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Surveillance for the prevention of colorectal cancer in people with polyps

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1. Introduction

This project report has been produced to document the methods and results of the systematic reviews and evidence syntheses undertaken by ScHARR. The systematic reviews addressed analytical questions to aid the development of the British Society of Gastroenterology (BSG) guideline, specifically the section of the BSG guideline addressing surveillance following detection of colorectal adenomas, specifically, the initiation and subsequent continuation, or discontinuation, of surveillance following detection of colorectal cancer.

ScHARRs remit was to provide systematic reviews and narrative syntheses for seven clinical questions, across sixteen prognostic factors and this report will present the methods and results of those reviews. Evidence sifting was undertaken for four additional clinical questions and details of that work can be found in appendix 1. ScHARR also undertook searches for additional questions (details of these searches can be found in appendix 2).

The overall aim was to identify and evaluate the evidence relating to the following seven clinical questions (CQs) and to present a narrative synthesis of the evidence for each question. For CQ1, 2, 4, 5 and 6 the evidence was to be presented by sixteen prognostic factors that were either polyp, patient, or procedure related (see Table 2. For details);

- CQ 1 - Who is at increased risk of developing CRC or advanced adenomas post-polypectomy (polyp clearance) at index colonoscopy?
- CQ 2 - What is the evidence that 1st surveillance (as opposed to index colonoscopy polyp clearance) reduces future CRC risk?
- CQ3 - At what interval should 1st surveillance be performed?
- CQ4 - Who is at higher risk of developing CRC or advanced adenomas post-1st surveillance (Findings at 1st surveillance alone)?
- CQ5 - Who is at higher risk of developing CRC or advanced adenomas post-1st surveillance (Summative findings of index plus 1st surveillance)?
- CQ6 - What is the evidence that 2nd (and subsequent) surveillance reduces future CRC risk?
- CQ7 - At what interval should 2nd (and subsequent) surveillance be performed?

2. Methods

The systematic review was undertaken in accordance with the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (PRISMA, 2009).

Searching for the evidence

A systematic literature search was undertaken to identify all published evidence relevant to the review questions for the revised guideline. The search undertaken was in accordance with the parameters stipulated within the NICE guidelines manual (NICE, 2014). Databases were searched using relevant medical subject headings, free-text terms and study-type filters (such RCTs, systematic reviews and observational studies) where appropriate. Bibliographic search strategies were performed on 25th January 2018 in Medline [via Ovid], Embase [via Ovid] and Cochrane Library [via Wiley Online Library] and date limits applied from 2007 until 2018 using two search strategies combined into one:

1. Terms for colorectal cancer terms (1-2) were combined with terms for 'polyp' (3-6) and 'colonoscopy/surveillance' (7-9) and 'incidence/prevalence/risk' (14-19).

2. Terms for colorectal cancer terms (1-2) were combined with terms for 'polyp' (3-6) or 'colonoscopy' (7-8). The search was combined with 'surveillance/screening' (9).

An English language limit and exclusion publications filter (11-27) were applied. (see Appendix 2 for search terms)

In addition, we cross-checked against the reference lists of highly relevant papers or guidelines and asked the guideline committee members to highlight any additional studies.

Study selection

Citations were downloaded to EndNote bibliographic management software. All citations were sifted by one reviewer and checked by a second reviewer.

Inclusion criteria

Included studies were in populations of adults who had been diagnosed with at least one colorectal adenoma and all detected adenomas had been resected completely at index colonoscopy. The specific inclusion criteria for each question are presented in the population, exposure/intervention, comparator, outcome (PECO/PICO) format in Table 1. below.

Table 1. Inclusion criteria for questions 1 to 7

Clinical question	Population	Exposure / intervention	Comparator	Outcome
Who is at increased risk of developing CRC or advanced adenomas post-polypectomy (polyp clearance) at index colonoscopy?	Adults (18 years or over) who have been diagnosed with at least one colorectal adenoma and all detected adenomas have been resected completely.	Presence of prognostic factor (analyses presented separately for each prognostic factor listed in table 2.)	Absence of prognostic factor or comparator	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality
What is the evidence that 1st surveillance (as opposed to index colonoscopy polyp clearance) reduces future CRC risk?	Adults (18 years or over) who have been diagnosed with at least one colorectal adenoma and all detected adenomas have been resected completely.	Colonoscopic surveillance (analyses presented separately for each prognostic factor listed in table 2.)	No surveillance	Long-term CRC incidence; Long-term CRC mortality; with general population comparator where reported; to include health economic analyses
At what interval should 1st surveillance be performed?	Adults (18 years or over) who have been diagnosed with at least one colorectal adenoma and all detected adenomas have been resected completely.	Surveillance interval (e.g. 3 year surveillance)	Comparator surveillance interval (e.g.earlier than 3 year surveillance)	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality
Who is at higher risk of developing CRC or advanced adenomas post-1st surveillance?	Adults (18 years or over) who have completed first surveillance colonoscopy	Findings at 1st surveillance alone (analyses presented separately for each prognostic factor listed in table 2.)	Absence of I	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality
Who is at higher risk of developing CRC or advanced adenomas post-1st surveillance?	Adults (18 years or over) who have completed first surveillance colonoscopy	Summative findings of index plus 1st surveillance (analyses presented separately for each prognostic factor listed in table 2.)	Absence of I	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality

Clinical question	Population	Exposure / intervention	Comparator	Outcome
What is the evidence that 2nd (and subsequent) surveillance reduces future CRC risk?	Adults (18 years or over) who have completed first surveillance colonoscopy	2nd colonoscopic surveillance (analyses presented separately for each prognostic factor listed in table 2.)	No 2nd surveillance	Long-term CRC incidence; Long-term CRC mortality; with general population comparator where reported; to include health economic analyses
At what interval should 2nd (and subsequent) surveillance be performed?	Adults (18 years or over) who have completed first surveillance colonoscopy	3 year surveillance	earlier than 3 year surveillance	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality

An additional outcome measure was included during the course of the review as it was deemed important. The outcome measure was a composite outcome of advanced adenoma and colorectal cancer, usually termed advanced neoplasia (AN). Studies were included if they did not report AA or CRC outcomes separately but did report the outcome AN and the study population exceeded 1000 patients.

Table 2. Polyp, patient and Procedure related characteristics and comparators to be analysed across each CQ

Exposure (Polyp/Patient or Procedure characteristics)	Comparator
Polyp	
High grade dysplasia	Low grade dysplasia
Villous component ≥25% (tubulovillous or villous histology)	NO Villous component ≥25% (tubulovillous or villous histology)
Size of largest adenoma (variants: ≥10mm, or ≥20mm)	Size of largest adenoma NOT greater than (variants: ≥10mm, or ≥20mm)
Number of adenomas (variants: 1,2,3,4,5-9,10+; the main categories may be 1-2, 3-4 and 5+ but we would like to capture all reported variations)	N/a
Presence of adenoma in proximal colon	Absence of adenoma in proximal colon
Adenoma morphology (variants: pedunculated, sessile, flat)	N/a
Patient	
Male gender	Female gender
Family history of CRC	NO Family history of CRC
Younger age (e.g. <55 vs 55+; there will be other variants of age cut-off and we would like to capture these too)	NOT in Younger age range
Older age (e.g. <75 vs 75+; there will be other variants of age cut-off and we would like to capture these too)	NOT in Older age range
Smoking (variants: current, ex, never)	N/a
High body mass index (e.g. BMI>25)?	NOT High body mass index
Procedure	
Index colonoscopy Bowel prep quality (variants: good, adequate, inadequate/poor)	Inadequate/poor bowel prep
Index colonoscopy complete to caecum	incomplete colonoscopy
Index colonoscopy by high-quality colonoscopist	NOT high quality colonoscopist
Index colonoscopy using high-adenoma-detecting technologies (variants: HD scope, chromoendoscopy)	no high-adenoma-detecting technologies

In addition to assessing the evidence from electronic database searching, evidence reported in existing guideline documents, which met the inclusion criteria, were checked for inclusion in the review (Cairns et al., 2010; Atkin 2002; Hassan 2013).

Quality assessment

After identifying eligible studies for inclusion, methodological quality of the studies was assessed using the QUIPS tool for studies of prognostic factors, and a Cochrane risk of bias tool for non-randomised studies (ROBINS) of interventions, where applicable.

Data extraction

Data were extracted into a piloted data extraction form by one reviewer and checked by a second reviewer. Information on study characteristics and methods, participant characteristics, interventions and comparators evaluated, and clinical outcomes was extracted.

Synthesis

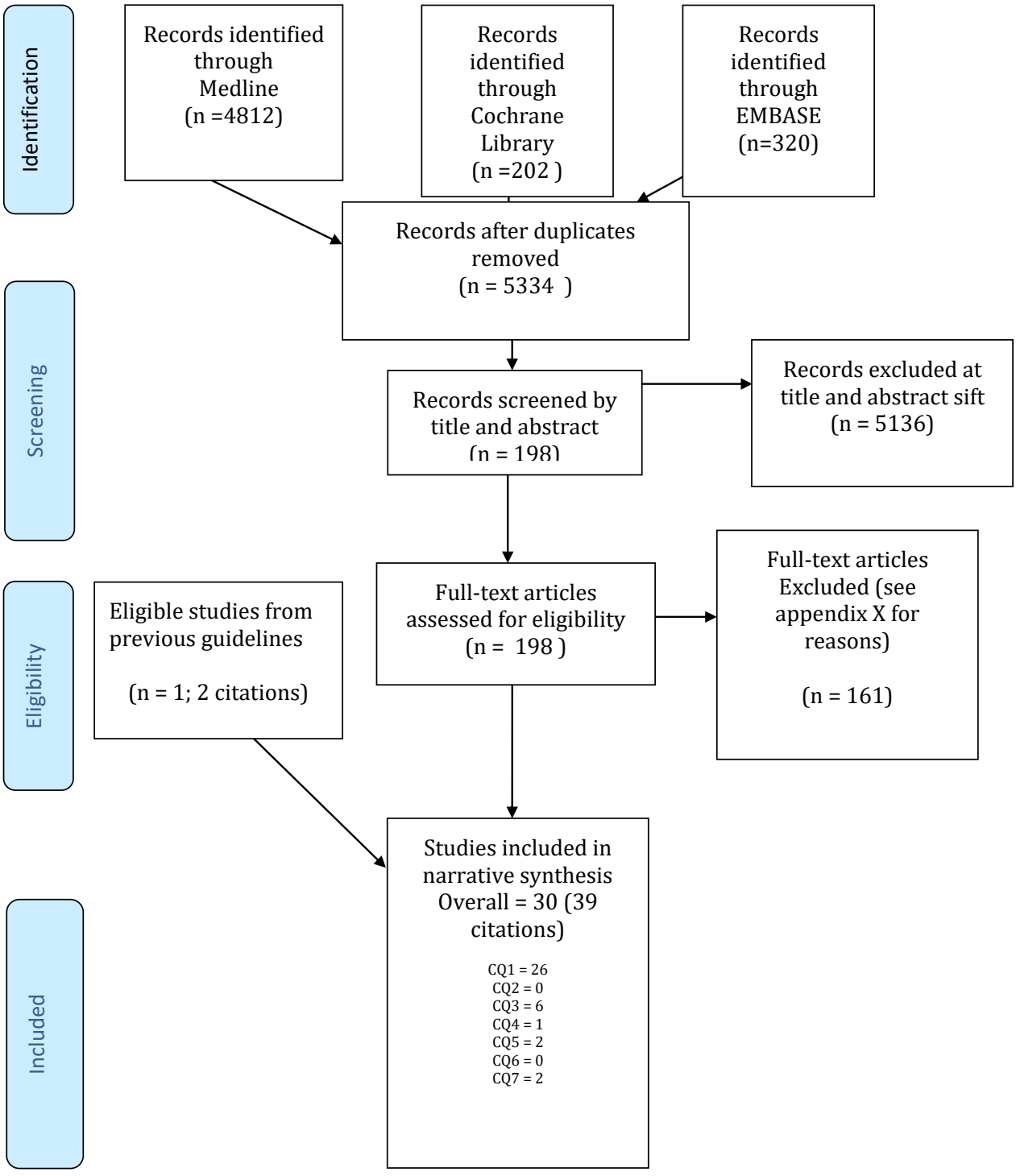
A narrative synthesis of included studies was undertaken, including tabulation of relevant study information and a GRADE assessment of the evidence.

