only patients with a complete baseline colonoscopy (*continued*)

Risk group/ subgroup	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
High-risk group						
Whole risk group						0.0046
Zero visits	780 (33.1)	17,847	33	421 (299 to 592)	1	
One visit	623 (26.5)	6181	19	307 (196 to 482)	0.51 (0.29 to 0.91)	
Two or more visits	951 (40.4)	5238	12	229 (130 to 403)	0.33 (0.16 to 0.68)	
Total	2354 (100)	19,266	64	332 (260 to 424)		
Higher-risk subgroup[e]						0.0030
Zero visits	174 (32.4)	1620	16	987 (605 to 1612)	1	
One visit	149 (27.8)	1414	7	495 (236 to 1038)	0.34 (0.14 to 0.85)	
Two or more visits	214 (39.9)	1199	3	250 (81 to 776)	0.15 (0.04 to 0.56)	
Total	537 (22.8)	4234	26	614 (418 to 902)		
Lower-risk subgroup[e]						0.26
Zero visits	606 (33.4)	6226	17	273 (170 to 439)	1	
One visit	474 (26.1)	4766	12	252 (143 to 443)	0.66 (0.31 to 1.41)	
Two or more visits	737 (40.6)	4039	9	223 (116 to 428)	0.49 (0.20 to 1.18)	
Total	1817 (77.2)	15,032	38	253 (184 to 347)		

a The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
b *p*-values were calculated with the LRT.
c The higher-risk subgroup comprised patients who had a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
d The higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have either of these factors were assigned to the lower-risk subgroup.
e The higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia at baseline. Patients who did not have this factor were assigned to the lower-risk subgroup.

TABLE 32 Cumulative incidence of CRC at 3, 5 and 10 years and age- and sex-SIRs, including only patients with a complete baseline colonoscopy

Risk group/ subgroup	Number of patients (%)	Number of person-years	3 years		5 years		10 years		*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
Low-risk group												
After baseline, with no surveillance[d]									< 0.0001			
Whole risk group	11,719 (100)	69,666	29	0.3 (0.2 to 0.4)	52	0.6 (0.5 to 0.8)	92	1.6 (1.3 to 2.1)		108	137	0.79 (0.65 to 0.95)
Higher-risk subgroup[e]	6484 (55)	36,763	23	0.4 (0.3 to 0.7)	41	0.9 (0.7 to 1.2)	63	2.1 (1.6 to 2.7)		77	77	1.00 (0.79 to 1.26)
Lower-risk subgroup[e]	5235 (45)	32,903	6	0.1 (0.1 to 0.3)	11	0.3 (0.2 to 0.5)	29	1.2 (0.8 to 1.7)		31	60	0.51 (0.35 to 0.73)
After first surveillance, with one surveillance visit[f]									0.066			
Whole risk group	5570 (100)	25,706	12	0.3 (0.2 to 0.5)	20	0.5 (0.3 to 0.8)	28	1.4 (0.8 to 2.4)		29	51	0.57 (0.38 to 0.82)
Higher-risk subgroup[e]	3139 (56)	14,296	7	0.3 (0.1 to 0.6)	13	0.6 (0.4 to 1.1)	20	2.1 (1.1 to 3.9)		21	30	0.70 (0.44 to 1.08)
Lower-risk subgroup[e]	2431 (44)	11,410	5	0.2 (0.1 to 0.6)	7	0.4 (0.2 to 0.8)	8	0.6 (0.2 to 1.4)		8	21	0.38 (0.16 to 0.74)
After second surveillance, with two or more surveillance visits[g]									0.97			
Whole risk group	2348 (100)	12,948	0		1	0.1 (0.0 to 0.6)	5	0.8 (0.3 to 1.9)		7	27	0.26 (0.10 to 0.53)
Higher-risk subgroup[e]	1349 (57)	7475	0		1	0.2 (0.0 to 1.1)	3	0.8 (0.2 to 2.6)		4	17	0.24 (0.07 to 0.62)
Lower-risk subgroup[e]	999 (43)	5472	0		0		2	0.7 (0.2 to 3.0)		3	10	0.29 (0.06 to 0.84)

Risk group/ subgroup	Number of patients (%)	Number of person-years	3 years		5 years		10 years		*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
Intermediate-risk group												
After baseline, with no surveillance[d]									0.0004			
Whole risk group	8967 (100)	40,921	35	0.5 (0.4 to 0.7)	55	1.1 (0.8 to 1.4)	74	2.1 (1.6 to 2.7)		85	88	0.97 (0.77 to 1.19)
Higher-risk subgroup[h]	4229 (47)	17,684	22	0.7 (0.5 to 1.1)	35	1.5 (1.1 to 2.2)	47	3.1 (2.2 to 4.4)		52	41	1.27 (0.95 to 1.66)
Lower-risk subgroup[h]	4738 (53)	23,237	13	0.4 (0.2 to 0.6)	20	0.7 (0.4 to 1.1)	27	1.3 (0.8 to 2.1)		33	47	0.70 (0.48 to 0.99)
After first surveillance, with one surveillance visit[f]									0.028			
Whole risk group	5362 (100)	24,087	10	0.2 (0.1 to 0.4)	22	0.8 (0.5 to 1.2)	39	2.9 (2.0 to 4.3)		41	53	0.77 (0.55 to 1.05)
Higher-risk subgroup[h]	2556 (48)	10,936	7	0.4 (0.2 to 0.7)	14	1.1 (0.6 to 1.8)	24	4.3 (2.6 to 7.3)		25	26	0.96 (0.62 to 1.42)
Lower-risk subgroup[h]	2806 (52)	13,151	3	0.1 (0.04 to 0.4)	8	0.5 (0.2 to 1.0)	15	1.9 (1.0 to 3.4)		16	27	0.59 (0.34 to 0.96)
After second surveillance, with two or more surveillance visits[g]									0.99			
Whole risk group	2797 (100)	15,565	6	0.3 (0.1 to 0.6)	10	0.5 (0.3 to 1.0)	18	1.7 (1.0 to 2.8)		24	36	0.66 (0.42 to 0.98)
Higher-risk subgroup[h]	1378 (49)	7482	3	0.3 (0.1 to 0.8)	4	0.4 (0.1 to 1.0)	8	1.7 (0.8 to 3.7)		11	18	0.61 (0.30 to 1.09)
Lower-risk subgroup[h]	1419 (51)	8082	3	0.3 (0.1 to 0.8)	6	0.6 (0.3 to 1.5)	10	1.7 (0.8 to 3.3)		13	18	0.72 (0.38 to 1.22)
High-risk group												
After baseline, with no surveillance[d]									< 0.0001			
Whole risk group	2354 (100)	7847	13	0.9 (0.5–1.6)	23	2.6 (1.7 to 4.0)	32	5.8 (3.8 to 8.9)		33	20	1.68 (1.15 to 2.35)
Higher-risk subgroup[i]	537 (23)	1620	6	2.1 (0.9 to 4.8)	10	5.4 (2.7 to 10.4)	15	14.4 (7.8 to 25.7)		16	4	3.76 (2.15 to 6.11)
Lower-risk subgroup[i]	1817 (77)	6226	7	0.6 (0.3 to 1.4)	13	1.9 (1.0 to 3.4)	17	3.8 (2.1 to 6.8)		17	15	1.10 (0.64 to 1.76)

continued

TABLE 32 Cumulative incidence of CRC at 3, 5 and 10 years and age- and sex-SIRs, including only patients with a complete baseline colonoscopy (*continued*)

Risk group/ subgroup	Number of patients (%)	Number of person-years	3 years		5 years		10 years		*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
After first surveillance, with one surveillance visit[f]									0.12			
Whole risk group	1574 (100)	6181	8	0.6 (0.3 to 1.3)	15	2.0 (1.2 to 3.5)	18	4.4 (2.1 to 8.9)		19	16	1.21 (0.73 to 1.89)
Higher-risk subgroup[i]	363 (23)	1414	3	1.1 (0.3 to 3.2)	7	4.5 (2.0 to 9.7)	7	4.5 (2.0 to 9.7)		7	4	1.82 (0.73 to 3.75)
Lower-risk subgroup[i]	1211 (77)	4766	5	0.5 (0.2 to 1.3)	8	1.3 (0.6 to 2.9)	11	4.4 (1.8 to 10.6)		12	12	1.01 (0.52 to 1.76)
After second surveillance, with two or more surveillance visits[g]									0.91			
Whole risk group	951 (100)	5238	2	0.3 (0.1 to 1.0)	7	1.1 (0.5 to 2.3)	12	2.8 (1.5 to 5.2)		12	14	0.85 (0.44 to 1.48)
Higher-risk subgroup[i]	214 (23)	1199	1	0.5 (0.1 to 3.6)	1	0.5 (0.1 to 3.6)	3	3.7 (1.0 to 13.2)		3	3	0.88 (0.18 to 2.58)
Lower-risk subgroup[i]	737 (78)	4039	1	0.2 (0.02 to 1.2)	6	1.3 (0.6 to 2.8)	9	2.4 (1.2 to 4.7)		9	11	0.83 (0.38 to 1.58)

a *p*-values were calculated with the log-rank test to compare cumulative incidence curves of the higher- and lower-risk subgroups.
b Total number of observed CRCs at end of follow-up.
c The numbers of expected CRCs were calculated by multiplying the sex- and 5-year age group-specific observed person-years by the corresponding sex- and age-specific incidence rates in the general population of England in 2007.
d The data were censored at the first surveillance visit.
e The higher-risk subgroup comprised patients who had a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
f Data were censored at second surveillance visit.
g Data were censored at end of follow-up.
h The higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia or proximal polyps at baseline. Patients who did not have either of these factors were assigned to the lower-risk subgroup.
i The higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia at baseline. Patients who did not have this factor were assigned to the lower-risk subgroup.

TABLE 33 Detection rate of AAs and CRC at first surveillance by interval length and risk subgroup, including only patients with a complete baseline colonoscopy

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Low-risk group																
< 18 months	326	14.0	9	2.8	521	17.1	23	4.4	328	13.9	2	0.6	527	17.0	6	1.1
2 years[c]	369	15.9	13	3.5	470	15.4	29	6.2	372	15.8	3	0.8	480	15.4	10	2.1
3 years[c]	588	25.3	28	4.8	853	28.0	61	7.2	590	25.1	2	0.3	868	27.9	15	1.7
4 years[c]	309	13.3	22	7.1	365	12.0	31	8.5	313	13.3	4	1.3	372	12.0	7	1.9
5 years[c]	430	18.5	28	6.5	494	16.2	43	8.7	435	18.5	5	1.1	499	16.1	5	1.0
6 years[c]	162	7.0	17	10.5	176	5.8	14	8.0	165	7.0	3	1.8	179	5.8	3	1.7
7 years[c]	86	3.7	8	9.3	104	3.4	14	13.5	86	3.7	0	0.0	110	3.5	6	5.5
8 years[c]	57	2.4	4	7.0	66	2.2	9	13.6	65	2.8	8	12.3	72	2.3	6	8.3
Total	2327	100	129	5.5	3049	100	224	7.3	2354	100	27	1.1	3107	100	58	1.9
p-value[d]			< 0.0001				< 0.0001				< 0.0001				0.0067	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.35 (1.08 to 1.69); 0.0077								1.64 (1.04 to 2.60); 0.0307							
Intermediate-risk group																
< 18 months	642	24.0	35	5.5	804	32.0	64	8.0	645	23.9	3	0.5	817	32.0	13	1.6
2 years[c]	399	14.9	24	6.0	432	17.2	42	9.7	407	15.1	8	2.0	437	17.1	5	1.1
3 years[c]	1024	38.2	68	6.6	801	31.9	93	11.6	1029	38.1	5	0.5	807	31.6	6	0.7
4 years[c]	255	9.5	29	11.4	225	9.0	18	8.0	256	9.5	1	0.4	234	9.2	9	3.8
5 years[c]	241	9.0	20	8.3	172	6.9	28	16.3	247	9.1	6	2.4	178	7.0	6	3.4
6 years[c]	117	4.4	15	12.8	76	3.0	8	10.5	118	4.4	1	0.8	78	3.1	2	2.6

continued

TABLE 33 Detection rate of AAs and CRC at first surveillance by interval length and risk subgroup, including only patients with a complete baseline colonoscopy (*continued*)

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	2678	100	191	7.1	2510	100	253	10.1	2702	100	24	0.9	2551	100	41	1.6
p-value[d]			0.0007				0.0093				0.28				0.064	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.46 (1.20 to 1.78); 0.0001								1.82 (1.10 to 3.03); 0.0180							
High-risk group																
< 15 months	513	47.5	76	14.8	150	44.8	24	16.0	516	47.4	3	0.6	153	44.7	3	2.0
1.5 years[f]	161	14.9	23	14.3	77	23.0	8	10.4	161	14.8	0	0.0	77	22.5	0	0
2 years[f]	104	9.6	11	10.6	35	10.4	5	14.3	107	9.8	3	2.8	37	10.8	2	5.4
2.5 years[f]	47	4.4	9	19.1	20	6.0	5	25.0	48	4.4	1	2.1	20	5.8	0	0
3 years[f]	184	17.0	35	19.0	38	11.3	9	23.7	185	17.0	1	0.5	39	11.4	1	2.6
3.5 years[f]	71	6.6	9	12.7	15	4.5	2	13.3	72	6.6	1	1.4	16	4.7	1	6.3
Total	1080	100	163	15.1	335	100	53	15.8	1089	100	9	0.8	342	100	7	2.0
p-value[d]			0.46				0.51				0.38				0.35	
OR (95% CI) for higher-risk vs. lower-risk; *p*-value[e]	1.06 (0.75 to 1.48); 0.75								2.51 (0.93 to 6.78); 0.080							

a Patients with CRC detected at first surveillance were excluded from the analyses of AA detection rates.
b In the low-risk group, the higher-risk subgroup comprised patients who had a tubulovillous or villous adenoma, or proximal polyps at baseline. In the intermediate-risk group, the higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia, or proximal polyps at baseline. In the high-risk group, the higher-risk subgroup comprised patients who had an adenoma with high-grade dysplasia at baseline. In all risk groups, the patients who did not have any of the previously stated factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.
f Interval ± 3 months.

