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]

[1]Cancer Screening and Prevention Research Group, Department of Surgery and Cancer, Imperial College London, London, UK
[2]Department of Gastroenterology, University Hospital of North Tees, Stockton-on-Tees, UK
[3]Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK
[4]Department of Gastroenterology, New Cross Hospital, Wolverhampton, UK
[5]Wolfson Unit for Endoscopy, St Mark's Hospital, London, UK
[6]Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK
[7]Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK

*Corresponding author amanda.cross1@imperial.ac.uk

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

Scientific summary

Colonoscopy surveillance following adenoma removal

Health Technology Assessment 2022; Vol. 26: No. 26
DOI: 10.3310/OLUE3796

NIHR Journals Library www.journalslibrary.nihr.ac.uk

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.

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/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

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.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).