3. Results

Bibliographic searches

After removing duplicates, 5334 articles were found. No systematic reviews were found as potentially relevant. 198 citations were considered potentially relevant and acquired in full text. In total 30 studies (relating to 39 citations) were included at full text sift across questions 1 - 7. 29 studies (relating to 37 citations) were identified from electronic database searching from 2007. An additional study (relating to 2 citations) were included from the previous guidelines (Atkin, 2002; Cairns, 2010). (See Figure 1. PRISMA flow chart). 161 studies were excluded because they did not meet the inclusion criteria (see appendix 3 for a list of excluded studies with reasons for their exclusion).

Figure 1. PRISMA Flow Diagram



Study characteristics

Of the 30 studies included at full text, 26 provided evidence for CQ1, no studies provided evidence for CQ2, 6 studies provided evidence for CQ3; 1 study provided evidence for CQ4; 2 studies provided evidence for CQ5; no studies provided evidence for CQ6; and 2 studies provided evidence for CQ7. All except one study (an RCT; Winawer 1993) were observational studies. Details of the study characteristics are presented in table 3.

Table 3 Study characteristics of the included studies.

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
Atkin 2017a&b	Retrospective cohort - To estimate CRC incidence after baseline colonoscopy in patients who are recommended 3-yearly surveillance, and assess the effect of surveillance on CRC incidence. The hypothesis was that a subgroup of patients exists in whom surveillance colonoscopy could be stopped earlier, or for whom surveillance is not necessary, on the basis of their CRC incidence.	AA CRC incidence at next surveillance Long term CRC incidence Cox proportional hazards models	Patients were eligible for inclusion in the study if they had a baseline colonoscopy and newly diagnosed intermediate-risk adenomas according to UK guidelines, defined as one-to-two large (≥10 mm) adenomas, or three to four small adenomas	Median follow up time 7·9 years, (IQR 5·6–11·1),	Advanced adenoma was defined as an adenoma of ≥ 10 mm, or with villous or tubulovillous histology, or HGD	Surveillance was associated with a substantially reduced incidence of CRC in intermediate-risk patients. First surveillance seemed to confer the most benefit and was associated with a significantly reduced CRC incidence rate compared with no surveillance; this reduction was maintained in patients who attended subsequent visits.
Chung 2013	Retrospective cohort study – To evaluate risk factors for the presence of high-risk adenomas at the time of a third colonoscopy based on the findings from two prior colonoscopic examinations, which will help determine optimal colonoscopic intervals	AA Cox regression analysis was used to identify clinical covariates predictive of high-risk adenoma at the third colonoscopy.	patients who underwent two consecutive surveillance colonoscopies after an initial polyp removal (size ≥ 5 mm and number ≥ 1) at the first colonoscopy	First and second surveillance - The median interval (min-max) between the first and second colonoscopy was 17 (6-101) months, while the median interval (min-max) between the second and third	AA was defined as an adenoma of diameter ≥10 mm or a villous component or HGD.	Patients with high risk adenoma at the first and/or second colonoscopy had increased sik of recurred high risk adenoma at second surveillance than the patients without high-risk adenoma at the first and second colonoscopy.

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
				colonoscopy was 24 (6-90) months.		
Chung 2011	Prospective cohort - The aim of this large-scale prospective study was to (1) estimate the 5-year cumulative incidence of advanced adenoma and compare differences among risk categories inherent to the guidelines and (2) determine whether purported risk factors for occurrence of colorectal neoplasia would also be predictive of its recurrence.	AA N and % only	Asymptomatic undergoing first time screening colonscopy with complete clearing at every examination	FS SS - FS <3years vs 3-5years	AA diameter ≥10 mm or a villous component or HGD.	For the 5-year incidence of advanced adenoma, the high-risk group exhibited a significantly higher rate of 12.2% as compared with rates of 2.0% for the normal group and 2.4% for the low-risk group. Among subjects in the low-risk group, 355 (52.9%) underwent their first surveillance within <3 years. Rates of advanced adenoma were similar irrespective of the timing of the first surveillance (1.7% at <3 years vs 2.2% at 3e5 years, p¼0.11). Almost all subjects in the high-risk group underwent their first surveillance within 3 years and the majority of them underwent repeat examinations. Notably, most advanced adenomas in the high-risk group were detected within <3 years, with 1-, 2- and 3-year cumulative rates of 4.6, 7.4 and 9.6%, respectively.
Coleman 2015	Retrospective cohort study / with nested case control study - The aim of this investigation was to quantify colorectal cancer risk following polypectomy of adenomas in a large population based study.	CRC incidence at next surveillance Cox proportional hazards models to investigate the association between CRC risk and demographics or incident polyp characteristics. Standardized colorectal cancer incidence ratios (SIR) were analysed per 100,000 population, and separately for males and females. Models	Cohort study - Patients in an adenoma register. Nested case-control study - Patients who developed CRC at least 6 months post-incident polyp diagnosis. Controls were matched 1:1 to CRC cases by age (1 year), sex, year of incident polyp diagnosis, and	Study conducted over a 6 year time period	NA	Colorectal cancer risk was elevated in individuals following polypectomy for adenoma, outside of screening programmes.

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
		adjusted for age at index, sex, year at index, number of polpys at index, and subsequent adenoma diagnosed. For the nested case–control study, CRC risk was assessed between comparative groups by applying conditional logistic regression analysis to generate odds ratios (OR) and 95% CI.	were alive at the time of their matched cases' CRC diagnosis.			
Cottet 2012	Retrospective cohort study - The aim of this study was to estimate the risk of colorectal cancer in patients with adenoma within the general population followed-up in routine practice, both overall and according to the initial characteristics of the patients and adenomas and to colonoscopic follow-up practices.	AA CRC incidence at next surveillance The number of person-years (from index to CRC diagnosis) was calculated by sex and 5-year age group. The sex and age-specific colorectal cancer incidence rates in the general population were obtained from the cancer registry. The ratio of observed to expected cases of colorectal cancer was reported as a standardised incidence ratio (SIR). Cumulative colorectal cancer probabilities were calculated using the Kaplan Meier method and expressed with 95% CI.	Patients were identified from the population-based registry of colorectal polyps, and comprised all patients diagnosed for the first time with a colorectal adenoma between 1 January 1990 and 31 December 1999.	FS (all patients had at least one FU) Median FU 7.7 year (IQR -5.2-10.5)	Advanced adenomas were defined as adenomas with a diameter <10 mm and/or a villous component and/or HGD.	The long-term risk of CRC remained higher in patients diagnosed for the first time with adenomas than in the general population. Both initial adenoma features and the conditions of colonoscopic surveillance in routine practice strongly affected the cancer risk. Compared with the general population, the risk of developing CRC after polypectomy only remained high in patients with advanced adenomas and without follow-up colonoscopy. Patients with initial advanced adenomas could largely benefit from colonoscopic surveillance, since the risk of cancer was similar to that in the general population when at least one follow-up colonoscopy was performed. The cancer risk was low in patients with non-advanced adenomas in comparison with the general population.

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
Cubiella 2016	Retrospective cohort study – To determine whether there are differences in the incidence of advanced neoplasia and CRC detection at the first surveillance between the two risks groups at 3 year interval.	Advanced Neoplasia (AN) (AA+CRC) Multivariate logistic regression.	Two groups – screening patients who met criteria for an intermediate group and high risk group.	1st surv after 2.8 (1.8) years for 65% of the study population.	NA	Variables independently associated with the risk of AN at fist surveillance were more than 5 adenomas, villous histology and HGD.
Emilsson 2017 (& Loberg 2014)	Retrospective cohort study – To evaluate CRC mortality in a large, population-based cohort with virtually complete follow-up for death from colorectal cancer. (Loberg) To assess the generalisability of our Norwegian study (Loberg), we took advantage of a large, independent cohort from Sweden, with the aim of providing reliable estimates for the risk of CRC death after adenoma removal. (Emilsson)	Long term CRC mortality Compared the observed mortality in the adenoma cohort with rates in the general population. Data on all patients in whom CRC was diagnosed were retrieved from the Cancer Registry, including age at the time of diagnosis, date of diagnosis, cancer location, and date and cause of death.	Cancer Registry for all patients who were 40 years of age or older and had at least one colorectal adenoma removed	The median follow-up was 7.2 years	N/A	The mortality rates for adenoma patients are low and are similar in Norway and Sweden and accordingly the differences in standardised mortality ratios reflect the different baseline risk in the two countries.
Facciorusso 2016a b	Retrospective cohort – The aim of this study was to develop and validate an easy to use numeric score point able to accurately predict ACA recurrence after colon polypectomy.	AA Unadjusted and adjusted: grade; size; number ACAs	All had advanced adenoma at baseline with complete adenoma resection, and complete follow-up data.	FS - 3 years	ACAs were identified according to Paris classification as: polypoid pedunculated type (0-1p), sessile (0-1s), non-polypoid (0-IIa, 0-IIb and 0-IIc)	ACAs >15mm representing HGD at pathologic examination are at higher risk and might benefit from more intensive surveillance. Single lesions +/=15mm without HGD show a very low risk of recurrence and could be considered for longer follow up intervals.
Fairley 2014	Retrospective cohort – To estimate the strength of associations between baseline adenoma attributes	AA CRC incidence at next surveillance	Patients with adenomas removed at screening colonoscopy .	FS+ (all patients had one or more screening / surveillance colonoscopies (Time NR)	Advanced adenoma: adenoma with +/= 1 risk attributes. Risk attributes were defined at namely	The results emphasise the need to mitigate excessive risk by performing timely surveillance colonoscopies in patients with