TABLE 34 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	14,401 (100.0)	138,903	189	136 (118 to 157)				
Number of surveillance visits[c]						< 0.0001		< 0.0001
Zero	7207 (50.0)	84,591	139	164 (139 to 194)	1		1	
One	3959 (27.5)	34,507	39	113 (83 to 155)	0.53 (0.37 to 0.77)		0.54 (0.38 to 0.79)	
Two	1943 (13.5)	12,986	8	62 (31 to 123)	0.26 (0.12 to 0.54)		0.27 (0.13 to 0.57)	
Three or more	1292 (9.0)	6818	3	44 (14 to 136)	0.17 (0.05 to 0.57)		0.18 (0.06 to 0.59)	
Sex						0.50		0.77
Women	6382 (44.3)	63,337	91	144 (117 to 176)	1		1	
Men	8019 (55.7)	75,567	98	130 (106 to 158)	0.91 (0.68 to 1.21)		0.96 (0.72 to 1.27)	
Age (years)						< 0.0001		< 0.0001
< 55	3569 (24.8)	40,422	21	52 (34 to 80)	1		1	
55–64	3991 (27.7)	42,121	43	102 (76 to 138)	1.98 (1.18 to 3.34)		1.93 (1.14 to 3.25)	
65–74	4258 (29.6)	38,799	76	196 (156 to 245)	3.88 (2.39 to 6.29)		3.54 (2.18 to 5.75)	
≥ 75	2583 (17.9)	17,561	49	279 (211 to 369)	5.81 (3.47 to 9.72)		4.79 (2.85 to 8.04)	
Year of baseline visit						0.80		0.57
1984–99	1640 (11.4)	23,185	30	129 (90 to 185)	1		1	
2000–4	5168 (35.9)	56,134	83	148 (119 to 183)	1.10 (0.71 to 1.71)		0.96 (0.61 to 1.50)	
2005–10	7593 (52.7)	59,585	76	128 (102 to 160)	0.99 (0.63 to 1.58)		0.81 (0.50 to 1.32)	

continued

TABLE 34 Long-term CRC incidence after baseline among low-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Length of baseline visit						0.84		0.71
1 day	11,354 (78.8)	110,143	148	134 (114 to 158)	1		1	
2 days to 3 months	1373 (9.5)	12,314	18	146 (92 to 232)	1.10 (0.67 to 1.79)		1.14 (0.69 to 1.87)	
3–6 months	950 (6.6)	9309	15	161 (97 to 267)	1.19 (0.70 to 2.03)		1.36 (0.80 to 2.33)	
≥ 6 months	724 (5.0)	7137	8	112 (56 to 224)	0.83 (0.41 to 1.69)		0.96 (0.47 to 1.97)	
Colonoscopy completeness						0.36		0.0672
Complete	11,719 (81.4)	108,319	142	131 (111 to 155)	1		1	
Incomplete	1140 (7.9)	10,674	25	234 (158 to 347)	1.17 (0.84 to 1.64)[d]		1.39 (0.99 to 1.95)[d]	
Unknown	1542 (10.7)	19,910	22	110 (73 to 168)	1.17 (0.84 to 1.64)[d]		1.39 (0.99 to 1.95)[d]	
Bowel preparation quality						0.0782		0.18
Excellent or good	5145 (35.7)	52,129	84	161 (130 to 200)	1		1	
Satisfactory	2540 (17.6)	22,051	30	136 (95 to 195)	0.85 (0.56 to 1.29)		0.81 (0.53 to 1.23)	
Poor	968 (6.7)	7970	14	176 (104 to 297)	1.10 (0.63 to 1.94)		1.02 (0.58 to 1.81)	
Unknown	5748 (39.9)	56,754	61	107 (84 to 138)	0.67 (0.48 to 0.93)		0.71 (0.51 to 0.98)	
Number of adenomas						0.21		0.54
One	11,762 (81.7)	113,729	148	130 (111 to 153)	1		1	
Two	2639 (18.3)	25,175	41	163 (120 to 221)	1.25 (0.89 to 1.77)		1.12 (0.79 to 1.59)	
Adenoma histology						0.0744		0.0446
Tubular	11,138 (77.3)	107,018	132	123 (104 to 146)	1		1	
Tubulovillous	2113 (14.7)	20,130	38	189 (137 to 259)	1.47 (1.03 to 2.10)[e]		1.50 (1.05 to 2.15)[e]	
Villous	190 (1.3)	1906	2	105 (26 to 420)	1.47 (1.03 to 2.10)[e]		1.50 (1.05 to 2.15)[e]	
Unknown	960 (6.7)	9849	17	173 (107 to 278)	1.39 (0.84 to 2.30)		1.52 (0.92 to 2.52)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.38		0.40
Low grade	13,242 (92.0)	125,812	168	134 (115 to 155)	1		1	
High grade	357 (2.5)	3469	8	231 (115 to 461)	1.72 (0.85 to 3.49)		1.69 (0.82 to 3.48)	
Unknown	802 (5.6)	9623	13	135 (78 to 233)	0.99 (0.56 to 1.74)		0.94 (0.53 to 1.69)	
Proximal polyps						0.0019		0.0013
No	8133 (56.5)	80,118	88	110 (89 to 135)	1		1	
Yes	6268 (43.5)	58,785	101	172 (141 to 209)	1.57 (1.18 to 2.09)		1.62 (1.21 to 2.17)	
Hyperplastic polyps						0.24		0.12
No	11,535 (80.1)	110,804	144	130 (110 to 153)	1		1	
Yes	2866 (19.9)	28,099	45	160 (120 to 214)	1.23 (0.88 to 1.72)		1.31 (0.94 to 1.85)	
Hyperplastic polyp $\geq$ 10 mm in size						0.82		0.84
No	14,263 (99.0)	137,656	187	136 (118 to 157)	1		1	
Yes	138 (1.0)	1247	2	160 (40 to 641)	1.18 (0.29 to 4.75)		1.16 (0.29 to 4.67)	
Family history of cancer/CRC[f]						0.13		0.48
No	12,936 (89.8)	121,702	172	141 (122 to 164)	1		1	
Yes	1465 (10.2)	17,201	17	99 (61 to 159)	0.69 (0.42 to 1.14)		1.21 (0.72 to 2.03)	

a *p*-values were calculated with the LRT.
b The multivariable model contained number of surveillance visits, age, completeness of colonoscopy, adenoma histology and proximal polyps. The variables that were selected for inclusion in the final multivariable model for low-risk patients in the main analysis as presented in *Table 4*. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e For the adenoma histology variable the HRs for the tubulovillous and villous categories are for these two categories combined.
f Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 35 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	11,852 (100.0)	111,270	217					
Number of surveillance visits[c]						0.0053		0.0113
Zero	4683 (39.5)	53,927	111	206 (171 to 248)	1		1	
One	3343 (28.2)	33,284	59	177 (137 to 229)	0.64 (0.46 to 0.89)		0.65 (0.47 to 0.91)	
Two	2279 (19.2)	15,477	29	187 (130 to 270)	0.55 (0.36 to 0.86)		0.59 (0.38 to 0.92)	
Three or more	1547 (13.1)	8582	18	210 (132 to 333)	0.49 (0.28 to 0.84)		0.48 (0.27 to 0.84)	
Sex						0.0948		0.0215
Women	5271 (44.5)	51,049	88	172 (140 to 212)	1		1	
Men	6581 (55.5)	60,221	129	214 (180 to 255)	1.26 (0.96 to 1.65)		1.38 (1.05 to 1.82)	
Age (years)						< 0.0001		< 0.0001
< 55	2097 (17.7)	24,995	27	108 (74 to 158)	1		1	
55–64	3158 (26.6)	33,530	47	140 (105 to 187)	1.36 (0.85 to 2.19)		1.33 (0.83 to 2.14)	
65–74	3915 (33.0)	35,391	89	251 (204 to 310)	2.64 (1.71 to 4.08)		2.55 (1.65 to 3.95)	
≥ 75	2682 (22.6)	17,354	54	311 (238 to 406)	3.67 (2.29 to 5.88)		3.20 (1.98 to 5.18)	
Year of baseline visit						0.0332		0.0676
1984–99	1870 (15.8)	25,329	73	288 (229 to 363)	1		1	
2000–4	4222 (35.6)	42,957	82	191 (154 to 237)	0.69 (0.50 to 0.97)		0.68 (0.48 to 0.96)	
2005–10	5760 (48.6)	42,983	62	144 (112 to 185)	0.62 (0.42 to 0.90)		0.67 (0.44 to 1.00)	
Length of baseline visit						0.14		0.0547
1 day	6697 (56.5)	63,453	108	170 (141 to 206)	1		1	
2 days to 3 months	2343 (19.8)	21,669	50	231 (175 to 304)	1.38 (0.99 to 1.94)		1.52 (1.08 to 2.14)	
3–6 months	1403 (11.8)	13,277	28	211 (146 to 305)	1.25 (0.83 to 1.90)		1.30 (0.85 to 1.98)	
≥ 6 months	1409 (11.9)	12,871	31	241 (169 to 342)	1.43 (0.96 to 2.13)		1.50 (1.00 to 2.25)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Colonoscopy completeness						0.0014		0.0024
Complete	8967 (75.7)	80,572	131	163 (137 to 193)	1		1	
Incomplete	1321 (11.2)	11,545	44	381 (284 to 512)	1.58 (1.20 to 2.09)[d]		1.59 (1.18 to 2.15)[d]	
Unknown	1564 (13.2)	19,152	42	219 (162 to 297)	1.58 (1.20 to 2.09)[d]		1.59 (1.18 to 2.15)[d]	
Bowel preparation quality						0.14		0.18
Excellent or good	3974 (33.5)	37,493	65	173 (136 to 221)	1		1	
Satisfactory	1903 (16.1)	15,451	30	194 (136 to 278)	1.19 (0.77 to 1.84)		1.36 (0.88 to 2.12)	
Poor	660 (5.6)	4840	16	331 (203 to 540)	1.99 (1.15 to 3.45)		1.77 (1.02 to 3.07)	
Unknown	5315 (44.8)	53,485	106	198 (164 to 240)	1.10 (0.81 to 1.50)		1.09 (0.79 to 1.49)	
Number of adenomas						0.67		0.36
One	7793 (65.8)	74,791	147	197 (167 to 231)	1		1	
Two	3053 (25.8)	27,502	56	204 (157 to 265)	1.07 (0.78 to 1.45)		0.93 (0.67 to 1.29)	
Three or four	1006 (8.5)	8977	14	156 (92 to 263)	0.82 (0.48 to 1.42)		0.67 (0.38 to 1.19)	
Adenoma size (mm)						0.22		0.28
< 10	1006 (8.5)	8977	14	156 (92 to 263)	1		1	
10–19	6802 (57.4)	64,716	118	182 (152 to 218)	1.14 (0.65 to 1.98)		1.39 (0.79 to 2.46)	
≥ 20	4044 (34.1)	37,577	85	226 (183 to 280)	1.41 (0.80 to 2.49)		1.57 (0.87 to 2.85)	
Adenoma histology						0.0003		0.0300
Tubular	4694 (39.6)	44,369	69	156 (123 to 197)	1		1	
Tubulovillous	5537 (46.7)	51,211	99	193 (159 to 235)	1.26 (0.92 to 1.71)		1.18 (0.86 to 1.61)	
Villous	1134 (9.6)	10,108	22	218 (143 to 331)	1.42 (0.88 to 2.29)		1.11 (0.67 to 1.83)	
Unknown	487 (4.1)	5581	27	484 (332 to 705)	2.92 (1.86 to 4.58)		2.38 (1.37 to 4.12)	

continued

TABLE 35 Long-term CRC incidence after baseline among intermediate-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.0017		0.0134
Low grade	9399 (79.3)	87,581	150	171 (146 to 201)	1		1	
High grade	1979 (16.7)	17,402	41	236 (173 to 320)	1.39 (0.98 to 1.96)		1.28 (0.90 to 1.82)	
Unknown	474 (4.0)	6287	26	414 (282 to 607)	2.18 (1.42 to 3.33)		1.94 (1.25 to 3.02)	
Proximal polyps						0.0161		0.0023
No	8254 (69.6)	79,798	141	177 (150 to 208)	1		1	
Yes	3598 (30.4)	31,471	76	241 (193 to 302)	1.42 (1.07 to 1.88)		1.58 (1.19 to 2.12)	
Hyperplastic polyps						0.75		0.56
No	9793 (82.6)	91,902	178	194 (167 to 224)	1		1	
Yes	2059 (17.4)	19,367	39	201 (147 to 276)	1.06 (0.75 to 1.50)		1.11 (0.78 to 1.59)	
Hyperplastic polyp ≥ 10 mm in size						0.81		0.84
No	11,668 (98.4)	109,499	214	195 (171 to 223)	1		1	
Yes	184 (1.6)	1771	3	169 (55 to 525)	0.87 (0.28 to 2.73)		0.89 (0.28 to 2.79)	
Family history of cancer/CRC[e]						0.33		0.94
No	11,366 (95.9)	105,842	209	197 (172 to 226)	1		1	
Yes	486 (4.1)	5428	8	147 (74 to 295)	0.72 (0.35 to 1.46)		1.03 (0.50 to 2.11)	

a *p*-values were calculated with the LRT.
b The multivariable model included number of surveillance visits, age, year of baseline visit, length of baseline visit, completeness of colonoscopy, adenoma dysplasia and proximal polyps. The variables that were selected for inclusion in the final multivariable model for intermediate-risk patients in the main analysis as presented in *Table 5*. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 36 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Total	2719 (100.0)	22,961	77	335 (268 to 419)				
Number of surveillance visits[c]						0.0006		0.0003
Zero	911 (33.5)	9243	40	433 (317 to 590)	1		1	
One	695 (25.6)	7144	23	322 (214 to 484)	0.49 (0.29 to 0.83)		0.48 (0.28 to 0.81)	
Two	593 (21.8)	4018	8	199 (100 to 398)	0.26 (0.12 to 0.57)		0.24 (0.11 to 0.53)	
Three or more	520 (19.1)	2555	6	235 (105 to 523)	0.30 (0.12 to 0.77)		0.28 (0.11 to 0.72)	
Sex						0.56		0.85
Women	799 (29.4)	6997	26	372 (253 to 546)	1		1	
Men	1920 (70.6)	15,963	51	319 (243 to 420)	0.87 (0.54 to 1.39)		0.95 (0.59 to 1.53)	
Age (years)						0.012		0.0844
< 55	283 (10.4)	3191	5	157 (65 to 376)	1		1	
55–64	750 (27.6)	7082	19	268 (171 to 421)	1.76 (0.65 to 4.70)		1.94 (0.72 to 5.23)	
65–74	1065 (39.2)	8735	31	355 (250 to 505)	2.37 (0.92 to 6.12)		2.41 (0.93 to 6.22)	
≥ 75	621 (22.8)	3953	22	557 (366 to 845)	3.87 (1.46 to 10.29)		3.08 (1.15 to 8.20)	
Year of baseline visit						0.38		0.31
1984–99	329 (12.1)	3948	9	228 (119 to 438)	1		1	
2000–4	874 (32.1)	8250	30	364 (254 to 520)	1.63 (0.75 to 3.56)		1.66 (0.75 to 3.68)	
2005–10	1516 (55.8)	10,762	38	353 (257 to 485)	1.66 (0.75 to 3.68)		1.85 (0.80 to 4.24)	
Length of baseline visit						0.76		0.98
1 day	1184 (43.5)	10,106	30	297 (208 to 425)	1		1	
2 days to 3 months	562 (20.7)	4556	17	373 (232 to 600)	1.25 (0.69 to 2.27)		1.06 (0.58 to 1.93)	
3–6 months	442 (16.3)	3738	12	321 (182 to 565)	1.08 (0.55 to 2.10)		0.99 (0.50 to 1.95)	
≥ 6 months	531 (19.5)	4561	18	395 (249 to 626)	1.34 (0.75 to 2.40)		1.13 (0.61 to 2.07)	

continued

TABLE 36 Long-term CRC incidence after baseline among high-risk patients by number of surveillance visits and baseline characteristics, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion (*continued*)