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
	and the risk of adenoma recurrence and invasive CRC.	Multivariate logistic regression, adjusting for sex, smoking status, family history (of CRC), and age (age at diagnosis of recurrent adenoma or CRC, or age at the end of follow-up for patients who did not have these outcomes.			the number (+/=3) and size (+/=10 mm) of adenomas, and the presence of HGD or villous morphology.	baseline adenomas displaying high-risk attributes.
Huang 2012	Retrospective cohort - To assess 5-year risk of colorectal neoplasia after normal colonoscopy in asymptomatic Chinese Mongolian over 50 years of age	AA Multiple logistic regressions.	All patients who had undergone colonscopic removal of adenomas and received colonsocpic surveillance within 5 years.(sub cohort)	FS- 5 years	A tubular adenoma 10mm or larger in diameter, villous or tubulovillous adenoma, or any adenoma with HGD.	The results provide support for follow-up colonoscopy of at least 5 years for entire cohort (which includes those who had no baseline adenoma – data not extracted)
Huang 2010	Retrospective cohort – To analyse the actual recurrence rate of adenoma and advanced adenoma in a Chinese patient population with adenoma on the initial colonoscopy and assess the relationship between the characteristics of baseline adenoma and the recurrence of adenoma. Also estimated possible colonoscopy surveillance intervals after polypectomy.	AA Cox proportional hazard model to assess the relative risk of recurrence of advanced adenoma based on size, presence of villous, and number of baseline adenomas and to control for the age and sex of the patient.	Colorectal adenoma removed by colonoscopy , complete colonoscopy was performed at every examination; at least one surveillance colonoscopy was performed within 6 months after the initial colonoscopy, with the aim of removing missed adenomas; follow up data available.	Patients underwent more than one surveillance colonoscopy within 1-20 years of the baseline examination.	One or more of the following features: a tubular adenoma 10 mm or larger in diameter, villous or tubulovillous adenoma, or the presence of HGD.	The recurrence rate of advanced adenoma in various surveillance intervals was higher among patients with advanced adenomas at baseline than in those with non-advanced adenomas at baseline. The recurrence of any adenoma and advanced adenoma was associated with the size, number, and histological features of the baseline adenoma as well as with the age and sex of the patients.
Huang 2012a	Retrospective cohort - To evaluate the risk and cause of ICC in patients with adenoma within 5 years after polypectomy and to provide some beneficial information for improvement of the current colonoscopic surveillance strategies.	Interval CRC Multivariate logistic regression adjusting for age, sex, stage (advanced or non-advanced), size (<10mm/≥ 10mm, pathology (tubular vs tubulovillus and villous adenoma), dysplasia and number of adenomas (<2/≥3)	Colorectal adenoma removed by colonoscopy , complete colonoscopy was performed at every examination, patients had to have had a surveillance colonoscopy within 5 years.	FS at least one surveillance mean 2.67 years	One or more of the following features: a tubular adenoma 10 mm or larger in diameter, villous or tubulovillous adenoma, or the presence of HGD.	Among patients undergoing surveillance colonoscopy within 5 years after polypectomy the incidence density of ICC was 2.9 cases per 1000 person years. The majority of interval cancers originated from incomplete resection and AA and missed cancers. Age >60 yrs, presence of villous and HGD sig

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
						associated with ICC on surveillance colonoscopy.
Jang 2015	Retrospective cohort - To evaluate risk factors related to recurrent high-risk polyps	AA (referred to as high risk polyps)	Of patients who were found to have polyps at first colonoscopy, clinical data from consecutive patients with high-risk polyps was collected retrospectively.	FS Surveillance colonoscopy performed within more than 1 year of the index colonoscopy.	High-risk polyps defined as adenoma ≥10mm, ≥adenomas, ≥20% villous histology, or HGD.	Male patients and those with poor bowel preparation for colonoscopy or higher numbers of adenomas were more likely to experience recurrent high-risk polyps.
Jung 2016	Retrospective cohort study – to compare the risk for advanced colorectal neoplasia recurrence according to the number of high risk findings at the index colonoscopy.	Advanced Neoplasia (AA+CRC) Cox proportional hazards.	Patients who had one or more high risk adenomas at index (all adenomas removed at index) and underwent follow up 2.5 or more years after index.	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	NA	A 3 year surveillance interval for patient with multiple high risk findings appears reasonable.
Laish 2017	Retrospective cohort - To stratify the risk for advanced adenoma and CRC based on both pathology and polyp size at baseline colonoscopy	AA Multivariate analysis performed by development of backwards logistic regression model.	All adult patients above the age of 18 who had a documented neoplasia at baseline colonoscopy and a surveillance colonoscopy.	FS Interval between procedures was at least 1 year and less than 5 years	Advanced tubular adenoma (either>10mm or with HGD histology).	The size of the polyp and the number of advanced lesions are more important than its histology for predicting the risk of high-risk metachronous lesions at follow-up.
Laiyamo 2008; Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010 (only follow up data)	Prospective study – Polyp Prevention Trial - To measure the ability of adenoma characteristics at baseline to predict subsequent advanced adenoma recurrence within 4 years. To examine the rate of interval CRC in the PPT continued follow-up study	AA Long term CRC incidence Log-binomial modelling . Age, sex, BMI, nonsteroidal anti-inflammatory drug use, adenoma characteristics (location, size, HGD. and villous component), family history of CRC adjusted for in multivariate	Patients completing the PPT trial by having end point colonoscopy. Inclusion in PPT was patients aged 35 or older who had at least 1 histologically confirmed adenoma removed during a screening or diagnostic colonoscopy within 6 months of random assignment.	At 4 years; (and follow up data 6.2 years after the end of the PPT for CRC incidence)	adenomas ≥1 cm in diameter or with a villous histology or HGD.	Missed lesions are more likely to be in the proximal colon. Recurrent adenomas and advanced adenomas are more likely to be in the proximal colon. Risk of adenoma recurrence increases with increased body size, but short-term weight change over 4 years does not affect risk of adenoma recurrence. Advancing age was associated with an increased risk of proximal advanced adenoma recurrence.
Lee 2017	Retrospective cohort - To estimate the risk of metachronous neoplasia and	AA	Patients who underwent complete colonoscopic polypectomies and after	FS at 3 or 5 years (comparison)	HRA was defined as advanced adenoma, ≥10 mm in diameter,	Patients had a surveillance colonoscopy before the recommended guidelines

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
	optimal surveillance interval in the Korean population.	Logistic regression analysis, adjusted for age, male sex, smoking, multiple adenomas, large adenoma, and 3-year surveillance interval.	index colonoscopy, underwent one or more surveillance colonoscopies.		containing >25% villous structure or HGD, or three or more adenomas.	despite a low risk of metachronous neoplasia. However, the risk of metachronous advanced adenoma was increased in elderly patients and those with a 3 or more year surveillance interval.
Lee 2013	Retrospective cohort - To describe the findings at 12-month surveillance colonoscopy in high risk individuals and to identify baseline patient and clinical characteristics that may predict the risk of having AA or CRC at surveillance.	Advanced Neoplasia (AA+CRC) MV logistic regression model	individuals who were assigned to the high-risk group as a result of the baseline screening	FS – 1 year he mean interval between the first colonoscopy in the screening episode and surveillance colonoscopy was 387 (SD = 89) days	NA	Patients at high risk of future neoplasia, had an incidence at 12 months of 0.8% for CRC and 6.1% for advanced adenomas. 12-month surveillance in high-risk group of patients is recommended.
Martinez 2009	Pooled analysis of 8 retrospective studies - To estimate absolute risks of metachronous advanced adenoma, CRC, and their combination (advanced colorectal neoplasia) and to identify patient characteristics and adenoma features that are independently associated with risk of these outcomes.	Advanced Neoplasia (AA+CRC) – Logistic regressions, adjusting for study, age, sex, race, smoking status, BMI, family history of CRC, history of polyp or adenoma prior to baseline examination, baseline adenoma characteristics.	Studies including >800 participants; protocol requiring complete baseline colonoscopy with removal of one or more adenomas and removal of all visualised lesions; specified schedule of surveillance follow-up colonoscopies; availability of end-point data regarding the number, size, and histopathology of adenomas and CRC detected at follow-up examination.	Median follow-up was 47.2 months, range 36.9 to 59.0	NA	Development of metachronous advanced colorectal neoplasia was associated with the number, size, location, and histological features of prior adenomas, as well as age and sex of patients.
Miller 2010	Retrospective cohort - To provide descriptive statistics to help define the risk of identifying advanced neoplasia or any neoplasia on follow-up colonoscopies in a patient who has had 1-2 small tubular adenomas removed on colonoscopy.	AA Primary outcome, presence of an advanced adenoma or any adenoma on 3rd procedure.	Patients aged 49 or older who had at least 3 colonoscopies each at least 11 months apart. Inclusion required that the first of 3 colonoscopies be a complete colonoscopy to the cecum performed as an outpatient with the identification and	FS SS subsequent - Median time between Index and FS 32.6m (range 11-78) and between 2nd and 3rd 37.6m(range 11-102m).	An advanced adenoma was defined as any adenoma greater than or equal to 1 cm or any adenoma with tubulo-villous or villous histology or HGD.	There is a high percentage of patients who have adenomatous polyps on follow-up colonoscopies even after two low risk colonoscopies. After having two low risk colonoscopies (i.e. two or fewer small tubular adenomas), 30% of patients were found to have

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			removal of 1 or 2 small tubular adenomas without tubulo-villous or villous histology or HGD.			adenomatous polyps within approximately 3 years after their most recent colonoscopy, and 2.4% had advanced adenomas.
Morelli 2013(and Imperiale, 2014)	Retrospective cohort - To quantify the yield of advanced colorectal findings (high risk findings, advanced adenoma on the second surveillance colonoscopy based on finding from the index and first surveillance colonoscopies using data generated from clinical practice.	AA (High risk findings, defined as an advanced adenoma). Multivariable logistic regression models were used to examine the association of age, sex, and findings on a previous colonoscopy with the likelihood of advanced adenoma on the subsequent surveillance colonoscopy	Eligible for study inclusion were patients with a history of neoplastic polyps (tubular adenomas, tubulovillous adenomas, and villous adenomas) on an index colonoscopy, which could have been done for any indication except for surveillance for previous adenomatous polyps or CRC. Patients had to have undergone at least 2 surveillance colonoscopies.	FS SS - The overall mean (median) SD interval between index and first surveillance colonoscopies was 33.9 (36.3) 20.2. overall mean (median) SD interval between the first and second surveillance colonoscopies was 44.1 (38.5) 18.6 months.	AA = a tubular adenoma 10 mm or larger in diameter, villous or tubulovillous adenoma, or the presence of HGD. Or three or more NAAs.	The risk of high risk findings on the second surveillance was found to be most dependent on whether high risk findings were present on the first surveillance and less so on the index. Patients with high risk findings on the index and first surveillance or on the first surveillance alone have a high subsequent risk of high risk findings. Patients with low risk or non AA on the index and first surveillance, a surveillance interval longer than 5 years may be considered, due to the low subsequent risk of advanced neoplasia in these subgroups.
Nusko 2008	Prospective cohort study – To identify differences between initial adenomas and metachronous lesions detected during a large series of subsequent follow-up examinations in order to evaluate the effect of long-term surveillance	AA Relative risk (RR) for the development of metachronous adenomas of advanced pathology.	Patients with adenomas at the initial examination and had at least one surveillance.	FS SS + Patients who had only single initial adenomas were re-examined at 4-year, those with multiple adenomas at 2-year, intervals. All patients had at least one follow up.	Adenoma of advanced pathology was defined as large (≥10 mm) or tubulovillous or villous or an adenoma bearing HGD.	Patients who had, at baseline, large adenomas or tubulovillous or villous adenomas or multiple adenomas have a significantly higher risk for those lesions also at follow up.
Park 2016	Retrospective cohort study - To investigate the risk of developing advanced colorectal neoplasm in young patients after removing high-risk adenoma detected at	Advanced Neoplasia (AA+CRC) – Cox proportional hazard regression analysis after adjusting for potentially confounding variables to assess	Patients with high-risk adenoma detected at index colonoscopy and who underwent colonoscopy at the last follow-up ≥ 2.5 years after index colonoscopy were included.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	advanced colorectal neoplasm was defined as cancer or advanced adenoma.	Age is a significant risk factor for developing overall and advanced colorectal neoplasms after removing high-risk adenoma detected at index colonoscopy

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
	index colonoscopy compared with that in older patients	risk factors of developing colorectal neoplasm.				
Pinksy 2009	Retrospective cohort study (SCU) nested in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening trial - To obtain information about the utilisation of and the findings from surveillance colonoscopy after a baseline colonoscopy	AA (and any adenoma) Multivariate model controlled for time to surveillance, sex, family history of CRC, aspirin use, age and smoking status.	All screening arm PLCO subjects randomised before January 1, 2000 and presumed alive on January 5, 2005, with no cancer diagnosis and who had a positive baseline FSG screen with a follow-up (baseline) colonoscopy within 18 months and	Mean times from baseline colonoscopy to FS Advanced adenoma at baseline, 3.4 years, Non-advanced adenoma at baseline, 4.3 years Non-adenomatous polyp at baseline, 4.5 years, No polyp at baseline, 4.7 years	adenoma, ≥10 mm, villous or tubulovillous or showing severe dysplasia	Time interval from baseline to first colonoscopy had virtually no effect on the rate of adenoma or advanced adenoma at FS. Location of the initial adenoma, and male sex were associated with adenoma recurrence.
Solakoglu 2017	Prospective cohort study - To determine the predictive value of 3-year recurrence adenoma characteristics at baseline conventional colonoscopy in patients with high-risk adenoma	AA Logistic regression	Patients with a first-time diagnosis of at least one histologically confirmed adenoma, which was removed during the diagnostic complete colonoscopy, and over 20 years of age; High-risk patients were defined as having tubular adenomas ≥10 mm, 3 or more adenomas, adenomas with at least 20% villous elements, or HGD.	FS-3 years	AA: diameter ≥10 mm or a villous component or HGD.	There was no association between adenoma recurrence and age or sex in patients with high-risk adenoma. In addition, initial adenoma features (size: ≥1cm, number: ≥3, location and villous component, and /or HGD) were not associated with adenoma / AA recurrence at the 3-year follow-up colonoscopy in patients with high risk adenoma. AA detected at the initial colonoscopy was also not a determinant of adenoma recurrence. AA should be monitored in shorter intervals independently for the component that makes an adenoma an AA.
Tae 2017	Retrospective cohort study – To determine whether index obesity is associated with metachronous CRA in terms	AA Logistic multivariate analyses - In all statistical models, we	Patients who underwent an index colonoscopy, who subsequently underwent at least one or more	Mean follow up period 3 years, patients underwent 1.3	Any polyp with one or more of the following features: ≥	This study demonstrated a dose-dependent association between index BMI and the multiplicity of metachronous

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
	of prevalence, multiplicity, and advanced adenoma on surveillance colonoscopy within 5 years.	adjusted for age, sex, index BMI status, current smoking, family history of CRC, use of aspirin or NSAID, index colonoscopic findings, follow-up period, and frequency of surveillance.	surveillance colonoscopies whose polyps were removed at the index colonoscopy.	surveillance colonoscopies	10 mm, villous histology, or HGD.	CRAs on surveillance within 5 year ager index. This association between BMI and the risk of multiple CRAs persisted in analyse of men but not in women.
Van Enckevort 2014	Retrospective cohort – To determine predictive factors for the development of adenomas and advanced neoplasia after polypectomy. Based on the results, a proposal for appropriate surveillance intervals is formulated.	AA Cox regression analyses.	18 years or older and had undergone polypectomy of at least one histologically proven adenoma during a complete colonoscopy.	Median FU period was 85 months (range 9-260). The median number of colonoscopies that had been performed during follow-up was 2 (mean 2.3, range 1-7). Data reported here combines all time intervals.	Adenoma with HGD reported here in the multivariate model. The term AA is used is absolute values for incidence stats, but is different to the definition used in the MV analyses.	Adenoma development after polypectomy occurs in a regular and repetitive way. Our data suggest that only the interval between the initial colonoscopy and the first follow up colonoscopy should be based on initial findings and that subsequent colonoscopies can be planned at predetermined intervals.
Van Heijningen 2013	Retrospective cohort study – To determine independent adenoma-related and colonoscopy related predictors and their associated odds rations for advance colorectal adenomas during clinical surveillance practice in a large community-based study.	Advanced Neoplasia (AA+CRC) Multivariate logistic regression.	Patients undergoing polypectomy and had at least one surveillance	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	NA	A high adenoma number, larger adenoma, villous histology, and proximal location are important independent predictors for AA during surveillance, as is quality of index colonoscopy.
Vemulapalli 2014	Retrospective cohort study – To evaluate the effect of using UK guidelines in a US cohort.	Advanced Neoplasia (AA+CRC) Univariate logistic regression	Patients with 1 or more adenomas and a follow up more than 200 days after baseline.	FS >200 days and less than 3 years.	NA	The rate of advanced lesions at first follow up is increased in patients with 3 or more baseline adenomas and at least 1 that is 10mm or larger.
Winawer 1993 Winawer 1993a	RCT – To evaluate whetheher follow-up colonoscopy at three years will detect important colonic lesions as effectively as follow-up at both one and three years.	CRC at next surveillance.	Patients referred for initial colonoscopy or polypectomy who did not have familial polyposis, inflammatory bowel disease or a person history of polypectomy or CRC, who had a complete colonoscopy to caecum,	1st - 1&3 vs 3 years follow-up: 3 years (Winnawer 1993); 6 years (Winnawer 1993a)	NA	Follow-up at 3 years detects important clinical lesions as effectively as follow-up at both one year and three years

First author, year	Study design and Aims and objectives	End points and Statistical model	Patient inclusion criteria	F/U [planned surveillance intervals]	Definition of AA	Summary of findings
			removal of all polyps, found to have one or more adenomas.	Group A: 2 surveillance: 1 & 3 years Group B: 1 surveillance: 3 years		

AA advanced adenoma; CRC colorectal cancer; AN advanced neoplasia; FS First surveillance; SS Second surveillance; FU follow up; HGD high grade dysplasia

Study quality

The quality of the included studies was assessed using the Quality In Prognosis Studies tool – QUIPS and Cochrane risk of bias tool for non-randomised studies of interventions ROBINS-I. Table 4 summarizes the decisions made regarding the 6 bias domains. The majority of studies were assessed as having a low risk of bias using these tools, although in a number of studies there were areas of uncertainty, around study participation and how confounding factors were controlled for, giving rise to uncertain risk of bias or high risk of bias in some studies.

Table 4. Results of the quality assessment of the studies using QUIPS and ROBINS-I

Study and date	1. Study Participation	2. Study Attrition	3. Prognostic Factor Measurement	4. Outcome Measurement	5. Study Confounding	6. Statistical Analysis and Reporting
Atkin 2017						
Park 2016						
Chung 2011						
Chung 2013						
Lee 2013						
Cubiella 2016						
Jung 2016						
Vemulapalli 2014						
Van Heijningen 2013						
Miller 2008						
Martinez 2009						
Laiyamo 2008						
Huang 2012						
Huang 2012a						
Kim 2012						
Facciorusso 2016						
Pinsky 2009						
Van Enckevort 2014						
Fairley 2014						
Huang 2010						
Nusko 2008						
Lee 2017						
Emilsson 2017						
Coleman 2015						
Solakoglu 2017						
Laish 2017						

Study and date	1. Study Participation	2. Study Attrition	3. Prognostic Factor Measurement	4. Outcome Measurement	5. Study Confounding	6. Statistical Analysis and Reporting	
Jang 2015							
Tae 2017							
Imperial 2014							
Cottet 2012							
ROBINS-I	**1. Confounding**	**2. Selection of participants**	**3. Classification of interventions**	**4. Deviations from intended interventions**	**5. Missing data**	**6. Measurement of outcomes**	**7. Selection of the reported result**
Winawer 1993							

Synthesis of findings

Due to the design of the studies included in the review the synthesis of findings was limited to a narrative synthesis. As part of the narrative synthesis an assessment of risk of bias was undertaken using the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach which incorporates the findings of the quality assessment with other factors study factors to make an assessment of the strength of the evidence per synthesised finding. Table 5. summarises the factors contributing to the overall grade assessment.