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Colonoscopy completeness						0.0984		0.0730
Complete	2354 (86.6)	19,266	59	306 (237 to 395)	1		1	
Incomplete	123 (4.5)	1009	6	595 (267 to 1324)	1.60 (0.94 to 2.72)[d]		1.67 (0.98 to 2.86)[d]	
Unknown	242 (8.9)	2686	12	447 (254 to 787)	1.60 (0.94 to 2.72)[d]		1.67 (0.98 to 2.86)[d]	
Bowel preparation quality						0.80		0.82
Excellent or good	1119 (41.2)	9788	32	327 (231 to 462)	1		1	
Satisfactory	411 (15.1)	3106	11	354 (196 to 640)	1.09 (0.55 to 2.17)		1.02 (0.51 to 2.04)	
Poor	143 (5.3)	980	5	510 (212 to 1226)	1.61 (0.63 to 4.13)		1.54 (0.60 to 3.98)	
Unknown	1046 (38.5)	9086	29	319 (222 to 459)	0.98 (0.59 to 1.61)		0.94 (0.57 to 1.56)	
Number of adenomas						0.53		0.37
Three	1227 (45.1)	10,577	33	312 (222 to 439)	1		1	
Four	557 (20.5)	4704	13	276 (160 to 476)	0.89 (0.47 to 1.69)		0.94 (0.49 to 1.79)	
Five	454 (16.7)	3697	17	460 (286 to 740)	1.47 (0.82 to 2.64)		1.58 (0.88 to 2.85)	
Six or more	481 (17.7)	3983	14	351 (208 to 593)	1.14 (0.61 to 2.12)		1.36 (0.72 to 2.56)	
Adenoma size (mm)						0.44		0.83
< 10	264 (9.7)	2374	5	211 (88 to 506)	1		1	
10–19	1344 (49.4)	11,361	35	308 (221 to 429)	1.46 (0.57 to 3.74)		1.25 (0.49 to 3.20)	
≥ 20	1084 (39.9)	8951	36	402 (290 to 558)	1.92 (0.75 to 4.89)		1.48 (0.57 to 3.86)	
Unknown	27 (1.0)	275	1	364 (51 to 2585)	1.68 (0.20 to 14.38)		1.45 (0.17 to 12.65)	
Adenoma histology						0.60		0.84
Tubular	1038 (38.2)	8994	30	334 (233 to 477)	1		1	
Tubulovillous	1293 (47.6)	10,701	34	318 (227 to 445)	0.97 (0.59 to 1.58)		0.87 (0.53 to 1.44)	
Villous	328 (12.1)	2648	12	453 (257 to 798)	1.38 (0.70 to 2.69)		1.07 (0.54 to 2.14)	
Unknown	60 (2.2)	619	1	162 (23 to 1147)	0.47 (0.06 to 3.49)		0.55 (0.07 to 4.15)	

Variable	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Unadjusted HR (95% CI)	*p*-value[a]	Multivariable adjusted HR (95% CI)[b]	*p*-value[a]
Adenoma dysplasia						0.0058		0.0020
Low grade	2035 (74.8)	17,109	47	275 (206 to 366)	1		1	
High grade	616 (22.7)	5080	29	571 (397 to 821)	2.09 (1.31 to 3.31)		2.21 (1.39 to 3.51)	
Unknown	68 (2.5)	772	1	130 (18 to 919)	0.47 (0.07 to 3.44)		0.38 (0.05 to 2.78)	
Proximal polyps						0.99		0.45
No	663 (24.4)	5934	20	337 (217 to 522)	1		1	
Yes	2056 (75.6)	17,027	57	335 (258 to 434)	1.00 (0.60 to 1.67)		1.22 (0.72 to 2.08)	
Hyperplastic polyps						0.25		0.13
No	1929 (70.9)	16,037	49	306 (231 to 404)	1		1	
Yes	790 (29.1)	6923	28	404 (279 to 586)	1.32 (0.83 to 2.10)		1.44 (0.90 to 2.30)	
Hyperplastic polyp ≥ 10 mm in size						0.95		0.82
No	2650 (97.5)	22,388	75	335 (267 to 420)	1		1	
Yes	69 (2.5)	573	2	349 (87 to 1395)	1.04 (0.26 to 4.25)		1.18 (0.29 to 4.82)	
Family history of cancer/CRC[e]								
No	2621 (96.4)	21,902	83	379 (306 to 470)				
Yes	98 (3.6)	1059	0	0				

a *p*-values were calculated with the LRT.
b The multivariable model included number of surveillance visits, completeness of colonoscopy and adenoma dysplasia. The variables that were selected for inclusion in the final multivariable model for high-risk patients in the main analysis as presented in *Table 6*. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
c The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
d For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
e Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.

TABLE 37 Detection rate of AAs and CRC at first surveillance by interval length and risk subgroup, excluding all CRCs deemed likely to have arisen from an incompletely resected baseline lesion

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Low-risk group																
< 18 months	326	14.0	9	2.8	803	17.4	56	7.0	328	13.9	2	0.6	814	17.3	11	1.4
2 years[c]	369	15.9	13	3.5	726	15.7	50	6.9	372	15.8	3	0.8	743	15.8	17	2.3
3 years[c]	588	25.3	28	4.8	1284	27.8	85	6.6	590	25.1	2	0.3	1303	27.7	19	1.5
4 years[c]	309	13.3	22	7.1	616	13.3	53	8.6	313	13.3	4	1.3	627	13.3	11	1.8
5 years[c]	430	18.5	28	6.5	667	14.4	68	10.2	435	18.5	5	1.1	675	14.3	8	1.2
6 years[c]	162	7.0	17	10.5	279	6.0	20	7.2	165	7.0	3	1.8	283	6.0	4	1.4
7 years[c]	86	3.7	8	9.3	143	3.1	21	14.7	86	3.7	0	0.0	150	3.2	7	4.7
8 years[c]	57	2.4	4	7.0	104	2.3	14	13.5	65	2.8	8	12.3	113	2.4	9	8.0
Total	2327	100	129	5.5	4622	100	367	7.9	2354	100	27	1.1	4708	100	86	1.8
p-value[d]			< 0.0001				0.0002				< 0.0001				0.0072	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.35 (1.08 to 1.69); 0.0077								1.60 (1.04 to 2.48); 0.0273							
Intermediate-risk group																
< 18 months	642	24.0	35	5.5	1311	31.0	118	9.0	645	23.9	3	0.5	1330	30.9	19	1.4
2 years[c]	401	14.9	24	6.0	819	19.3	83	10.1	407	15.1	6	1.5	827	19.2	8	1.0
3 years[c]	1024	38.2	68	6.6	1195	28.2	136	11.4	1029	38.1	5	0.5	1203	28.0	8	0.7
4 years[c]	255	9.5	29	11.4	428	10.1	43	10.0	256	9.5	1	0.4	442	10.3	14	3.2
5 years[c]	244	9.1	20	8.2	313	7.4	55	17.6	247	9.1	3	1.2	320	7.4	7	2.2

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
6 years[c]	117	4.4	15	12.8	169	4.0	23	13.6	118	4.4	1	0.8	176	4.1	7	4.0
Total	2683	100	191	7.1	4235	100	458	10.8	2702	100	19	0.7	4298	100	63	1.5
p-value[d]			0.0007				0.0002				0.72				0.0063	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.58 (1.33 to 1.89); < 0.0001								2.10 (1.25 to 3.52); 0.0028							
High-risk group																
< 15 months	516	47.6	76	14.7	222	40.8	34	15.3	516	47.4	0	0	226	40.6	4	1.8
1.5 years[f]	161	14.9	23	14.3	127	23.3	13	10.2	161	14.8	0	0	127	22.8	0	0
2 years[f]	104	9.6	11	10.6	66	12.2	8	12.1	107	9.8	3	2.8	69	12.4	3	4.3
2.5 years[f]	47	4.3	9	19.1	38	7.0	8	21.1	48	4.4	1	2.1	39	7.0	1	2.6
3 years[f]	184	17.0	35	19.0	62	11.4	10	16.1	185	17.0	1	0.5	65	11.7	3	4.6
3.5 years[f]	71	6.6	9	12.7	29	5.3	5	17.2	72	6.6	1	1.4	31	5.6	2	6.5
Total	1083	100	163	15.1	544	100	78	14.3	1089	100	6	0.6	557	100	13	2.3
p-value[d]			0.44				0.53				0.035				0.030	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	0.94 (0.71 to 1.27); 0.70								4.31 (1.63 to 11.41); 0.0020							

a Patients with CRC detected at first surveillance were excluded from the analyses of AA detection rates.
b In the low-risk group, the higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. In the intermediate-risk group, the higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, an adenoma with high-grade dysplasia or proximal polyps at baseline. In the high-risk group, the higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, or an adenoma with high-grade dysplasia at baseline. In all risk groups, the patients who did not have any of the previously stated factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.
f Interval ± 3 months.

TABLE 38 Incidence of CRC after baseline by number of surveillance visits among intermediate-risk patients, with poor bowel preparation and adenomas ≥ 20 mm in size additionally included in the definition of the higher-risk subgroup

Visits	Number of patients (%)	Number of person-years	Number of CRCs	Incidence rate per 100,000 person-years (95% CI)	Comparison of incidence in the presence and absence of surveillance[a]	
					Unadjusted HR (95% CI)	*p*-value[b]
Whole intermediate-risk group						0.0001
Zero	4683 (39.5)	53,927	135	250 (211 to 296)	1	
One	3343 (28.2)	33,284	62	186 (145 to 239)	0.58 (0.42 to 0.79)	
Two or more	3826 (32.3)	24,059	49	204 (154 to 269)	0.50 (0.34 to 0.73)	
Total	11,852 (100)	111,270	246	221 (195 to 251)		
Higher-risk subgroup[c]						0.0001
Zero	3387 (38.6)	38,286	117	306 (255 to 366)	1	
One	2446 (27.9)	24,957	54	216 (166 to 283)	0.54 (0.39 to 0.76)	
Two or more	2948 (33.6)	19,167	45	235 (175 to 314)	0.48 (0.32 to 0.71)	
Total	8781 (74.1)	82,411	216	262 (229 to 299)		
Lower-risk subgroup[c]						0.22
Zero	1296 (42.2)	15,641	18	115 (73 to 183)	1	
One	897 (29.2)	8327	8	96 (48 to 192)	0.66 (0.28 to 1.60)	
Two or more	878 (28.6)	4892	4	82 (31 to 218)	0.37 (0.11 to 1.21)	
Total	3071 (25.9)	28,859	30	104 (73 to 149)		

a The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
b *p*-values were calculated with the LRT.
c The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, poor bowel preparation, an adenoma ≥ 20 mm in size or with high-grade dysplasia, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.

TABLE 39 Cumulative incidence of CRC at 3, 5 and 10 years and age- and sex-SIRs among intermediate-risk patients, with poor bowel preparation and adenomas ≥ 20 mm in size additionally included in the definition of the higher-risk subgroup

Risk group/ subgroup	Number of patients (%)	Number of person-years	3 years		5 years		10 years		*p*-value[a]	Number of observed CRCs[b]	Number of expected CRCs[c]	SIR (95% CI)
			Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)	Number of CRCs	Cumulative incidence, % (95% CI)				
After baseline, with no surveillance[d]									< 0.0001			
Whole intermediate-risk group	11,852 (100.0)	53,927	57	0.6 (0.5 to 0.8)	88	1.3 (1.0 to 1.6)	121	2.6 (2.1 to 3.3)		135	117	1.16 (0.97 to 1.37)
Higher-risk subgroup[e]	8781 (74.1)	38,286	49	0.7 (0.6 to 1.0)	78	1.6 (1.3 to 2.1)	107	3.3 (2.6 to 4.2)		117	85	1.37 (1.13 to 1.64)
Lower-risk subgroup[e]	3071 (25.9)	15,641	8	0.3 (0.2 to 0.7)	10	0.5 (0.2 to 0.9)	14	1.0 (0.5 to 2.0)		18	31	0.58 (0.34 to 0.91)
After first surveillance, with one surveillance visit[f]									0.0296			
Whole intermediate-risk group	7169 (100.0)	33,284	17	0.3 (0.2 to 0.5)	34	0.8 (0.6 to 1.2)	57	2.6 (1.9 to 3.6)		62	73	0.85 (0.65 to 1.08)
Higher-risk subgroup[e]	5394 (75.2)	24,957	15	0.3 (0.2 to 0.6)	30	1.0 (0.7 to 1.4)	50	3.1 (2.2 to 4.4)		54	56	0.96 (0.72 to 1.25)
Lower-risk subgroup[e]	1775 (24.8)	8327	2	0.1 (0.03 to 0.5)	4	0.4 (0.1 to 1.0)	7	1.1 (0.5 to 2.6)		8	17	0.47 (0.20 to 0.93)
After second surveillance, with two or more surveillance visits[g]									0.0477			
Whole intermediate-risk group	3826 (100.0)	24,059	10	0.3 (0.2 to 0.6)	19	0.7 (0.4 to 1.1)	36	2.0 (1.4 to 2.9)		49	56	0.87 (0.65 to 1.16)
Higher-risk subgroup[e]	2948 (77.1)	19,167	9	0.3 (0.2 to 0.7)	17	0.8 (0.5 to 1.2)	32	2.2 (1.5 to 3.2)		45	45	1.00 (0.73 to 1.34)
Lower-risk subgroup[e]	878 (22.9)	4892	1	0.2 (0.02 to 1.2)	2	0.4 (0.1 to 1.4)	4	1.3 (0.4 to 3.9)		4	11	0.36 (0.10 to 0.93)

a *p*-values were calculated with the log-rank test to compare cumulative incidence curves of the higher- and lower-risk subgroups.
b Total number of observed CRCs at end of follow-up.
c The numbers of expected CRCs were calculated by multiplying the sex- and 5-year age group-specific observed person-years by the corresponding sex- and age-specific incidence rates in the general population of England in 2007.
d Data were censored at first surveillance visit.
e The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, poor bowel preparation, an adenoma ≥ 20 mm or with high-grade dysplasia, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
f Data were censored at second surveillance visit.
g Data were censored at end of follow-up.

TABLE 40 Detection rate of AAs and CRC at first surveillance among intermediate-risk patients by interval length and risk subgroup, with poor bowel preparation and adenomas ≥ 20 mm in size additionally included in the definition of the higher-risk subgroup

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
< 18 months	353	21.1	22	6.2	1600	30.5	131	8.2	354	21.0	1	0.3	1621	30.5	21	1.3
2 years[c]	224	13.4	14	6.2	996	19.0	93	9.3	227	13.5	3	1.3	1007	18.9	11	1.1
3 years[c]	684	40.8	37	5.4	1535	29.3	167	10.9	687	40.8	3	0.4	1545	29.1	10	0.6
4 years[c]	162	9.7	18	11.1	521	9.9	54	10.4	163	9.7	1	0.6	535	10.1	14	2.6
5 years[c]	178	10.6	16	9.0	379	7.2	59	15.6	179	10.6	1	0.6	388	7.3	9	2.3
6 years[c]	74	4.4	7	9.5	212	4.0	31	14.6	75	4.5	1	1.3	219	4.1	7	3.2
Total	1675	100	114	6.8	5243	100	535	10.2	1685	100	10	0.6	5315	100	72	1.4
p-value[d]			0.067				< 0.0001				0.62				0.0093	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.56 (1.26 to 1.92); < 0.0001								2.30 (1.18 to 4.47); 0.0065							

a Patients with CRC detected at first surveillance were excluded from the analyses of AA detection rates.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, poor bowel preparation, an adenoma ≥ 20 mm in size or with high-grade dysplasia, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.