Table 5. GRADE assessment of risk of bias for the included studies

			Quality of evidence contributing to overall GRADE assessment		
Reference	**Design**	**N patients**	**Study limitations (QUIPS)**	**Imprecision:**	**Publication bias:**
Atkin 2017	Observational	N = 11 944	Low risk of bias – Although only Intermediate risk patients included	For some prognostic factors the number of events at index were very small despite a large sample.	NA
Chung 2011	Observational	N = 1210	Low risk of bias	NA	NA
Chung 2013	Observational	N = 131	Low risk of bias	NA	NA
Miller 2011	Observational	N = 88	Low risk of bias	Due to the very small sample size the number of events was very small.	NA
Facciorusso 2016	Observational	N = 843	Low risk of bias – although only high risk patients at baseline.	Number of events unclear due to incomplete reporting	NA
Enckevort 2014	Observational	N= 433	Low risk of bias.	Number of events unclear due to incomplete reporting	Not all relevant prognostic factors were reported.
Fairley 2014	Observational	N= 3300	Low risk of bias	Number of events unclear due to incomplete reporting	Not all relevant prognostic factors were reported.
Huang 2012	Observational	N = 197	Low to moderate risk of bias	For some prognostic factors the number of events at index and follow up were very small due to the small sample size.	NA
Huang 2012a	Observational	N= 1794	Low to moderate risk of bias	For some prognostic factors the number of events at index and follow up were very small due to the small sample size.	NA

			Quality of evidence contributing to overall GRADE assessment		
Reference	**Design**	**N patients**	**Study limitations (QUIPS)**	**Imprecision:**	**Publication bias:**
Huang 2010	Observational	N= 1356	Low risk of bias	NA	NA
Laiyamo 2008	Observational	N = 1905	Low to moderate risk of bias	NA	NA
Nusko 2008	Observational	N = 1091	High risk of bias – only patients with adenoma at surveillance included in analyses. No regression model presented.	NA	NA
Park 2016	Observational	N = 1479	Moderate risk of bias - High risk patients only	Number of events unclear due to incomplete reporting	Not all relevant prognostic factors were reported.
Lee 2013	Observational	N = 1760	Moderate risk of bias - High risk patients only	Number of events unclear due to incomplete reporting	Only significant factors are reported
Martinez 2009	Observational	N = 9167	Low risk of bias	NA	NA
Cubiella 2016	Observational	N = 5401	High risk of bias - Intermediate risk and high risk patients only	NA	NA
Van Heijningen 2013	Observational	N=2990	Moderate risk of bias	For a small number of prognostic factors the number of events are small.	NA
Lee 2017	Observational	N= 399	Low risk of bias	For some prognostic factors the number of events at index and follow up were very small due to the small sample size.	NA
Emilsson 2017	Observational	N= 90,864	Low risk of bias	NA	NA
Coleman 2015	Observational	N= 6972	Low risk of bias	NA	Not all relevant prognostic factors were reported.
Jung 2016	Observational	N = 1646	Moderate risk of bias - High risk patients only	Number of events unclear due to incomplete reporting	Not all relevant prognostic factors were reported.
Solakoglu 2017	Observational	N = 47	High risk of bias	For some prognostic factors the number of events at index and follow up were very small due to the small sample size.	NA
Cottet 2012	Observational	N= 5779	Low risk of bias	Number of events unclear due to incomplete reporting	NA
Laish 2017	Observational	N=1165	Low risk of bias	NA	Not all relevant prognostic factors were reported.
Jang 2015	Observational	N = 434	Low risk of bias – Although high risk patients only	Number of events unclear due to incomplete reporting.	NA
Tae 2017	Observational	N = 2904	Low risk of bias	NA	Not all relevant prognostic factors were reported. Age, sex and BMI only.
Pinksy 2009	Observational	N = 2607	Low risk of bias.	Number of events unclear due to incomplete reporting.	Not all relevant prognostic factors were reported. Sex only.
Imperiale, 2014	Observational	N = 965	Low risk of bias	NA	Not all relevant prognostic factors were reported. Only age and sex reported.

			Quality of evidence contributing to overall GRADE assessment		
Reference	**Design**	**N patients**	**Study limitations (QUIPS)**	**Imprecision:**	**Publication bias:**
Vemulapalli 2014	Observational	N=1414	Moderate risk of bias.	Number of events unclear due to incomplete reporting.	Not all relevant prognostic factors reported.
Winawer 1993	RCT	N= 1418	High risk of bias – high attrition rate.	NA	NA

In the following sections evidence relating to each of the CQs will be presented separately. The number of studies relating to each CQ will be stated together with a table of findings for each sub CQ and the table will be followed by a narrative synthesis of those findings for each sub CQ. It should be noted that not all studies presented multivariate analyses (adjusted for covariates) in addition to univariate analyses, therefore where non significant multivariate analyses follow significant univariate analyses, this should be considered.

Results relating to CQ1

Evidence was reported in twenty six observational studies for CQ1. The studies examined, patient, polyp and colonoscopy related predictors for advanced colorectal adenomas (AA) incidence at first surveillance after polypectomy at index colonoscopy, colorectal cancer (CRC) incidence at first surveillance after polypectomy at index colonoscopy, long term CRC incidence, and long term CRC mortality. Most of the included studies were rated as either low or moderate risk of bias with four studies rated as having a high risk of bias. The evidence relating to each of the prognostic factors is presented in Table 6.

Table 6. Findings from studies included for CQ1 for each of the prognostic factors.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
CQ1.1 High grade dysplasia v low grade								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance. Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance) Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref low grade (n=483/14.09%) OR (95%) (n=4608) High grade(n=162/19.06%) (1.44 (1.18 - 1.75) Unknown(n=78/23.56%) 1.88 (1.43 - 2.47)	UV Ref low grade (n51/1.49%) OR (95%)(n=4608) High grade (n26/3.06%) 2.09 (1.29 - 3.37) Unknown (n7/2.11%) 1.43 (0.64 - 3.18) MV FS: Model 1 interval as categorical Low grade (ref) High grade 1.81 (1.09 to 3.02) MV FS: Model 2 interval as continuous Low grade (ref) High grade 1.74 (1.04 to 2.90)	UV HR (95% CI): (n=11944) (vs low grade n139/94) High grade (n51/1994) 1·85 (1·34–2·55) ; Unknown (20/474) 1·71 (1·06–2·77) p= 0.0005 MV HR (95% CI):(vs low grade) High grade 1·69 (1·21–2·36) Unknown 1·69 (1·04–2·76) p=0.0033		Low risk of bias
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%).	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*High grade dysplasia: Ref none: : None 14.2% (12-.9-15.5) (at least one 12.1 (9.7-14.4) OR (95%CI) 0.7 (0.5-0.98).				High risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		Sex = Male HR 74.9%; IR 67.4%.						
Faccioruss o 2016a b	Retrospective cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male	FS at 3 years.	UV OR (95% CI) 3.25 (1.23 - 5.60), p<0.001 MV OR 4.25 (2.11-7.5), p<0.001				Low risk of bias
Fairley 2014	Retrospective cohort	N= 3300 Age = NR for sub cohort Sex = NR for sub cohort	FS+ (all patients had one or more screening / surveillance colonoscopies (Time NR)	OR (95%CI) 4.3 (2.2, 8.4; p0.0001)	OR (95%CI) 13.2 (2.8, 62.1; 0.001)			Low risk of bias
Huang 2012a	Retrospective cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years		Interval CRC, OR (95% CI) Low grade: 1 (n7/50%) High grade: (n7/50%) 1.61 (1.07 - 2.42), p=0.023			Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cumulative recurrence 1 – 20 years	high-grade dysplasia: (LG n66/5.7%: HG n 57/27.7%) (HR 1.61; 95% CI 1.07–2.42) P=0.023				Low risk of bias
Laiyamo 2008; (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Presence of high grade dysplasia (ref no HDG 109/1752) RR AA (15/145) v NAA (47/145) 1.11 (0.62-1.97); RR AA v no A (83/145) 1.11 (0.64-1.90)				Low to moderate risk of bias
*Lee 2013	Retrospective cohort study	N = 1760 (high-risk adenoma at index) Age = 65.8±3.5 Sex = 76% Male	1 year – mean interval between index and surveillance 387 (SD = 89) days	*MV OR (95% CI) HGD NS- high-grade dysplasia (P = 0.280),				Moderate risk of bias
*Martinez 2009	Pooled analysis of 8	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	*HDG No is reference [AA 10.6% (95% CI 9.8–11.3) CRC 0.5% (0.4–0.7)				Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
	restrospective studies			Yes AA 16.0% (13.2–18.7) CRC 1.3% (0.5–2.2)] Yes adjusted OR 1.05 (0.81-1.35)				
Nusko 2008	Prospective cohort	N = 1091 Age = 57.06 Sex = 64.16%	Up to 4 surveillance intervals.(at 2 or 4 yr intervals)	At index: High grade dysplasia n=51, 8.9%) 1st recurrence (FS) n=15, 2.6) p<0.00001				High risk of bias
*Park 2016	Retrospective cohort study	N = 1479 (high-risk adenoma at index, and last surveillance ≥ 2.5 years after index) Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): HDG 0.94 (0.66–1.34)				Moderate risk of bias
Van Enckevort 2014	Retrospective cohort	N= 433 Age = 55 (range 24-82) Sex = 41% Male	Median follow-up period was 85 months (range 9-260).	HR=1.73; 95% CI 1.13-2.64; p=0.012				Moderate risk of bias
*Van Heijningen 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	*MV OR (95%CI) HDG (AA 34 (8.1%); CRC 13 (3.1%) OR 1.2 (0.8-1.8)				Moderate risk of bias
CQ 1.2 Polyp: Villous component ≥25% (tubulovillous or villous histology) Polyp: NO Villous component ≥25% (tubulovillous or								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0)	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9	UV Ref Tubular (n171/9.92%) OR (95%)(n=4608) Tubulovillous (n374/17.51%) 1.93 (1.59 to 2.34) Villous (n115/25.05%) 3.03 (2.33 to 3.95) Unknown (n63/21.72%) 2.52 (1.83 to 3.47)	UV Ref Tubular (n18/1.04%) OR (95%)(n=4608) Tubulovillous (n39/1.83%) 1.76 (1.00 to 3.09)	UV HR (95% CI): (vs tubular n64/4742) (n=11944) Tubulovillous (n99/5576) 1·36 (1·00–1·87) ; Villous (24/1142) 1·65 (1·03–2·64); Unknown		Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		<55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	years, (IQR 5·6–11·1),	MV FS: Model 1 interval as categorical Worst adenoma histology, Tubular (ref) Tubulovillous 1.42 (1.15 to 1.76) Villous 1.59 (1.17 to 2.18) MV FS: Model 2 interval as continuous Worst adenoma histology, Tubular (ref) Tubulovillous 1.42 (1.15 to 1.75) Villous 1.59 (1.17 to 2.17)	Villous (n19/4.14%) 4.09 (2.13 to 7.86) Unknown (n8/2.76%) 2.69 (1.16 to 6.24) MV FS: Model 1 interval as categorical Worst adenoma histology, Tubular (ref) Tubulovillous 1.46 (0.82 to 2.60) Villous 2.55 (1.28 to 5.08) MV FS: Model 2 interval as continuous Worst adenoma histology, Tubular (ref) Tubulovillous 1.52 (0.85 to 2.71) Villous 2.94 (1.48 to 5.82)	(n23/484) 2·61 (1·61–4·23) p= 0·0018 Mulitvariate HR (95% CI):(vs tubular) Tubulovillous 1·16 (0·84–1·61); Villous 1·16 (0·71–1·91); Unknown 2·50 (1·40–4·47) p=0·0348		
Coleman 2015	Retrospective cohort with nested case control	N= 6972 Age = 62.3 (13.1) Sex =54.7 Male	Study conducted over a 6 year time period		MV HR ref tubular (1771/36): villous/tubulovillous (3368/97) 1.51 (1.02-2.23)			Low risk of bias
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Villous%: None 11.7 (10.2-13.3); at least one 15.5% (13.9-17.7) OR 1.4 (1.1-1.7)				High risk of bias
Emilsson 2017 (and Loberg 2014)	Retrospective cohort	N= 90,864 Age = median 67.7yr) 40–49 (7.9%) 50–59 (19.7%) 60–69 (29.4%) 70–79 (29.3%) =/+ 80 (13.7%)	Long term follow up - Median follow-up was 7.2 years [Does not report number of follow ups]				UV HR(95%CI): Villous or tubulovillous (v tubulous) 1.56 (1.36–1.79) P<.01	Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		Sex = 51.5 Male					MV analysis: 1.30 (1.13–1.50) P<.01."	
Faccioruss o 2016a b	Retrospectiv e cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male)	FS at 3 years.	UV OR (95% CI) Ref: Tubular Tubulo-Villous 1.49 (0.47-5.18) Villous 1.73 (0.68 - 4.45)				Low risk of bias
Fairley 2014	Retrospectiv e cohort	N= 3300 Age = NR for sub cohort Sex = NR for sub cohort	FS+ (all patients had one or more screening / surveillance colonoscopies (Time NR)	Villous - present or absent: OR (95%CI) 3.7 (2.9, 4.7; p0.0001)	Villous - present or absent OR (95%CI) 7.4 (2.5, 21.5; 0.01)			Low risk of bias
Huang 2012a	Retrospectiv e cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years		Interval CRC Tubular: 1 Tubulovillous and villous adenoma: 1.38 (1.03 - 1.85), p=0.030			Low risk of bias
Huang 2010	Retrospectiv e cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	Tubular ref (n20/2.1%) tubulovillous and villous histology(n103/26.1%) (HR 2.57; 95% CI 1.24–5.32) p=0.011				Low risk of bias
Laish 2017	Retrospectiv e cohort	N=1165 Age = 62.4±9.6 Sex = 54.2% male	Interval between procedures was at least 1 year and less than 5 years	Small TVA odds ratio 0.63 (0.36-1.12); Large TVA OR 2.11 (1.40-3.19)	Small TVA 3/199 (1.5%), of which 2 were IMC and 1 was invasive; Large TVA 3/233 (1.3%), of which all were invasive.			Low risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013;	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Villous /tubulovillous component (ref no villous component 78/1521) RR AA (47/347) v NAA (111/384) 2.38 (1.56-3.64); AA v No A (226/384) 2.25 (1.49-3.39)				Low to moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
Leung 2010)								
*Lee 2013	Retrospective cohort study	N = 1760 patients with high-risk adenoma detected at index colonoscopy Age = 65.8±3.5 Sex = 76% Male	1 year – mean interval between index and surveillance 387 (SD = 89) days	*MV OR (95% CI) *Villous = 1.98 (1.11 - 3.53), p=0.020 (absolute rates = 101 (6.2%) of 1634 vs 15 (11.9%) of 126].				Moderate risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	*Tubular is reference (AA 9.7% (95%CI 9.0–10.4) CRC 0.6% (95%CI 0.4–0.7). Tubulovillous/villous (AA 16.8% (15.1–18.5); CRC 0.9% (0.5–1.4) adjusted OR 1.28 (1.07-1.52)				Low risk of bias
Nusko 2008	Prospective cohort	N = 1091 Age = 57.06 Sex = 64.16%	Up to 4 surveillance intervals.(at 2 or 4 yr intervals)	At index: villous n=201, 35.1%) at 1st recurrence (FS) n = 121 (21.2%) p<0.0001				High risk of bias
*Park 2016	Retrospective cohort study	N = 1479 patients with high-risk adenoma detected at index colonoscopy who underwent their last colonoscopic surveillance ≥ 2.5 years after index colonoscopy were identified. Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): TVA or VA 1.29 (0.92–1.81)				Moderate risk of bias
Solakoglu 2017	Prospective Cohort	N = 47 Age =55.81 ±10.84 Sex = 72.3%	3 years	MV OR: 2.700, 95%CI: 0.405, 18.002, p = 0.990				High risk of bias
*Van Heijningen 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m)	*MV OR (95%CI) Villous (AA 20 (13%); CRC 6 (3.8%) OR 2.0 (1.2-3.2)				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
			Mean number of surveillances 1.7 (range 1-5)					
CQ1.3 Polyp: Size of largest adenoma (variants: ≥10mm, or ≥20mm) Polyp: Size of largest adenoma NOT greater than (variants: ≥10mm, or ≥20mm)								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref <10mm (n42/12.00%) OR (95%) (n=4608) 10–14 (n190/12.05%) 1.00 (0.7 to 1.43) 15–19 (n122/12.80%) 1.08 (0.74 to 1.57) ≥ 20 (n369/21.35%) 1.99 (1.41 to 2.80) MV FS: Model 1 interval as categorical Largest adenoma (mm) < 20 (ref) ≥ 20 1.69 (1.39 to 2.06) MV FS: Model 2 interval as continuous Largest adenoma (mm) < 20 (ref) ≥ 20 1.69 (1.39 to 2.06)	UV Ref <10mm (n1/0.29%) OR (95%)(n=4608) 10–14 (n29/1.84%) 6.54 (0.89 to 48.16) 15–19 (n16/1.68%) 5.96 (0.79 to 45.10) ≥ 20 7.85 (n38/2.20%) (1.07 to 57.34)	UV HR (95% CI): (n=11944) (vs<10mm n10/1029) 10-19mm (n116/6857) 1·62 (0·85–3·09) ; =/+20mm (n84/4058) 2·02 (1·05–3·89) p= 0·0495 Mulitvariate HR (95% CI):(vs<10mm)10-19mm 1·97 (1·01–3·81) =/+20mm 2·28 (1·16–4·50) p=0·0335		Low risk of bias
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Size%: <10mm 12.8 (10.6-13.1); 10-19mm 14.0 (12.3-15.6); =>20mm 14.5 (12.2-16.7. OR 10-19mm(ref <10mm) 1.2 (0.9-1.5); OR =>20mm (ref<10mm) 1.2 (0.9-1.6).				High risk of bias
Faccioruss o 2016a b	Retrospective cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male)	FS at 3 years.	UV OR (95%) (ref 15mm or more): 2.84 (1.75-4.19)p<0.001 MV OR >15mm (ref 15mm or less): 3.96 (1.87-7.55) <0.0001				Low risk of bias
Fairley 2014	Retrospective cohort	N= 3300 Age = NR for sub cohort	FS+ (all patients had one or more	size +/= 10mm versus 1-9 : OR (95%CI)	size +/= 10mm versus 1-9 : OR (95%CI)			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		Sex = NR for sub cohort	screening / surveillance colonoscopies (Time NR)	3.6 (2.8, 4.5; p0.0001)	5.2 (1.8, 15.1; 0.03)			
Huang 2012a	Retrospective cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years		Interval CRC <10 mm: 1 (n4/28.6%) ≥ 10mm: (n10/71.4%) 1.44 (0.35 - 5.94), p=0.612			Moderate risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cumulative recurrence 1 – 20 years.	(vs =/-10mm) (n149/20.2%) adenoma=/+20 mm (n 163/81.1%) (HR 2.35; 95% CI 1.09–5.06) p=0.029 10-19mm (n147/35.1%) (HR 1.25; 95% CI 0.60–2.62) p=0.584				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	n/s p=0.055				Low risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Size ≥1 cm (ref <1 cm 67/1204) RR AA (44/560) v NAA (167/560) 1.06 (0.69-1.61); AA v No A (349/560) 0.93 (0.61-1.41)				Low to moderate risk of bias
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years	UV analysis OR (95%CI): Large (≥10 mm) 1.501 (0.589-3.827)P=0.395. MV analysis: 1.441 (0.538-3.860) P=0.468				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
*Lee 2013	Retrospective cohort study	N = 1760 patients with high-risk adenoma detected at index colonoscopy Age = 65.8±3.5 Sex = 76% Male	1 year – mean interval between index and surveillance 387 (SD = 89) days	*MV OR (95% CI) Size NS one or more very large (≥ 40 mm) adenomas (P = 0.160)				Moderate risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	*Size <5mm is reference (AA 7.7% (95%CI 6.6–8.7) CRC 0.5 (0.2–0.8). 5-<10mm (AA 8.7 (7.7–9.7) CRC 0.5 (0.2–0.7) adjusted OR 1.17 (0.95-1.42); 10-<20mm (AA 15.9% (95%CI 14.5–17.4) CRC 0.8 (0.5–1.2) OR 2.27 (1.84-2.78); 20+mm (AA 19.3% (95%CI 16.4–22.3) CRC 1.2 (0.4–2.0) OR 2.99 (2.24-4.00)				Low risk of bias.
Nusko 2008	Prospective cohort	N = 1091 Age = 57.06 Sex = 64.16%	Up to 4 surveillance intervals.(at 2 or 4 yr intervals)	Numbers and % of patients with size +/=10mm at index and each surveillance, plus p value for difference between numbers at each time point. Index n 273 (47.6%) 1st rec n = 98 (17.1%) p<0.00001				High risk of bias
*Park 2016	Retrospective cohort study	N = 1479 (high-risk adenoma at index and last surveillance ≥ 2.5 years after index). Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): Size =/+10mm 1.81 (1.28–2.55) =/+3 1.25 (0.91–1.72)				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
Solakoglu 2017	Prospective Cohort	N = 47 Age =55.81 ±10.84 Sex = 72.3%	3 years	Size (≥1cm vs. <1 cm) MV OR: 1.330, 95%CI: 0.818, 2.162, p = 0.667				High risk of bias
*Van Heijningen 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	*MV OR (95%CI) Size =>10mm (AA 88 (7.5%; CRC 20 (1.7%) OR 1.7 (1.2-3.2)				Moderate risk of bias
CQ1.4 Polyp: Number of adenomas (variants: 1,2,3,4,5-9,10+; the main categories may be 1-2, 3-4 and 5+ but we would like to capture all reported variations) N/a								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref 1 adenoma (n470/15.13%) OR (95%)(n=4608) 2 (n211/18.33%) 1.26 (1.05 to 1.51) 3 (n25/10.42%) 0.65 (0.43 to 1.00) 4 (n17/15.45%) 1.03 (0.61 to 1.74) MV FS: Model 1 interval as categorical Number of adenomas, 1 (ref) 2 1.25 (1.02 to 1.54) 3 1.22 (0.76 to 1.96) 4 2.05 (1.14 to 3.67) MV FS: Model 2 interval as continuous Number of adenomas, 1 (ref) 2 1.25 (1.02 to 1.53) 3 1.22 (0.76 to 1.96) 4 2.05 (1.14 to 3.67)	UV Ref 1 adenoma(n62/2.00%) OR (n=4608) (95%) 2 (n21/1.82%) 0.91 (0.55 to 1.50) 3 (n1/0.42%) 0.21 (0.03 to 1.49)	UV HR (95% CI): (n=11944) (vs1 n143/7842) 2(n57/3073): 1·12 (0·82–1·52) ; 3or4 (n10/1029) 0·58 (0·31–1·11) p=0·12		Low risk of bias
Coleman 2015	Retrospective cohort with nested case control	N= 6972 Age = 62.3 (13.1) Sex =54.7 Male	Study conducted over a 6 year time period		MV HR vref 1 (5414/161) 2 or more (1558/32) 0.67 (0.45-0.97)			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
Cottet 2012	Retrospective cohort study	N= 5779 Age = 61.1 (12.9) years in men; 62.2 (13.6) years in women (p<0.001). <60 years: 41% 60-79: 50.8% =/+80 8.2% Sex = 58.4% Male	FS Median follow up 7.7 year (IQR -5.2-10.5)		AA at index: SIR (95% CI) 1 adenoma 2.32 (1.62-3.21) 2 or more 2.07 (1.21 to 3.32) Non AA at index: 1 adenoma 0.71 (0.44 to 1.10) 2 or more 0.59 (0.21 to 1.28)			Low risk of bias
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Number%: <3: 11.4 (9.9-12.9; 3-4: 14.8 (12.7-16.8); 5-9: 18.4 (15.5-21.4) OR 3-4 (ref <3) 1.3 (1.0-1.7); OR 5-9 (ref <3) 1.7 (1.2-2.3).				High risk of bias
Emilsson 2017 (and Loberg 2014)	Retrospective cohort	N= 90,864 Age = median 67.7yr) 40–49 (7.9%) 50–59 (19.7%) 60–69 (29.4%) 70–79 (29.3%) =/+ 80 (13.7%) Sex = 51.5 Male	Long term follow up - Median follow-up was 7.2 years				UV analysis HR(95%CI): =/+2 (v 1) 1.40 (1.21–1.63)P<0.01. MV analysis: 1.30 (1.10–1.55) P<0.01.	Low risk of bias
Facciorusso 2016a b	Retrospective cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male)	FS at 3 years.	UV OR Number of ACAs >1 (ref 1): 2.69 (1.88-4.53) p<0.001 MV Number of ACAs >1 (ref 1): 3.22 (2.19-5.39) p<0.001				Low risk of bias
Fairley 2014	Retrospective cohort	N= 3300 Age = NR for sub cohort Sex = NR for sub cohort	FS+ (all patients had one or more screening / surveillance colonoscopies (Time NR)	number 3 or more vs 1 or 2: OR (95%CI) 2.4 (1.9, 3.0; p<0.0001)	number 3 or more vs 1 or 2: OR (95%CI) 4.3 (1.4, 12.9; 0.01)			Low risk of bias
Huang 2012	Retrospective cohort –	N = 197 Age = 52 +/- 6.4	FS- 5 years	2 or fewer adenomas (ref).				Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
	data for the sub cohort with baseline adenomas	Sex = NR for sub cohort		3 or more adenomas: 13 (33.3%) RR 1.24 (1.22-5.10) p 0.018				
Huang 2012a	Retrospective cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years		Interval CRC <2: 1 (n8/57.1%) ≥ 3: (n6/42.9%) 0.37 (0.98 - 1.42) p=0.142			Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	multiple adenomas vs 1(n37/4.6%): 2(n15/ 6.1%) (HR 1.92 (1.04–3.54) p=0.037) =/+3(n70/23.0%) (HR 1.87 (1.12–3.10) p= 0.016				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	MV OR 1.150 (1.069-1.237) (higher number of adenomas).				Low risk of bias
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	*HR (95%CI) 3 or more adenomas 1.10 (0.84-1.43)				Moderate risk of bias
Laish 2017	Retrospective cohort	N=1165 Age = 62.4±9.6 Sex = 54.2% male	Interval between procedures was at least 1 year and less than 5 years	1-2 NAAs reference: ≥3 NAAs OR 2.32 (1.63-3.54); MAAs 3.11 (1.90-5.09)	1-2 NAAs 5/470 (1.1%) of which 3 were IMC and 2 were invasive; ≥3 NAAs 2/74 (2.7%) of which 1 was IMC and 1 was invasive; MAAs 4/109 (3.7%) of which all were invasive.			Low risk of bias
Laiyamo 2008 (Laiyamo 2011;	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	≥3 (ref =/<2: 97/1623) AA (28/282) v NAA (142/282) RR 1.06 (0.62-1.55); AA v No A (112/282) RR 1.46 (0.96-2.22)				Low to moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
Laiyamo 2012; Laiyamo 2013; Leung 2010)								
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): Multiple (≥2) 2.051 (0.790–5.324) P=0.140. MV analysis: 1.963 (0.705–5.467) P=0.197				Moderate risk of bias
*Lee 2013	Retrospective cohort study	N = 1760 patients with high-risk adenoma detected at index colonoscopy Age = 65.8±3.5 Sex = 76% Male	1 year – mean interval between index and surveillance 387 (SD = 89) days	*MV OR (95% CI) Number NS - one or more large (≥ 10 mm) adenomas (P = 0.860), Number Ns multiple (≥ 10) adenomas (P = 0.395)				Moderate risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	*Number 1 is reference (AA 8.6% (95%CI 7.8–9.3) CRC 0.5 (0.4–0.7) 2: AA 12.7% (11.3–14.1) CRC 0.5% (0.2–0.9) OR 1.39 (1.17–1.66) 3: AA 15.3% (12.9–17.6) CRC 1.1% (0.4–1.8) OR 1.85 (1.46–2.34) 4: AA 19.6% (15.3–23.9) CRC 1.2 (0.0–2.4) OR 2.41 (1.71–3.40) 5+: AA 24.1 (19.8–28.5) CRC 0.8 (0.0–1.7) OR 3.87 (2.76–5.42)				Low risk of bias
Solakoglu 2017	Prospective Cohort	N = 47 Age =55.81 ±10.84 Sex = 72.3%	3 years	Number (per 1 increase): MV OR: 2.318, 95%CI: 0.415, 0.384, p = 0.445				High risk of bias
*Van Heijninge n 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m)	*MV OR (95%CI) Number (1 ref: AA n=83; 4%) CRC n = 25; 1.2%):				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
			Mean number of surveillances 1.7 (range 1-5)	2: (AA 39; 7%: CRC 9; 1.6%) OR1.6 (1.1-2.4) 3: (AA 21; 8.7%); CRC 4; 1.6%) OR 2.1 (1.3-3.4) 4: (AA 8 (11.7%) CRC 0) OR 2.0 (0.9-4.6) 5+ (AA 14 (17.7%) CRC 0) OR 3.3 (1.7-6.6)				
*Vemulapalli 2014	Retrospective cohort study	N=1414 Age = (split by 5 groups increasing in risk) Grp 1: 56.7 (10.4); Grp 2: 60.6 (9.4); Grp 3: 62.3 (9.4); Grp 4: 61.3 (11.3); Grp 5: 64.7 (10.2). Sex = Male Grp 1: 51.4%; Grp 2: 64.4%; Grp 3: 67.7%; Grp 4: 52.7%; Grp 5: 62.6%.	FS >200 days and less than 3 years.	UV OR(95% CI) Number: 1-2 <10mm (ref); 3-4 <10mm 1.2 (0.4-3.4) =>5 <10mm 3.1 (1.2-8.2) 3-4 with 1 =>10mm 5.6 (2.1-15.1) =>5 with 1 =>10mm 10.8 (4.5-25.7)				Moderate risk of bias
CQ1.5 Polyp: Presence of adenoma in proximal colon Polyp: Absence of adenoma in proximal colon								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref Not in Proximal (n519/15.60%) OR (95%)(n=4608) Proximal (n204/15.91%) 1.02 (0.86 to 1.22) MV FS: Model 1 interval as categorical Proximal polyp, No (ref) Yes 1.28 (1.04 to 1.58) MV FS: Model 2 interval as continuous Proximal polyp, No (ref) Yes 1.28 (1.04 to 1.58)	UV Ref Not in Proximal (n60/1.80%) OR (95%)(n=4608) Proximal (n24/1.87%) 1.04 (0.64 to 1.67)	UV HR (95% CI): (n=11944) (vs not proximal n137/8295) Proximal (n73/3649) 1·38 (n=11944) (1·04–1·84) p= 0·0285 MV HR (95% CI): (vs not proximal) Proximal 1·76 (1·30–2·38) p= 0·0004		Low risk of bias
Cottet 2012	Retrospective cohort study	N= 5779 Age = 61.1 (12.9) years in men; 62.2 (13.6) years in women (p<0.001). <60 years: 41% 60-79: 50.8%	FS Median follow up 7.7 year (IQR -5.2-10.5)		AA at index: SIR (95% CI) Adenoma location Proximal only 1.26 (0.25 to 3.67)			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		=/+80 8.2% Sex = 58.4% Male			Distal only 2.08 (1.33 to 3.09) Non AA at index: Proximal only 0.63 (0.20 to 1.47) Distal only 0.68 (0.34 to 1.22)			
Emilsson 2017 (and Loberg 2014)	Retrospective cohort	N= 90,864 Age = median 67.7yr) 40–49 (7.9%) 50–59 (19.7%) 60–69 (29.4%) 70–79 (29.3%) =/+ 80 (13.7%) Sex = 51.5 Male	Long term follow up - Median follow-up was 7.2 years				UV analysis HR(95%CI): Proximal (v distal) 0.96 (0.71-1.30)P=0.78. UV analysis HR(95%CI): Multiple or unspecified (v distal) 0.99 (0.79-1.24)P=0.94.	Low risk of bias
Huang 2012	Retrospective cohort – data for the sub cohort with baseline adenomas	N = 197 Age = 52 +/- 6.4 Sex = NR for sub cohort	FS- 5 years	Any proximal is reference(10/13.5%). Distal only: 15 (14.3%), RR 0.76 (0.45-1.24) p=0.359				Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	v any proximal(n77/13.7%): Distal only (n46/5.8%) (HR 0.77 (0.48–1.22) p=0.259				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	n/s p=0.831				Low risk of bias
Laiyamo 2008 (Laiyamo	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2	Proximal (ref distal 49/1030) AA (73/834) v NAA (316/834)				Low to moderat