TABLE 41 Detection rate of AAs and CRC at first surveillance among low-risk patients by interval length and risk subgroup with a maximum interval length of 6.5 years

Interval length to first surveillance	AAs[a]								CRC							
	Lower-risk subgroup[b]				Higher-risk subgroup[b]				Lower-risk subgroup[b]				Higher-risk subgroup[b]			
	Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate		Patients attending one or more surveillance visits		Detection rate	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
< 18 months	326	14.9	9	2.8	802	18.3	56	7.0	328	14.9	2	0.6	814	18.3	12	1.5
2 years[c]	369	16.9	13	3.5	725	16.7	50	6.9	372	16.9	3	0.8	743	16.7	18	2.4
3 years[c]	588	26.9	28	4.8	1282	29.3	85	6.6	590	26.8	2	0.3	1303	29.3	21	1.6
4 years[c]	309	14.1	22	7.1	616	14.1	53	8.6	313	14.2	4	1.3	627	14.1	11	1.8
5 years[c]	430	19.7	28	6.5	667	15.3	68	10.2	435	19.7	5	1.1	675	15.2	8	1.2
6 years[c]	162	7.4	17	10.5	279	6.4	20	7.2	165	7.5	3	1.8	283	6.4	4	1.4
Total	2184	100	117	5.4	4371	100	332	7.6	2203	100	19	0.9	4445	100	74	1.7
p-value[d]			< 0.0001				0.045				0.11				0.40	
OR (95% CI) for higher vs. lower risk; *p*-value[e]	1.45 (1.17 to 1.80); 0.0006								1.95 (1.17 to 3.23); 0.0063							

a Patients with CRC detected at first surveillance were excluded from the analyses of AA detection rates.
b The higher-risk subgroup comprised patients who had an incomplete colonoscopy or colonoscopy of unknown completeness, a tubulovillous or villous adenoma, or proximal polyps at baseline. Patients who did not have any of these factors were assigned to the lower-risk subgroup.
c Interval ± 6 months.
d *p*-values were from a test for trend.
e *p*-values were calculated with the LRT.

TABLE 42 Long-term CRC incidence after baseline by number of surveillance visits and baseline characteristics, with hospital included in the multivariable models

Variable	Risk group: Low risk — Multivariable adjusted HR (95% CI)[a]	*p*-value[b]	Intermediate risk — Multivariable adjusted HR (95% CI)[c]	*p*-value[b]	High risk — Multivariable adjusted HR (95% CI)[d]	*p*-value[b]
Number of surveillance visits[e]		< 0.0001		0.0003		0.0002
Zero	1		1		1	
One	0.54 (0.38 to 0.78)		0.57 (0.41 to 0.78)		0.46 (0.27 to 0.77)	
Two	0.26 (0.12 to 0.54)		0.53 (0.35 to 0.82)		0.25 (0.12 to 0.53)	
Three or more	0.18 (0.05 to 0.59)		0.41 (0.24 to 0.72)		0.25 (0.10 to 0.64)	
Sex		0.97		0.058		0.58
Women	1		1		1	
Men	0.99 (0.75 to 1.32)		1.28 (0.99 to 1.66)		0.88 (0.56 to 1.38)	
Age (years)		< 0.0001		< 0.0001		0.071
< 55	1		1		1	
55–64	2.01 (1.20 to 3.38)		1.41 (0.89 to 2.23)		1.78 (0.71 to 4.48)	
65–74	3.44 (2.12 to 5.60)		2.61 (1.70 to 4.00)		2.27 (0.94 to 5.46)	
≥ 75	4.72 (2.82 to 7.90)		3.64 (2.30 to 5.76)		2.92 (1.18 to 7.23)	
Year of baseline visit		0.14		0.010		0.51
1984–99	1		1		1	
2000–4	0.80 (0.51 to 1.25)		0.63 (0.45 to 0.88)		1.50 (0.69 to 3.24)	
2005–10	0.62 (0.38 to 1.02)		0.56 (0.38 to 0.83)		1.56 (0.70 to 3.51)	
Length of baseline visit		0.83		0.018		0.92
1 day	1		1		1	
2 days to 3 months	1.03 (0.63 to 1.69)		1.62 (1.18 to 2.24)		0.93 (0.51 to 1.70)	
3–6 months	1.26 (0.74 to 2.13)		1.31 (0.88 to 1.95)		0.87 (0.44 to 1.72)	
≥ 6 months	0.87 (0.42 to 1.78)		1.49 (1.02 to 2.18)		1.10 (0.62 to 1.98)	
Colonoscopy completeness		0.0051		0.0006		0.0208
Complete	1		1		1	
Incomplete	1.67 (1.18 to 2.37)[f]		1.68 (1.25 to 2.26)[f]		1.95 (1.14 to 3.34)[f]	
Unknown	1.67 (1.18 to 2.37).[f] Hospital was constrained to be included in the model		1.68 (1.25 to 2.26)[f]		1.95 (1.14 to 3.34)[f]	

TABLE 42 Long-term CRC incidence after baseline by number of surveillance visits and baseline characteristics, with hospital included in the multivariable models (*continued*)

Variable	Risk group					
	Low risk		Intermediate risk		High risk	
	Multivariable adjusted HR (95% CI)[a]	*p*-value[b]	Multivariable adjusted HR (95% CI)[c]	*p*-value[b]	Multivariable adjusted HR (95% CI)[d]	*p*-value[b]
Bowel preparation quality		0.25		0.50		0.62
Excellent or good	1		1		1	
Satisfactory	0.67 (0.43 to 1.03)		1.17 (0.77 to 1.78)		1.04 (0.52 to 2.06)	
Poor	1.04 (0.59 to 1.82)		1.49 (0.86 to 2.56)		1.27 (0.49 to 3.33)	
Unknown	0.83 (0.52 to 1.32)		1.02 (0.67 to 1.54)		0.68 (0.33 to 1.40)	
Number of adenomas		0.65		0.49		0.30
One	1		1			
Two	1.09 (0.76 to 1.54)		0.95 (0.70 to 1.29)			
Three			0.71 (0.40 to 1.27)[g]		1	
Four			0.71 (0.40 to 1.27)[g]		0.83 (0.44 to 1.55)	
Five					1.54 (0.87 to 2.73)	
Six or more					1.29 (0.70 to 2.40)	
Adenoma size (mm)				0.29		0.56
< 10			1		1	
10–19			1.30 (0.74 to 2.32)		0.91 (0.37 to 2.20)	
≥ 20			1.52 (0.84 to 2.75)		1.28 (0.52 to 3.11)	
Unknown					1.27 (0.15 to 10.91)	
Adenoma histology		0.10		0.0021		0.28
Tubular	1		1		1	
Tubulovillous	1.45 (1.01 to 2.08)[h]		1.24 (0.91 to 1.69)		0.78 (0.47 to 1.30)	
Villous	1.45 (1.01 to 2.08)[h]		1.40 (0.89 to 2.20)		1.42 (0.75 to 2.68)	
Unknown	1.36 (0.81 to 2.31)		2.86 (1.70 to 4.82)		0.53 (0.07 to 4.04)	
Adenoma dysplasia		0.082		0.0001		0.0024
Low grade	1		1		1	
High grade	2.05 (1.10 to 3.84)		1.49 (1.09 to 2.05)		2.13 (1.36 to 3.33)	
Unknown	1.37 (0.73 to 2.54)		2.66 (1.66 to 4.27)		0.38 (0.05 to 2.81)	
Proximal polyps		0.0006		0.0003		0.36
No	1		1		1	
Yes	1.67 (1.25 to 2.24)		1.69 (1.28 to 2.23)		1.27 (0.75 to 2.13)	
Hyperplastic polyps		0.16		0.61		0.27
No	1		1		1	
Yes	1.28 (0.91 to 1.80)		1.10 (0.78 to 1.54)		1.30 (0.82 to 2.04)	

continued

TABLE 42 Long-term CRC incidence after baseline by number of surveillance visits and baseline characteristics, with hospital included in the multivariable models (*continued*)

	Risk group					
	Low risk		Intermediate risk		High risk	
Variable	Multivariable adjusted HR (95% CI)[a]	*p*-value[b]	Multivariable adjusted HR (95% CI)[c]	*p*-value[b]	Multivariable adjusted HR (95% CI)[d]	*p*-value[b]
Hyperplastic polyp ≥ 10 mm in size		0.94		0.67		0.85
No	1		1		1	
Yes	1.06 (0.26 to 4.27)		0.79 (0.25 to 2.48)		1.15 (0.28 to 4.69)	
Family history of cancer/CRC[i]		0.11		0.59		0.25
No	1		1		1	
Yes	1.55 (0.93 to 2.57)		1.21 (0.61 to 2.39)		0.37 (0.05 to 2.70)	
Hospital[j]		0.0058		0.0097		0.22

a The multivariable model for the low-risk group included number of surveillance visits, age, completeness of colonoscopy, adenoma histology, proximal polyps and hospital. The variables that were selected for inclusion in the final multivariable model for low-risk patients in the main analysis are presented in *Table 4* with the addition of hospital. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
b *p*-values were calculated with the LRT.
c The multivariable model for the intermediate-risk group included number of surveillance visits, age, year of baseline visit, length of baseline visit, completeness of colonoscopy, adenoma dysplasia, proximal polyps and hospital. The variables that were selected for inclusion in the final multivariable model for intermediate-risk patients in the main analysis as presented in *Table 5* with the addition of hospital. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
d The multivariable model for the high-risk group included number of surveillance visits, completeness of colonoscopy, adenoma dysplasia and hospital. The variables that were selected for inclusion in the final multivariable model for high-risk patients in the main analysis as presented in *Table 6* with the addition of hospital. For these variables the adjusted HRs are from the multivariable model. For the remaining variables the adjusted HRs are for when the variable was added as an additional variable to the stated multivariable model.
e The number of surveillance visits was included as a time-varying covariate, meaning that patients who had any surveillance contributed person-years to more than a single category of number of surveillance visits.
f For the colonoscopy completeness variable the HRs for the incomplete and unknown categories are for these two categories combined.
g For the intermediate-risk group, for the number of adenomas variable, the HRs for three and four adenomas categories are for these two categories combined.
h For the low-risk group, for the adenoma histology variable, the HRs for the tubulovillous and villous categories are for these two categories combined.
i Family history of cancer/CRC was defined as 'family history of cancer or CRC reported at an examination before or during visit'. Seventy-two per cent of cases reported to have a 'family history of cancer' came from a specialist hospital for colorectal diseases. We assumed that these cases had a family history of CRC.
j Results for hospitals are not presented.

Appendix 3 Supplementary tables and figures for the economic evaluation

TABLE 43 Costs in the low-risk group when using only complete CRC staging data

Costs	Risk subgroup			
	Lower risk		Higher risk	
	No visits ($n = 2804$)	Visits ($n = 2431$)	No visits ($n = 4403$)	Visits ($n = 4763$)
CRC cases, *n*				
Dukes' stage A	9	4	17	7
Dukes' stage B	4	2	22	7
Dukes' stage C	3	3	19	10
Dukes' stage D	3	0	14	3
Dukes' stage unknown	12	2	40	14
Total	31	11	112	41
Person-years	32,903	16,882	51,688	37,429
Incidence per 1000 person-years	0.94	0.65	2.17	1.10
Costs				
CRC costs (£), mean (SD)				
Dukes' stage A	4 (108)	4 (136)	20 (307)	6 (173)
Dukes' stage B	6 (214)	7 (206)	18 (360)	14 (326)
Dukes' stage C	4 (124)	0 (0)	11 (239)	3 (120)
Dukes' stage D	37 (407)	23 (371)	98 (707)	43 (509)
Total and discounted costs (£), mean (SD)				
Total CRC cost	13 (235)	6 (155)	16 (270)	8 (225)
Total surveillance cost	13 (235)	6 (155)	16 (270)	8 (225)
Total cost per patient	37 (407)	1064 (793)	98 (707)	1274 (1090)
Discounted total cost per patient	30 (328)	937 (717)	83 (607)	1130 (988)
Discounted total cost per 1000 person-years	2597 (8.88)	134,873 (89.38)	7029 (11.66)	143,805 (61.98)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	132,276 (127,853 to 136,700); < 0.001		136,775 (132,883 to 140,668); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.29 (−0.80 to 0.22); 0.262		−1.07 (−1.59 to −0.55); < 0.001	
Incremental cost per CRC prevented	455,184		127,660	

Notes
Costs are reported in GBP.
p-values are from the Wald test.

TABLE 44 Costs in the intermediate-risk group when using only complete CRC staging data

Costs	Risk subgroup			
	Lower risk		Higher risk	
	No visits ($n = 1932$)	Visits ($n = 2806$)	No visits ($n = 2751$)	Visits ($n = 4363$)
CRC cases, *n*				
Dukes' stage A	11	8	13	15
Dukes' stage B	4	5	24	16
Dukes' stage C	8	3	18	24
Dukes' stage D	3	5	9	7
Dukes' stage unknown	7	8	38	20
Total	33	29	102	82
Person-years	23,237	21,233	30,690	36,110
Incidence per 1000 person-years	1.42	1.37	3.32	2.27
Costs				
CRC costs (£), mean (SD)				
Dukes' stage A	21 (295)	11 (219)	19 (294)	11 (207)
Dukes' stage B	9 (193)	4 (112)	33 (380)	12 (229)
Dukes' stage C	28 (499)	6 (191)	36 (496)	29 (433)
Dukes' stage D	3 (109)	9 (279)	13 (309)	4 (124)
Total and discounted costs (£), mean (SD)				
Total CRC cost	73 (663)	42 (472)	143 (853)	77 (644)
Total surveillance cost	0 (0)	1187 (826)	0 (0)	1427 (1095)
Total cost per patient	73 (663)	1229 (993)	143 (853)	1504 (1312)
Discounted total cost per patient	61 (532)	1099 (886)	123 (743)	1354 (1186)
Discounted total cost per 1000 person-years	5039 (14.73)	145,207 (82.70)	10,994 (18.93)	163,604 (67.31)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	140,168 (135,276 to 145,059); < 0.001		152,610 (147,517 to 157,703); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.05 (−0.75 to 0.64); 0.878		−1.05 (−1.86 to −0.24); 0.011	
Incremental cost per CRC prevented	2,576,614		144,970	

SD, standard deviation.

Notes
Costs are reported in GBP.
p-values are from the Wald test.

TABLE 45 Costs in the high-risk group when using only complete CRC staging data

Costs	Risk subgroup			
	Lower risk		Higher risk	
	No visits ($n = 606$)	Visits ($n = 1211$)	No visits ($n = 305$)	Visits ($n = 597$)
CRC cases, *n*				
Dukes' stage A	5	3	4	2
Dukes' stage B	3	6	9	7
Dukes' stage C	1	4	4	3
Dukes' stage D	1	2	0	4
Dukes' stage unknown	7	6	10	3
Total	17	21	27	19
Person-years	6226	8805	3017	4913
Incidence per 1000 person-years	273	239	895	387
Costs				
CRC costs (£), mean (SD)				
Dukes' stage A	30 (346)	10 (196)	58 (519)	11 (209)
Dukes' stage B	15 (221)	20 (313)	102 (636)	46 (461)
Dukes' stage C	8 (192)	22 (477)	52 (478)	28 (446)
Dukes' stage D	11 (278)	8 (187)	0 (0)	36 (496)
Total and discounted costs (£), mean (SD)				
Total CRC cost	110 (705)	79 (696)	279 (1015)	144 (906)
Total surveillance cost	0 (0)	1565 (1087)	0 (0)	1682 (1248)
Total cost per patient	110 (705)	1643 (1361)	279 (1015)	1826 (1605)
Discounted total cost per patient	95 (611)	1505 (1262)	235 (870)	1668 (1453)
Discounted total cost per 1000 person-years	9232 (38.51)	207,013 (153.33)	23,783 (88.79)	202,672 (203.12)
Incremental costs (£)				
Incremental cost per 1000 person-years (95% CI); *p*-value	197,781 (186,656 to 208,905); < 0.001		178,889 (160,796 to 196,982); < 0.001	
Incremental CRC per 1000 person-years (95% CI); *p*-value	−0.35 (−1.99 to 1.30); 0.681		−5.08 (−8.84 to −1.32); 0.008	
Incremental cost per CRC prevented	599,342		35,196	

Notes
Costs are reported in GBP.
p-values are from the Wald test.