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)			years after the end of the trial)	RR 1.58 (1.11-2.25); AA v No A (445/834) RR 1.84 (1.31-2.59) Proximal only adenoma at baseline had increased risk of AA recurrence (RR=1.50, 0.99-2.27)				e risk of bias
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): Proximal 0.608 (0.239–1.545)				Low risk of bias
*Lee 2013	Retrospectivecohort study	N = 1760 patients with high-risk adenoma detected at index colonoscopy Age = 65.8±3.5 Sex = 76% Male	1 year – mean interval between index and surveillance 387 (SD = 89) days	*MV OR (95% CI) Proximal = 1.76 (1.13-2.74, p=0.012 (89/116 = 7.7%) [27 (4.5%) of 606 vs 89 (7.7%) of 1154				Moderate risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR (95%CI) *Distal is reference (AA 8.5% (95%CI 7.7–9.3) CRC 0.4 (0.2–0.6) *Proximal only AA 11.8% (10.6–13.1) CRC 0.8% (0.5–1.2). OR 1.68 (1.43-1.98)				Low risk of bias
Solakoglu 2017	Prospective Cohort	N = 47 Age =55.81 ±10.84 Sex = 72.3%	3 years	Distal, OR: 1.419, 95%CI: 0.143, 3.536, p = 1.000; Both. OR: 0.800, 95%CI: 0.080, 8.007, p = 0.567				High risk of bias
*Van Heijningen 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	*MV OR (95%CI) Proximal (AA 77/950 (8%); CRC 13/950 (1.4%) OR 1.6 (1.2-2.3)				Moderate risk of bias
CQ1.6 Polyp: Adenoma morphology (variants: pedunculated, sessile, flat) N/a								
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%).	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Flat%: No 13.0 (11.8-14.2); Yes 15.4 (12.0-18.7) OR 1.2 (0.9-1.6)				High risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		Sex = Male HR 74.9%; IR 67.4%.						
Facciorusso 2016a b	Retrospective cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male)	FS at 3 years.	UV OR (95% CI) (ref pedunculated) Sessile 1.96 (1.12-2.43) nonpolypoid 2.43 (1.14-3.26)				Low risk of bias
Huang 2012	Retrospective cohort – data for the sub cohort with baseline adenomas	N = 197 Age = 52 +/- 6.4 Sex = NR for sub cohort	FS- 5 years	Pedunculated is reference. Flat: 5 (14.7%) RR 1.28 (0.95-2.26)				Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	v's peduculated(n86/7.8%): Flat (n37/14.3%) (HR 1.48 (0.97-2.24) p=0.067				Low risk of bias
CQ1.7 Patient: Male gender Patient: Female gender								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	Finding at FS (FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref Male (n398/ 15.60% OR (95%)(n=4608) Female(n325/15.80%) 1.02 (0.87-1.19)	UV Ref Male OR (95%)(n=4608) Female 0.72 (0.46-1.13)	UV HR (95% CI): (n=11944) (vs women n96/5319) men (n114/6625) 1·02 (0·77–1·33) p= 0·91 Mulitvariate HR (95% CI): (vs women) men 1·14 (0·86–1·50) p= 0·35		Low risk of bias
Coleman 2015	Retrospective cohort with nested case control	N= 6972 Age = 62.3 (13.1) Sex =54.7 Male	Study conducted over a 6 year time period		MV HR ref female (3157/68): Male (3815/125) 1.69 (1.26-2.27)			Low risk of bias
Cottet 2012	Retrospective cohort study	N= 5779 Age = 61.1 (12.9) years in men; 62.2 (13.6) years in women (p<0.001). <60 years: 41% 60-79: 50.8% =/+80 8.2% Sex = 58.4% Male	FS Median follow up 7.7 year (IQR -5.2-10.5)		AA at index: SIR (95% CI) Gender Men 2.08 (1.48 to 2.90) Women 2.59 (1.65 to 4.06) Non AA at index Men 0.64 (0.40 to 1.03)			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
					Women 0.77 (0.40 to 1.48)			
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Sex%: Female 11.5% (9.60-13.5) Male 14.7 (13.3-16.1) OR 1.1 (0.9-1.4).				High risk of bias
Emilsson 2017 (and Loberg 2014	Retrospective cohort	N= 90,864 Age = median 67.7yr) 40–49 (7.9%) 50–59 (19.7%) 60–69 (29.4%) 70–79 (29.3%) =/+ 80 (13.7%) Sex = 51.5% Male	Long term follow up - Median follow-up was 7.2 years				UV analysis HR(95%CI):Male (v female) 1.01 (0.88–1.16) MV: 0.89 (0.78-1.02)	Low risk of bias
Faccioruss o 2016a b	Retrospective cohort	n = 843 Age: Median 58 (IQR 52-67) Sex: 61.9% Male)	FS at 3 years.	UV OR (95% CI) (ref female) 1.47 (0.87-1.88)				Low risk of bias
Huang 2012a	Retrospective cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years	-	Interval CRC Male: 1 (n11/78.6%) Female: (n3/21.4%) 0.72 (0.19 - 2.69)	-	- -	Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	v's Female(n18/3.7%): Male sex (n105/12.2%) (HR 2.11; 95% CI 1.27–3.53) p=0.004				Low risk of bias
Huang 2012	Retrospective cohort – data for the sub cohort with baseline adenomas	N = 197 Age = 52 +/- 6.4 Sex = NR for sub cohort	FS- 5 years	Women is reference. Male: n21 RR 2.18 (1.13-3.06) p=0.003				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	Male gender OR 2.757 (1.015-7.489)				Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	HR (95%CI) Male 1.36 (0.97-1.92).				Moderate risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Male RR AA v NAA 1.22 (0.81-1.84); AA v No A RR 1.34 (0.90-2.01)		Of the new cases diagnosed during the PPT-CFS, 78% (7/9) were diagnosed in men.		Low to moderate risk of bias
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): Male sex 0.599 (0.195–1.845) MV analysis: 0.884 (0.227–3.436)				Low risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR (95%CI) *Female is reference (AA 9.8% (95%CI 8.7–10.9) CRC 0.3% (0.1-0.5) Male AA 11.7% (10.9–12.5) CRC 0.8 (0.6–1.0). OR 1.40 (1.19-1.65).				Low risk of bias
Morelli 2013 (Imperiale, 2014)	Retrospective cohort	N = 965 Age = 57.8 (9.8) Sex = 62% Male	Mean (median) SD interval between index and first surveillance colonoscopies was 33.9 (36.3) 20.2 months; and 44.1 (38.5) 18.6 months between first and second surveillance.	Men v women: MV OR (95% CI) FS 1.28 (0.79-2.08)				