TABLE 46 Estimates of cost-effectiveness from our extrapolation model, using QoL scores from Whyte *et al.*[48,a]

	Risk subgroup			
	Lower risk		Higher risk	
Estimates of cost-effectiveness	No visits	Visits	No visits	Visits
Low-risk group				
Cost of surveillance (£)	0	897	0	1091
Total CRC cost (£)	125	110	312	220
Discounted total cost (£)	83	742	207	971
Life-years	23	23	22	23
Discounted QALYs	12	12	12	12
Incremental cost (£)	660		764	
Incremental QALYs	0.005		0.028	
ICER (£)	133,751		27,169	
Intermediate-risk group				
Cost of surveillance (£)	0	1281	0	1522
Total CRC cost (£)	188	200	448	371
Discounted total cost (£)	124	1098	298	1406
Life-years	23	23	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	974		1108	
Incremental QALYs	−0.008		0.024	
ICER (£)	Dominated[b]		45,417	
High-risk group				
Cost of surveillance (£)	0	2144	0	2000
Total CRC cost (£)	343	358	1077	694
Discounted total cost (£)	228	1877	726	2019
Life-years	22	22	22	22
Discounted QALYs	12	12	11	11
Incremental cost (£)	1649		1293	
Incremental QALYs	−0.015		0.148	
ICER (£)	Dominated[b]		8745	

a We assessed the impact of using different QoL estimates from Whyte *et al.*[48] on the results from our extrapolation model in a sensitivity analysis.
b More costly and less effective.

Note
Costs are reported in GBP.

TABLE 47 Estimates of cost-effectiveness from our extrapolation model, using a simplified model structure[a]

	Risk subgroup			
	Lower risk		Higher risk	
Estimates of cost-effectiveness	No visits	Visits	No visits	Visits
Low-risk group				
Cost of surveillance (£)	0	897	0	1092
Total CRC cost (£)	125	103	314	217
Discounted total cost (£)	83	739	208	970
Life-years	23	23	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	657		762	
Incremental QALYs	0.007		0.037	
ICER (£)	90,666		20,423	
Intermediate-risk group				
Cost of surveillance (£)	0	1281	0	1522
Total CRC cost (£)	179	200	452	368
Discounted total cost (£)	118	1098	301	1405
Life-years	23	23	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	979		1104	
Incremental QALYs	−0.009		0.034	
ICER (£)	Dominated[b]		32,112	
High-risk group				
Cost of surveillance (£)	0	2144	0	2000
Total CRC cost (£)	340	353	1077	694
Discounted total cost (£)	226	1875	726	2019
Life-years	22	22	22	22
Discounted QALYs	12	12	12	12
Incremental cost (£)	1649		1293	
Incremental QALYs	−0.005		0.165	
ICER (£)	Dominated[b]		7821	

a We assessed the sensitivity of the results from our extrapolation model to the use of imputed CRC staging data by using a simplified model structure, in which the four Dukes' stages were collapsed into a single CRC state.
b More costly and less effective.

Note
Costs are reported in GBP.

TABLE 48 Age-adjusted incremental cost-effectiveness estimates

Baseline risk subgroup	Age-adjusted[a] incremental cost (£) per 1000 person-years	Age-adjusted[a] incremental CRC per 1000 person-years	Age-adjusted[a] incremental cost (£) per CRC prevented	Unadjusted incremental cost (£) per CRC prevented
Low-risk group				
Lower-risk subgroup	133,197	−0.01	12,973,410	453,221
Higher-risk subgroup	138,598	−0.76	182,799	127,945
Intermediate-risk group				
Lower-risk subgroup	142,383	0.11	Dominated[b]	2,587,860
Higher-risk subgroup	156,564	−0.57	274,042	145,729
High-risk group				
Lower-risk subgroup	196,221	−0.15	1,286,287	568,719
Higher-risk subgroup	185,191	−3.93	47,153	36,636

a These estimates are for a patient at the mean age for each risk subgroup.
b More costly and less effective.

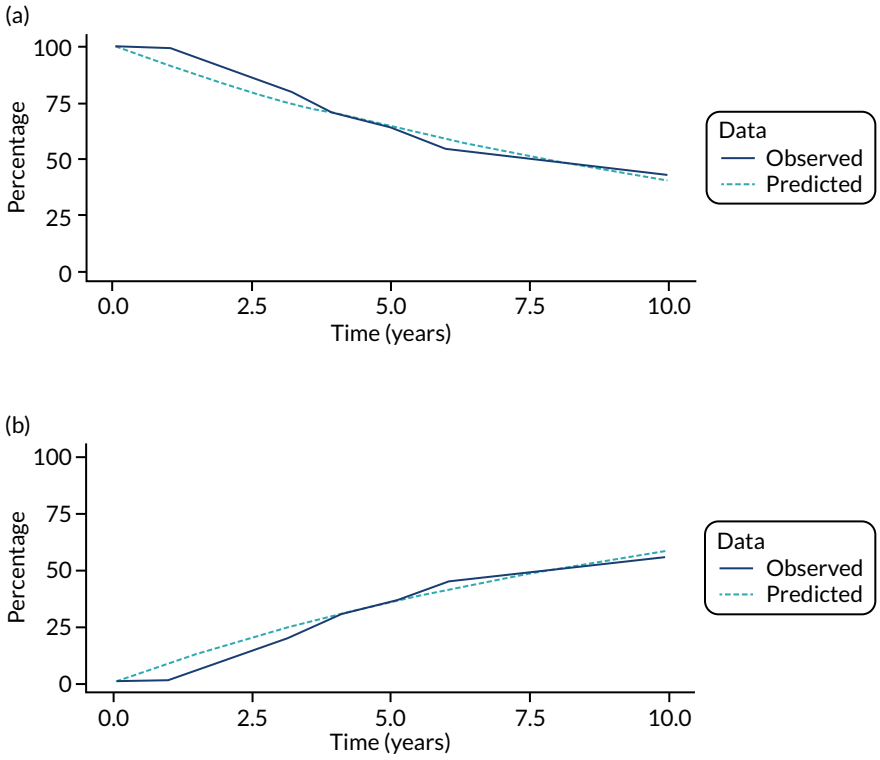

FIGURE 9 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the low-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state. (*continued*)

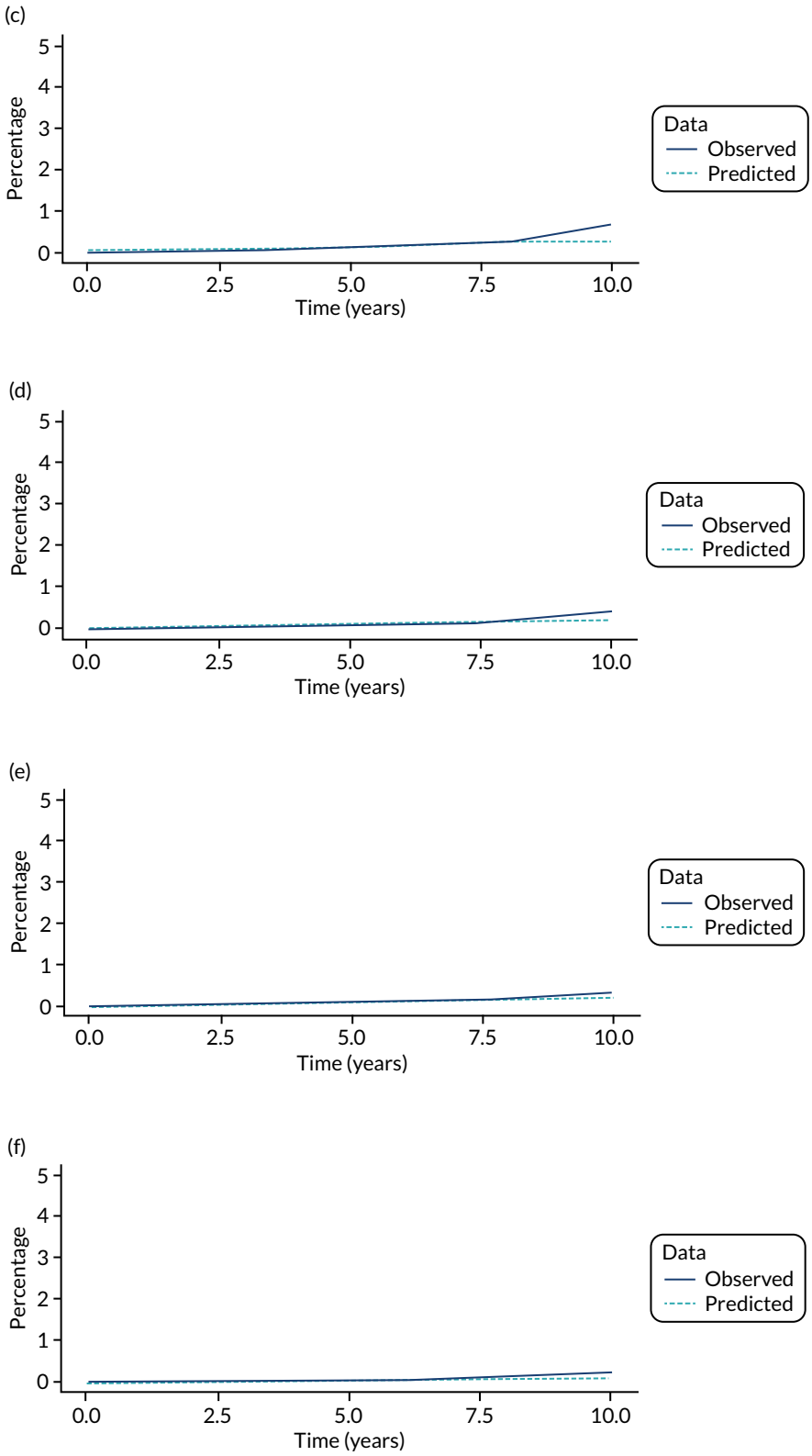

FIGURE 9 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the low-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state.

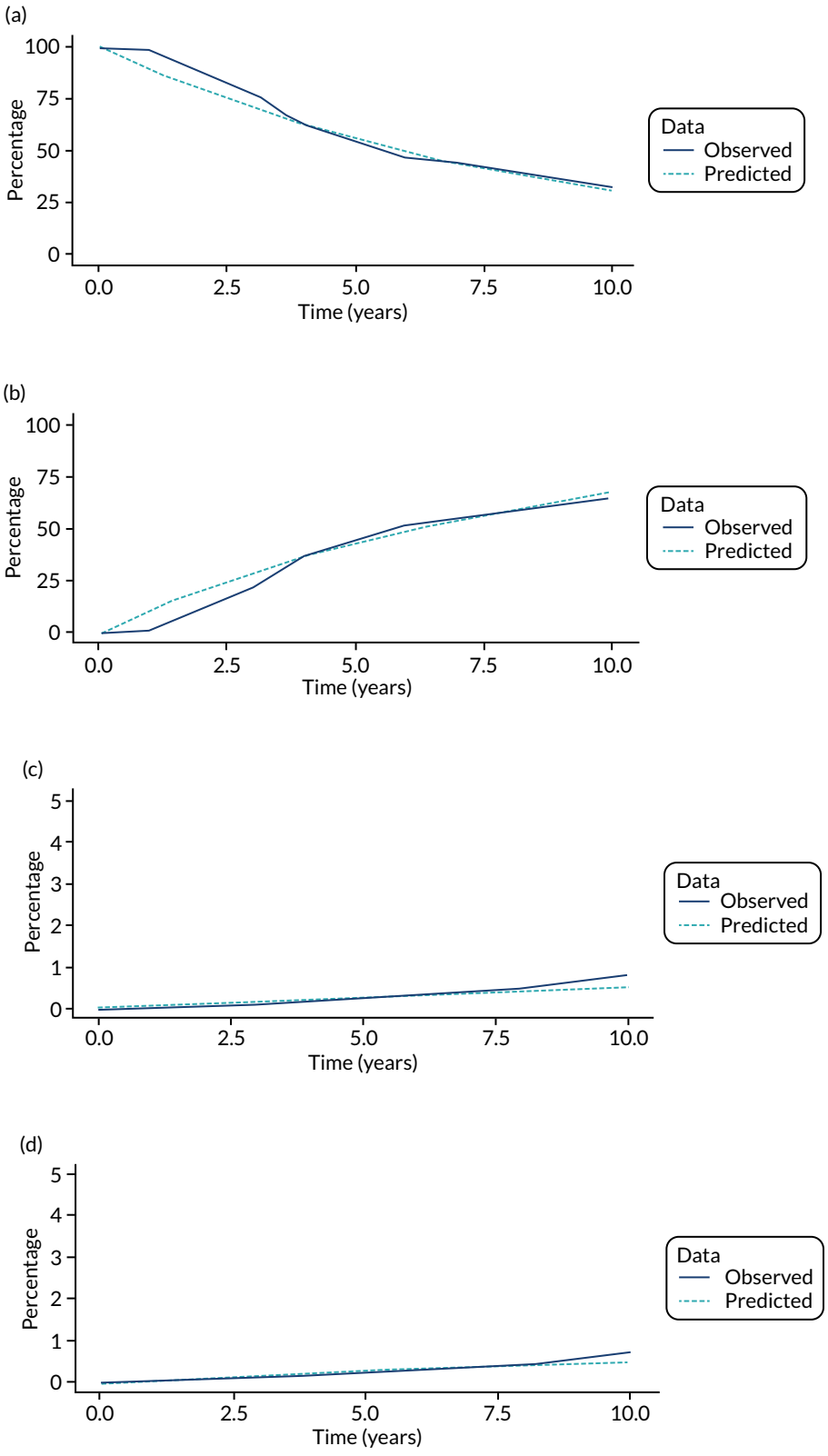

FIGURE 10 Comparison of model predictions with observed data from a single imputation for the higher-risk subgroup of the low-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state. (*continued*)

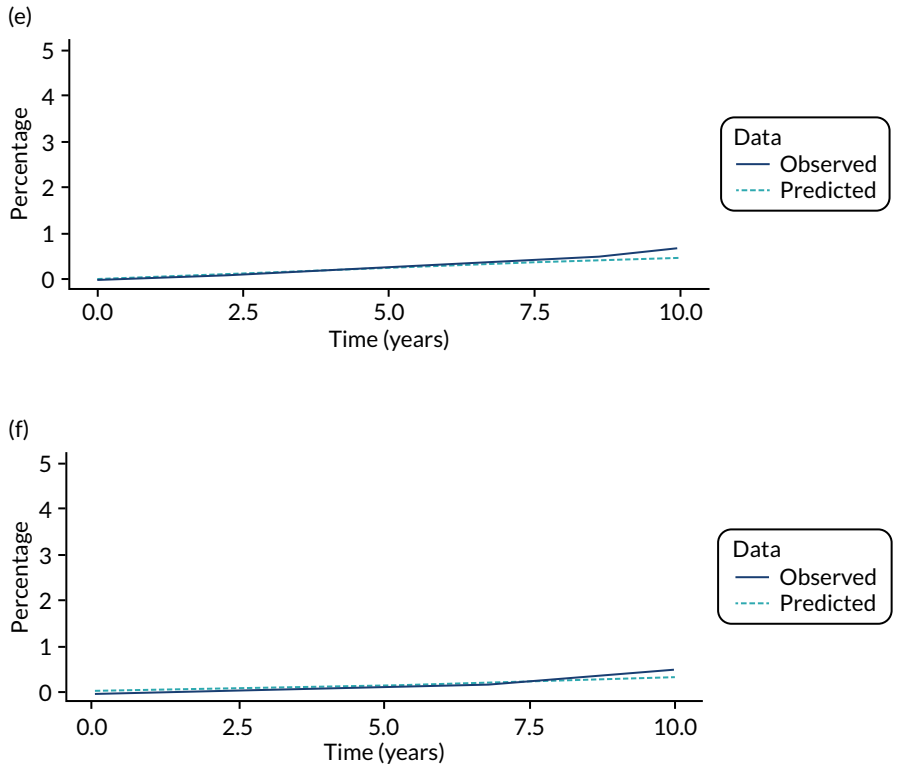

FIGURE 10 Comparison of model predictions with observed data from a single imputation for the higher-risk subgroup of the low-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state.

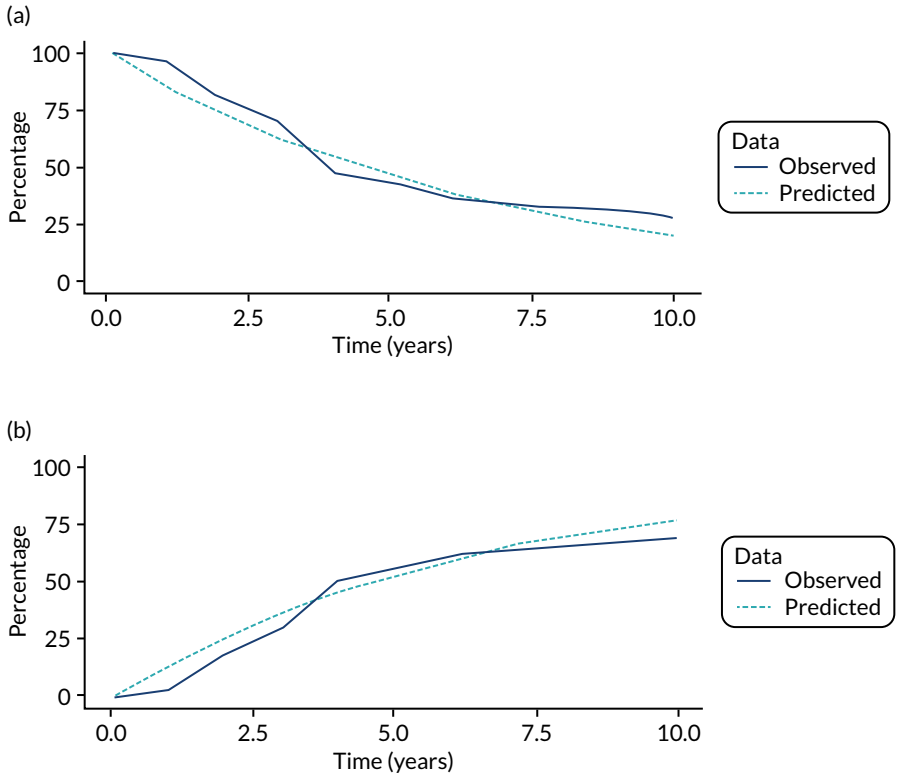

FIGURE 11 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the intermediate-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state. (*continued*)

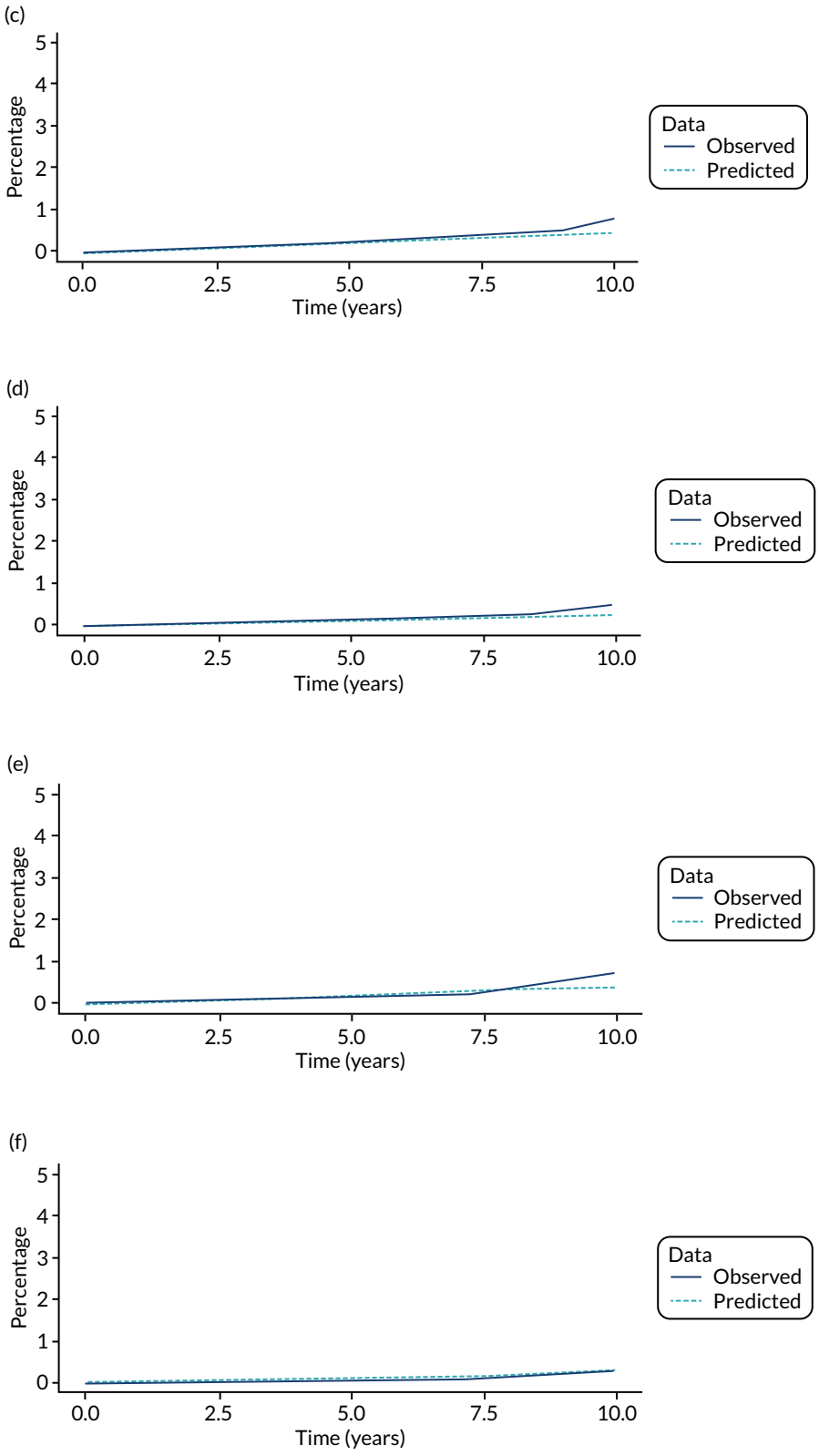

FIGURE 11 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the intermediate-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state.

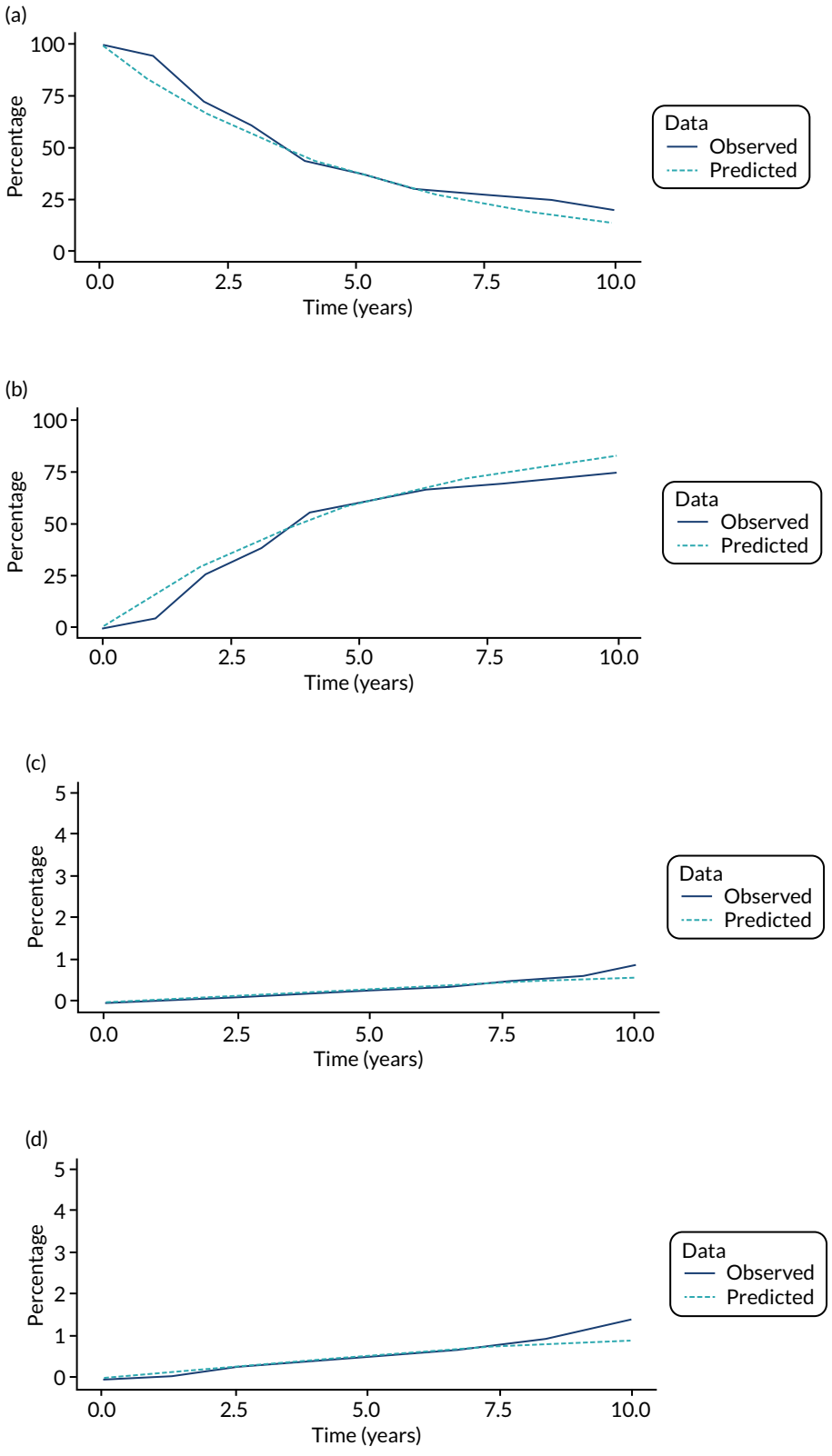

FIGURE 12 Comparison of model predictions with observed data from a single imputation for the higher-risk subgroup of the intermediate-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state. (*continued*)

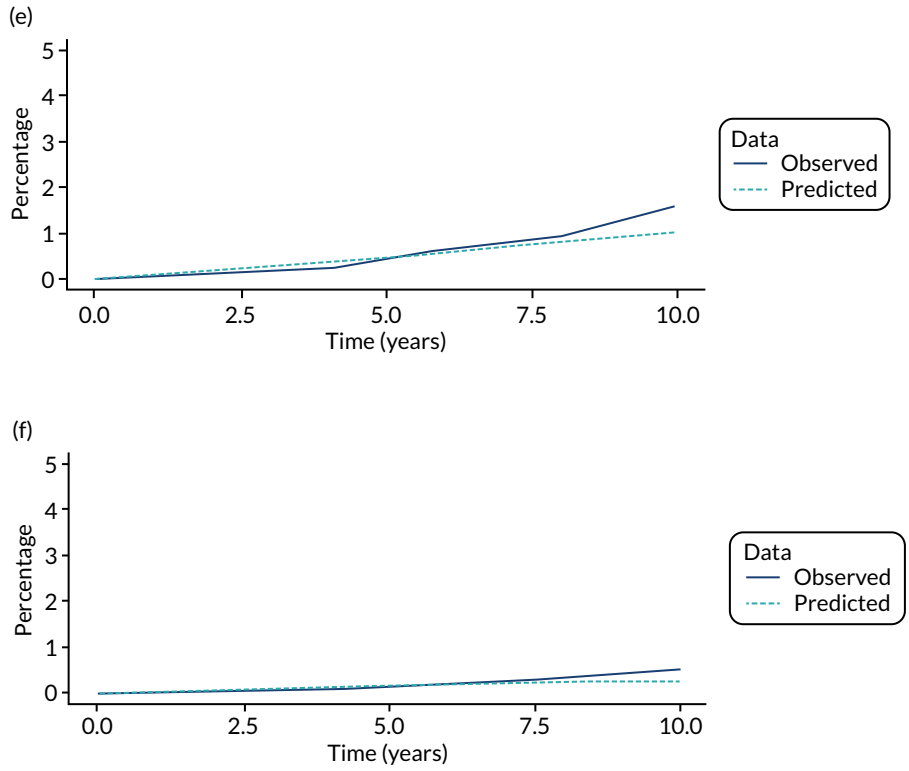

FIGURE 12 Comparison of model predictions with observed data from a single imputation for the higher-risk subgroup of the intermediate-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state.

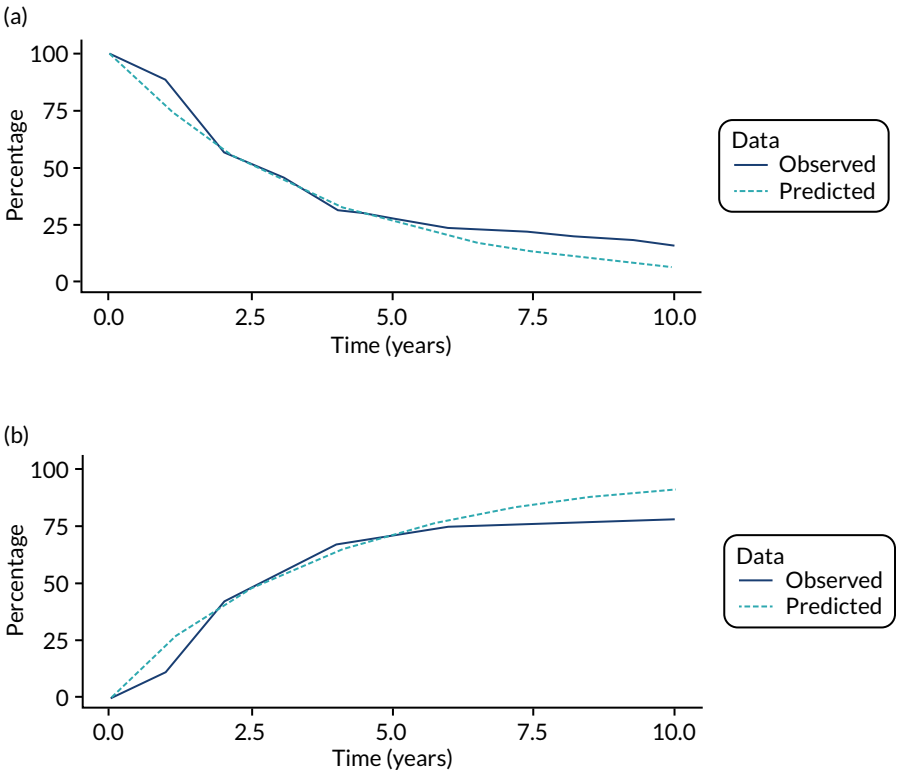

FIGURE 13 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the high-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state. (*continued*)

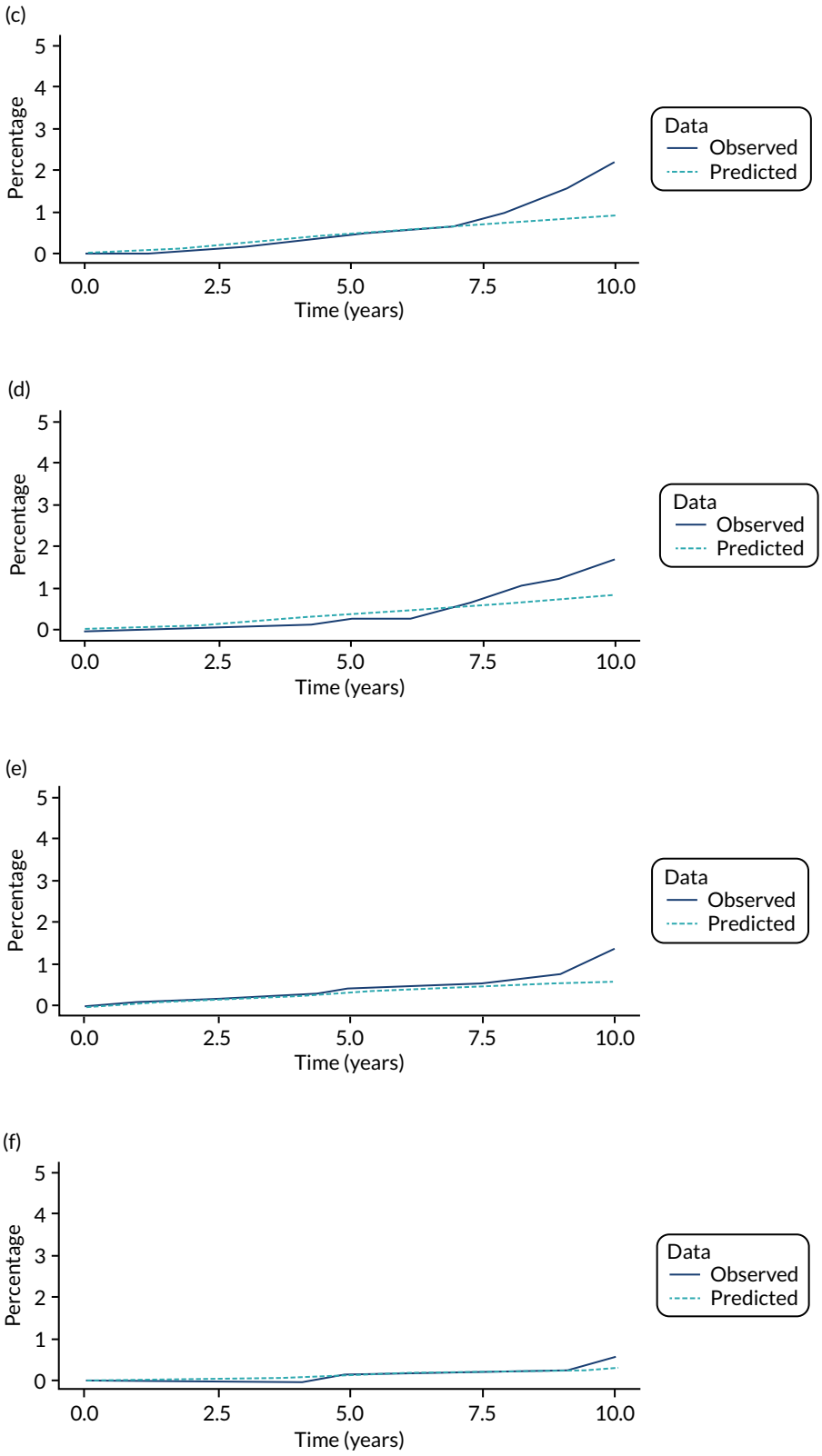

FIGURE 13 Comparison of model predictions with observed data from a single imputation for the lower-risk subgroup of the high-risk group. (a) No visits state; (b) visits state; (c) Dukes' stage A state; (d) Dukes' stage B state; (e) Dukes' stage C state; and (f) Dukes' stage D state.

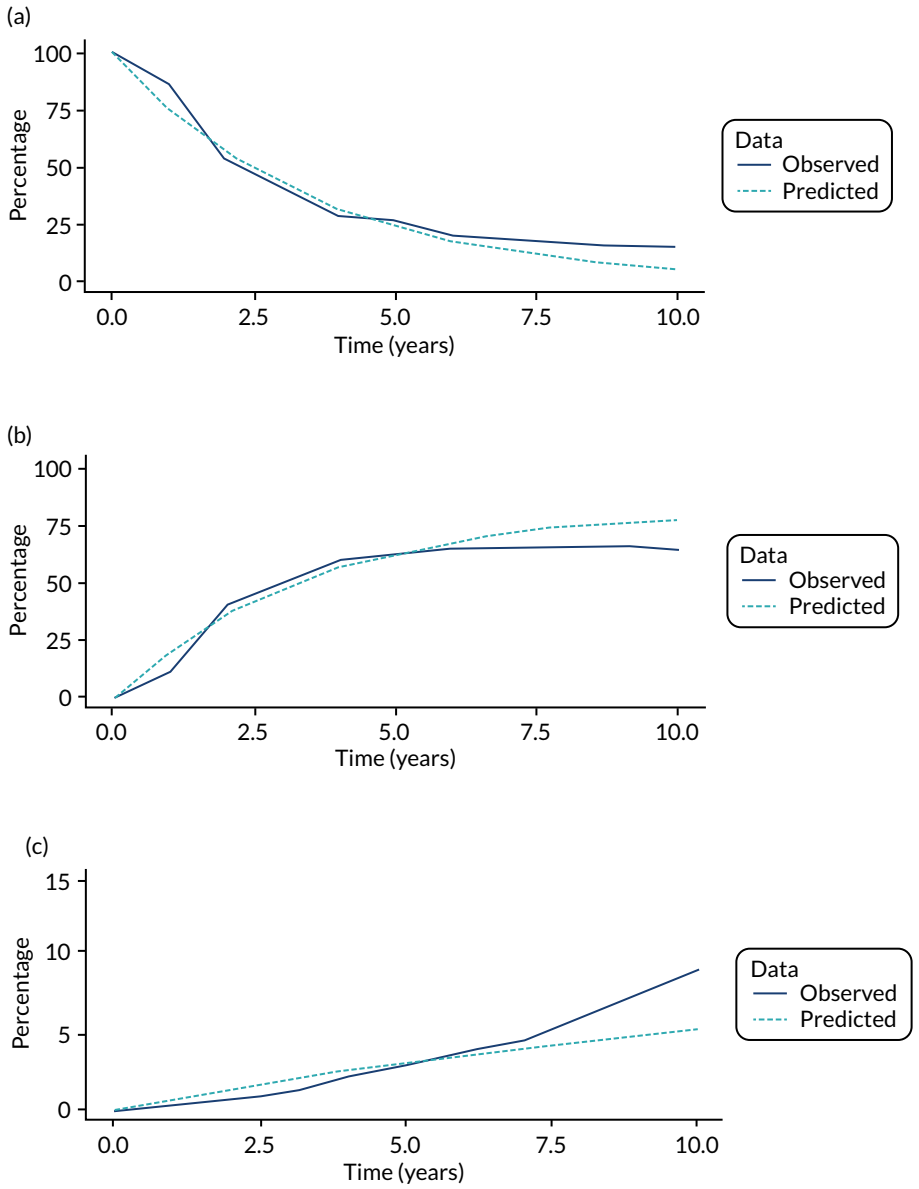

FIGURE 14 Comparison of model predictions with observed data from a single imputation for the higher risk subgroup of the high-risk group. (a) No visits state; (b) visits state; and (c) CRC state.

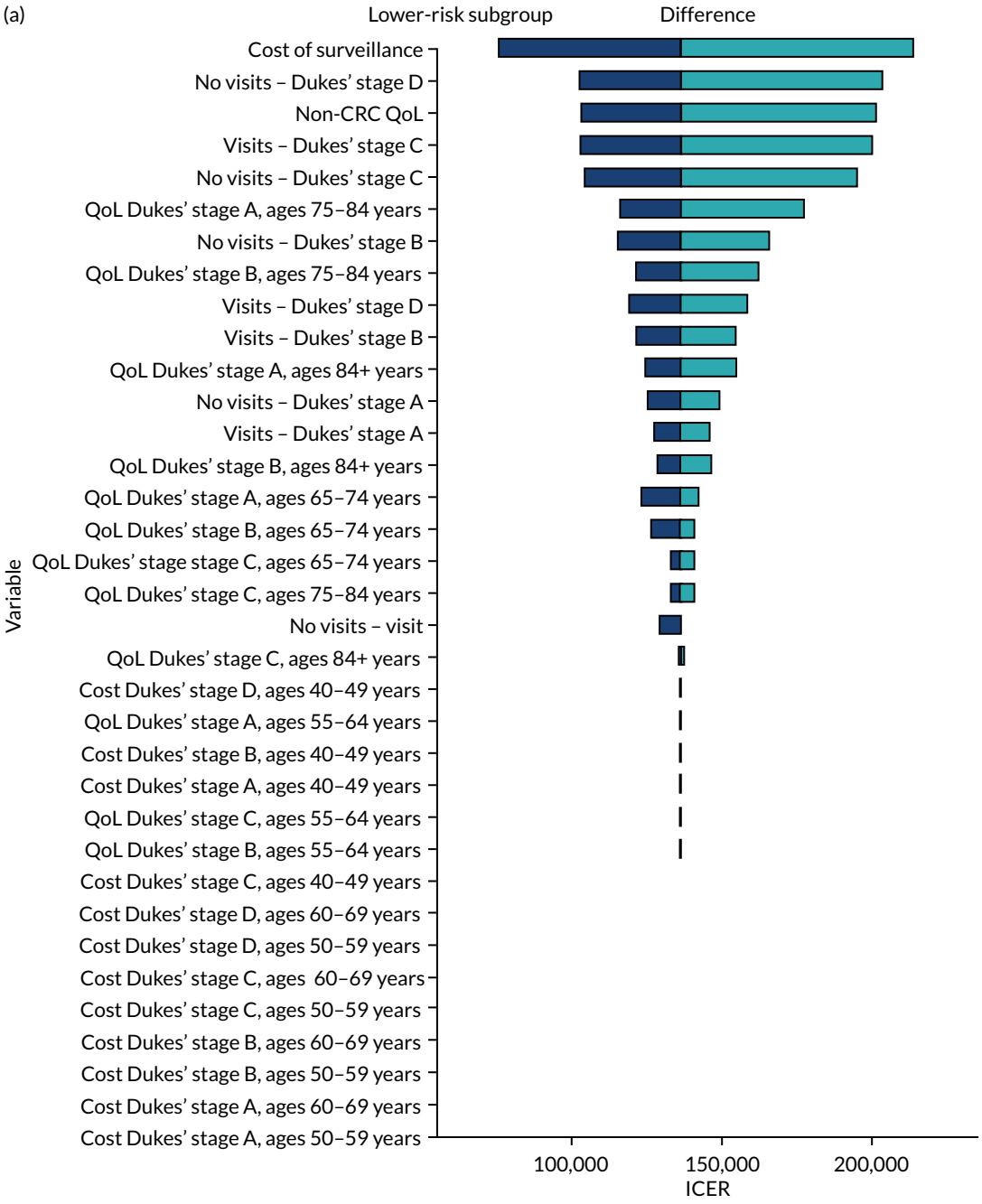

FIGURE 15 Effect of varying baseline parameters in a DSA on ICERs in the low-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup. (*continued*)

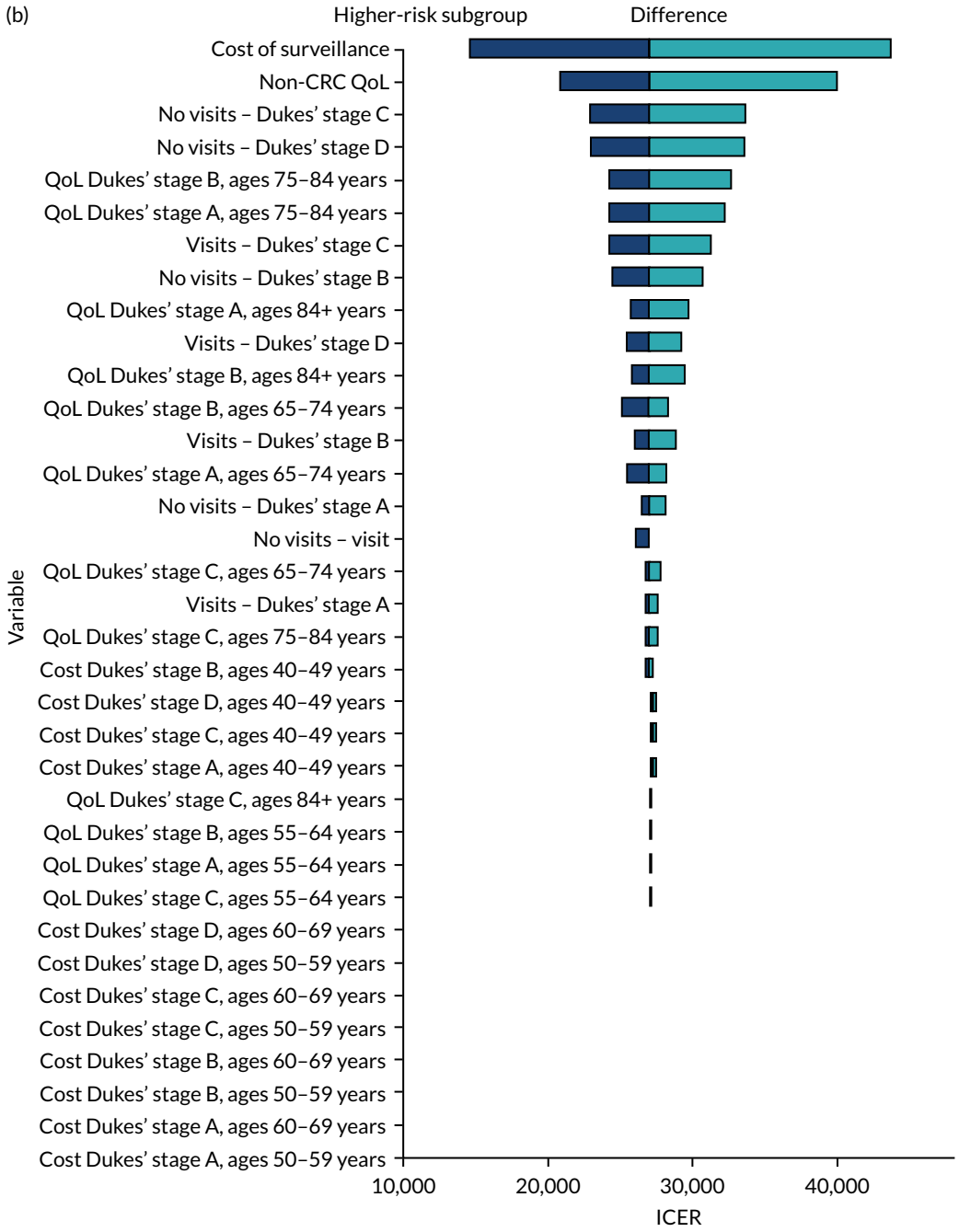

FIGURE 15 Effect of varying baseline parameters in a DSA on ICERs in the low-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup.

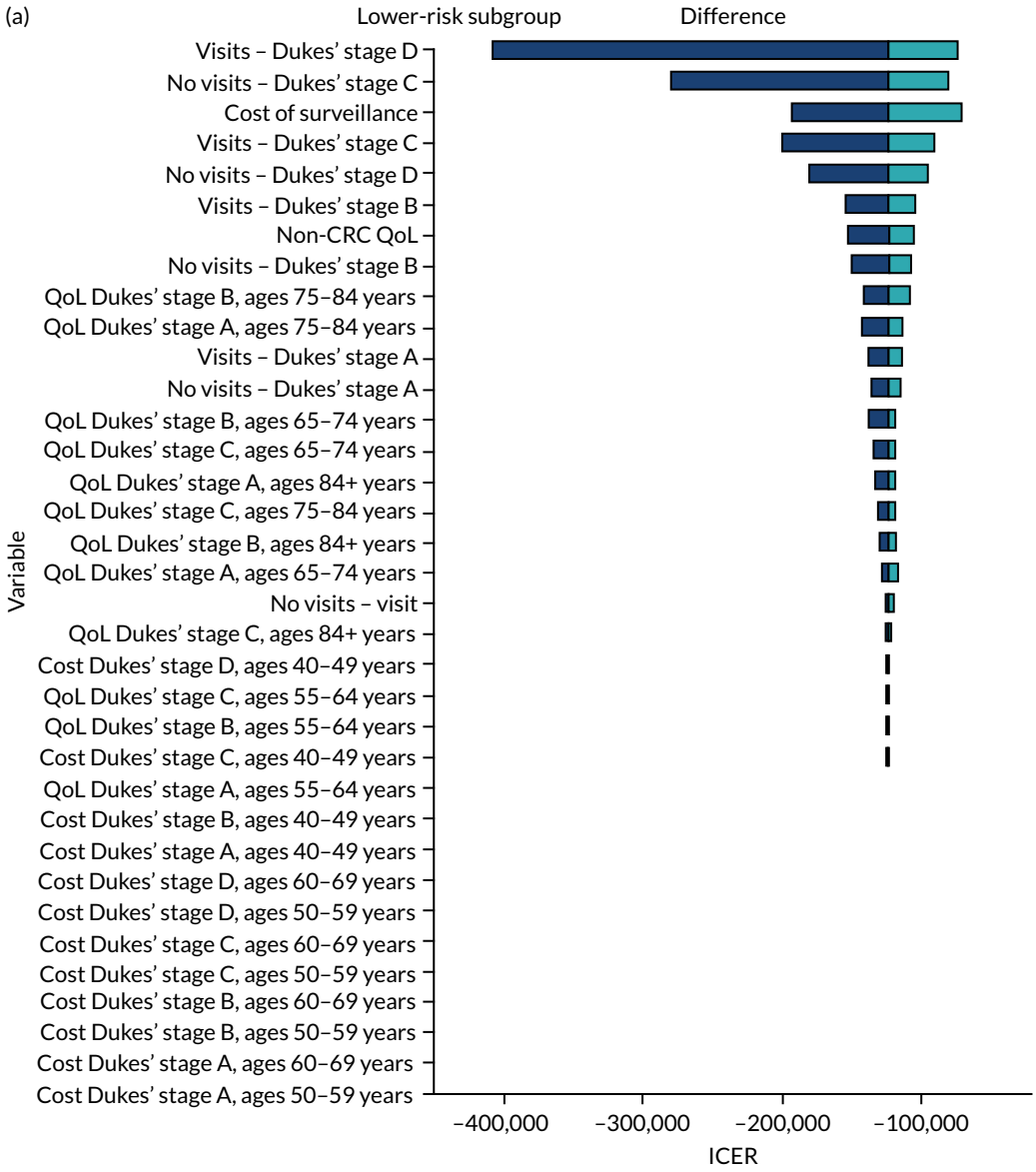

FIGURE 16 Effect of varying baseline parameters in a DSA on ICERs in the intermediate-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup. (*continued*)

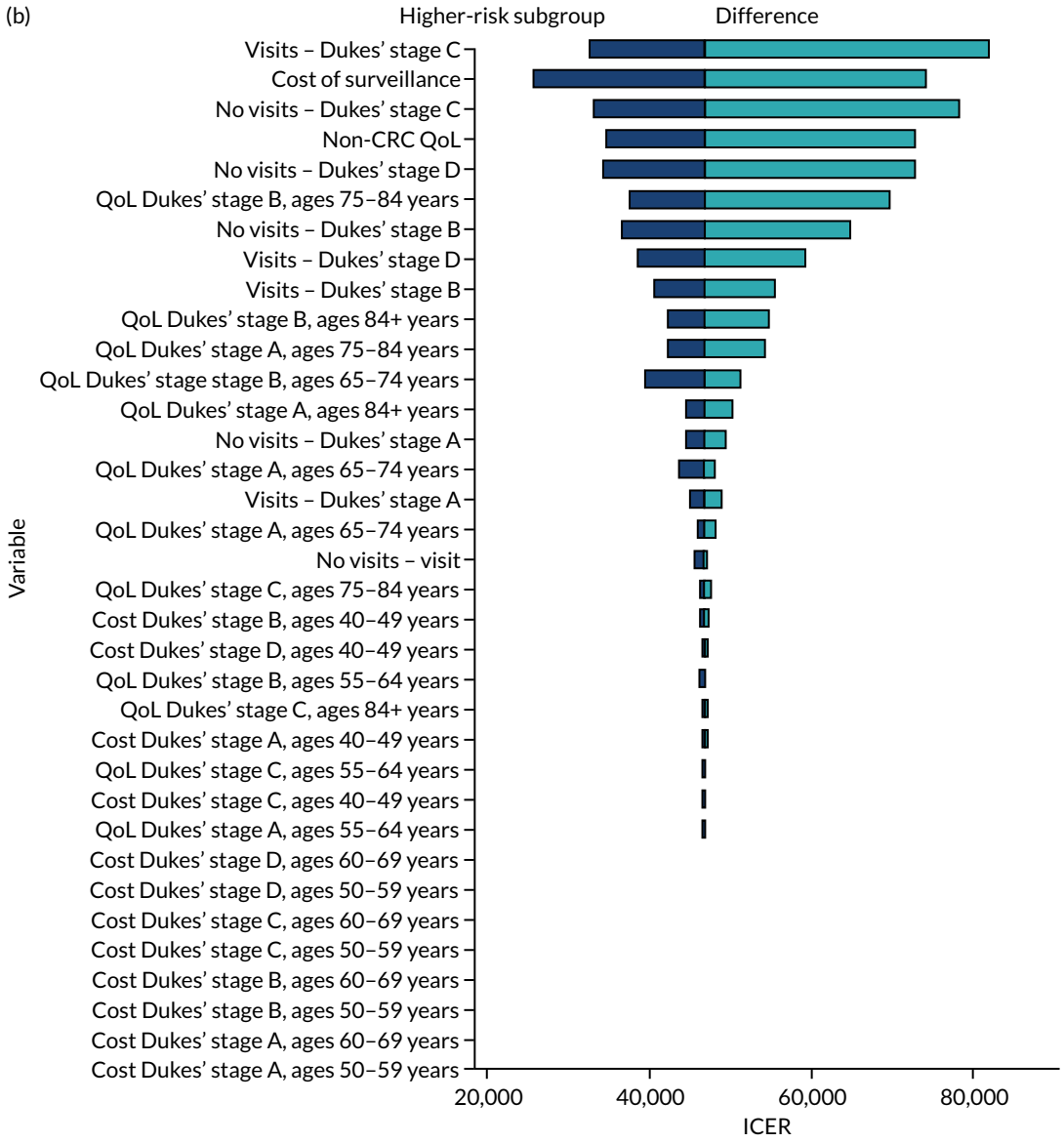

FIGURE 16 Effect of varying baseline parameters in a DSA on ICERs in the intermediate-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup.

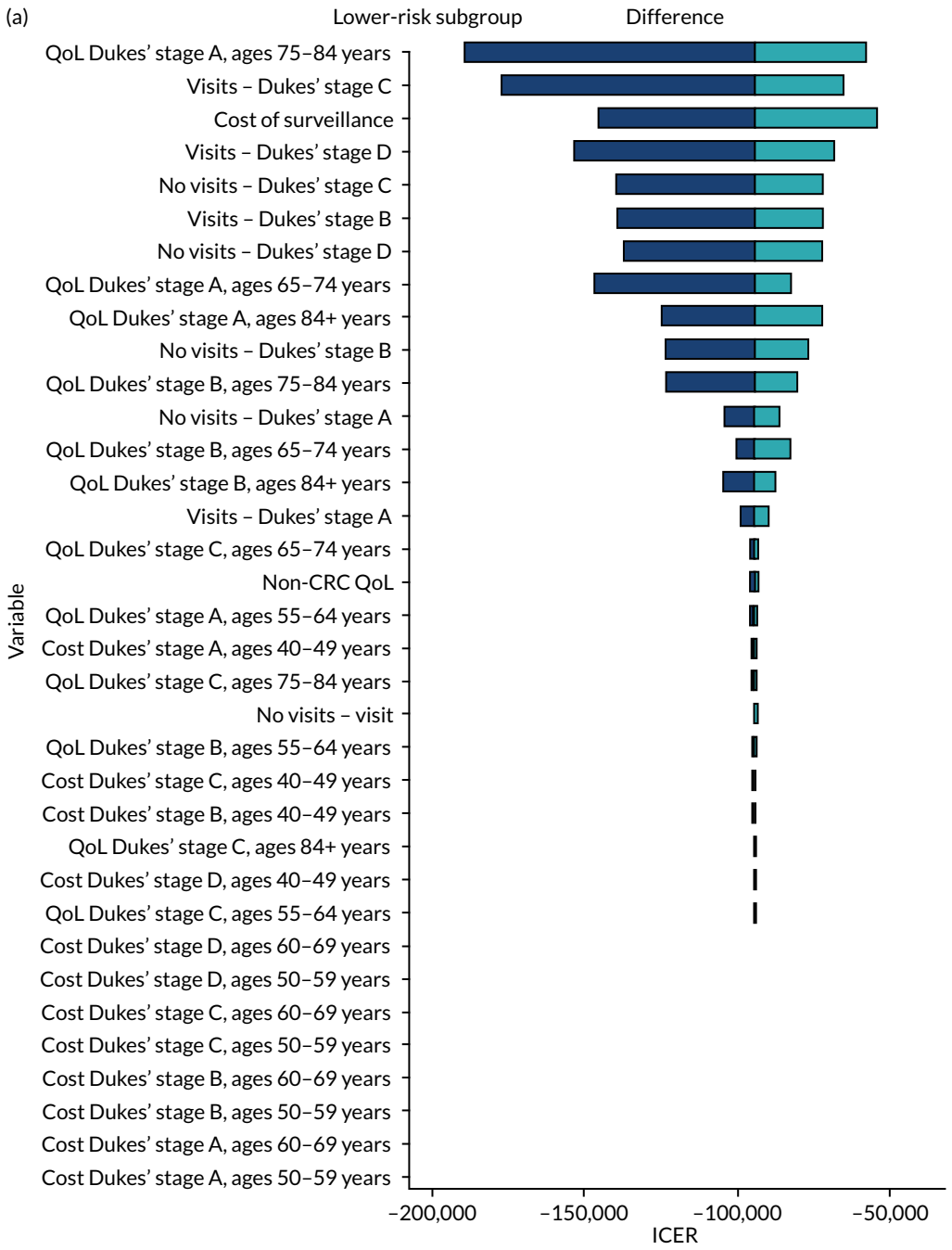

FIGURE 17 Effect of varying baseline parameters in a DSA on ICERs in the high-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup. (*continued*)

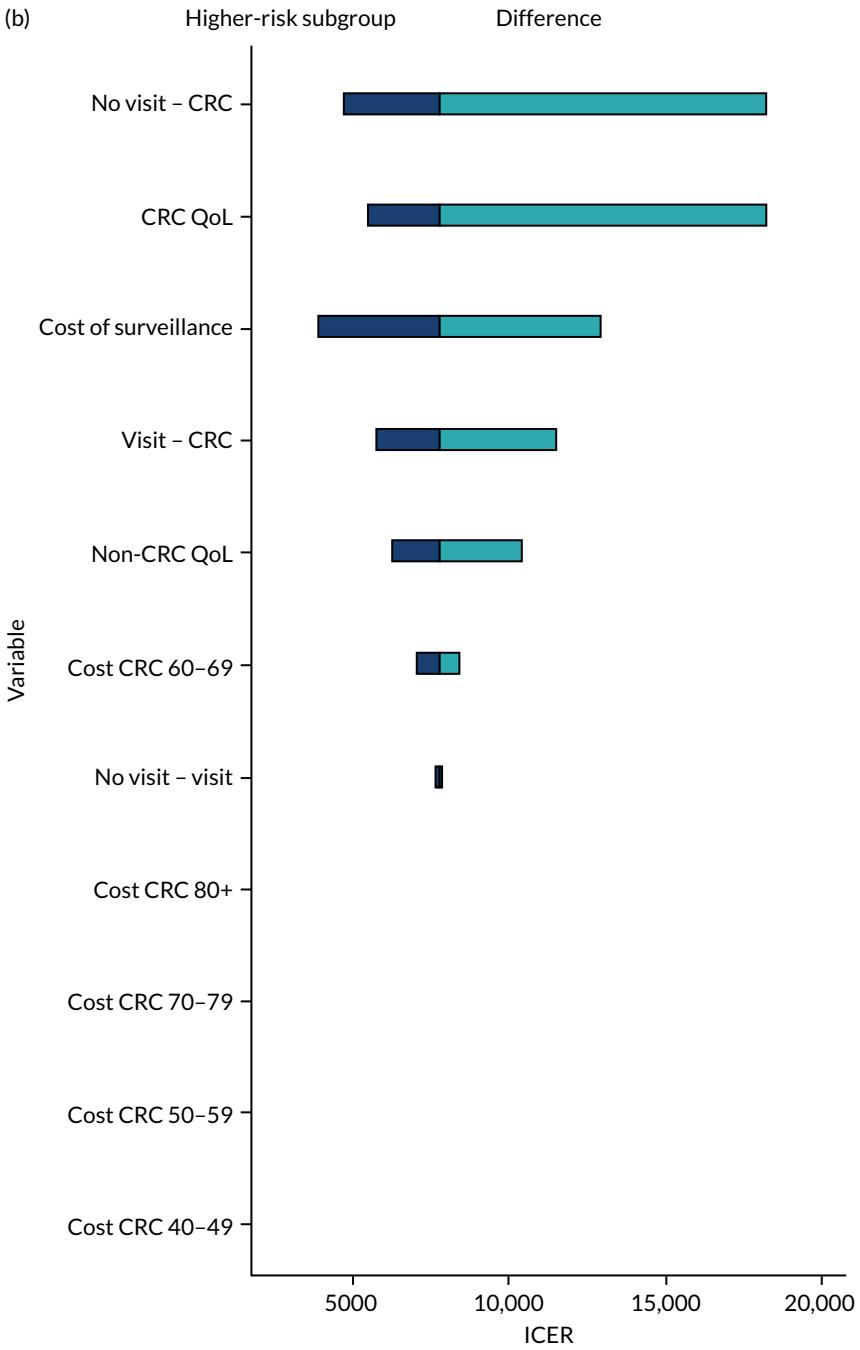

FIGURE 17 Effect of varying baseline parameters in a DSA on ICERs in the high-risk group. (a) Lower-risk subgroup; and (b) higher-risk subgroup.

EME
HSDR
HTA
PGfAR
PHR

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