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
*Park 2016	Retrospective cohort study	N = 1479 patients with high-risk adenoma detected at index colonoscopy who underwent their last colonoscopic surveillance ≥ 2.5 years after index colonoscopy were identified. Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): *Male sex 1.37 (0.91–2.08)				Moderate risk of bias
Pinksy 2009	Retropective cohort study	N = 2607 Age = 63 years Sex = 60% Male	FS mean 3.4 - 4.3 yrs (depending on index adenoma)	MV OR Ref: Female Male, 1.2 (0.9 to 1.8)				
Solakoglu 2017	Prospective Cohort	N = 47 (high risk only) Age =55.81 ±10.84 Sex = 72.3%	3 years	MV OR: Male 0.625, 95%CI: 0.063, 6.180, p = 0.517				High risk of bias
Tae 2017	Retrospective cohort study	N = 2904 Age = 57.5 ± 9.0 Sex = 71.3% Male	FS - Mean follow up period 3 years, patients underwent 1.3 surveillance colonoscopies	Male gender associated with AA: MV: OR (95% CI) 1.59 (1.09-2.34) p=0.017				Moderate risk of bias.
*Vemulapalli 2014	Retrospective cohort study	N=1414 Age = (split by 5 groups increasing in risk) Grp 1: 56.7 (10.4); Grp 2: 60.6 (9.4); Grp 3: 62.3 (9.4); Grp 4: 61.3 (11.3); Grp 5: 64.7 (10.2). Sex = Male Grp 1: 51.4%; Grp 2: 64.4%; Grp 3: 67.7%; Grp 4: 52.7%; Grp 5: 62.6%.	FS >200 days and less than 3 years.	*UV OR(95% CI) Male: 0.8 (0.4-1.4)				Moderate risk of bias
CQ1.8 Patient: Family history of CRC Patient: NO Family history of CRC								
Cottet 2012	Retrospective cohort study	N= 5779 Age = 61.1 (12.9) years in men; 62.2 (13.6) years in women (p<0.001). <60 years: 41%	FS Median follow up 7.7 year (IQR -5.2-10.5)		AA at index: SIR (95% CI) Known family history of colorectal cancer Yes 3.76 (1.51 to 7.75)			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		60-79: 50.8% =/+80 8.2% Sex = 58.4% Male			No 2.10 (1.54 to 2.81) Non AA at index Yes 0.77 (0.09 to 2.77) No 0.67 (0.43 to 1.00)			
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	n/s p=0.108				Low risk of bias
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	HR (95%CI) Family history of CRC 0.92 (0.43-1.96).				Moderate risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)			Of the new CRC cases diagnosed during the PPT-CFS, 44% (4/9) had a family history of CRC.		Low to moderate risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR(95%CI) *Family history of CRC. No is reference. (AA 11.0% (10.3–11.8) CRC 0.6% (0.4–0.8) Yes AA 11.6% (10.3–13.0) CRC 0.6% (0.3–0.9). OR 1.17 (0.99-1.38)				Low risk of bias.
*Park 2016	Retrospective cohort study	N = 1479 patients with high-risk adenoma detected at index colonoscopy who underwent their last colonoscopic surveillance ≥ 2.5 years after index colonoscopy were identified. Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): Family history of CRC 0.61 (0.23–1.67)				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		(n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.						
Tae 2017	Retrospective cohort study	N = 2904 Age = 57.5 ± 9.0 Sex = 71.3% Male	FS - Mean follow up period 3 years, patients underwent 1.3 surveillance colonoscopies	MV: OR (95%CI) 0.284 1.69 (0.81-3.46) p=0.168				Moderate risk of bias.
CQ1.9 Patient: Younger age (e.g. <55 vs 55+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Younger age range								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref <55yr (n 107/ 10.44%) OR (95%)(n=4608) ≥ 55 and <60 (n105/ 16.88%) 1.74 (1.30-2.33) ≥ 60 and< 65 (n116/ 14.72%) 1.48 (1.12 to 1.96) ≥ 65 and < 70 (n118/ 14.51%) 1.46 (1.10 to 1.93) ≥ 70 and < 75 (n137/ 19.19%) 2.04 (1.55 to 2.68) ≥ 75 and < 80 (n87 /21.07%) 2.29 (1.68 to 3.12) ≥ 80 (n53/ 22.75%) 2.53 (1.75 to 3.64) MV Effects of age as a risk factor on AA incidence at FS: Model 1 interval as categorical Age (years) < 55 (Ref) ≥ 55 and < 60 1.56 (1.14 to 2.13) ≥ 60 and < 65 1.37 (1.01 to 1.85) ≥ 65 and < 70 1.24 (0.91 to 1.68)	UV Ref <55yr OR (95%)(n=4608) (n8/ 0.78%) ≥ 55 and <60 (n2/ 0.32%) 0.41 (0.09 to 1.94) ≥ 60 and< 65 (n9 /1.14%) 1.47 (0.56 to 3.82) ≥ 65 and < 70 (n15 /1.85%) 2.39 (1.01 to 5.66) ≥ 70 and < 75 (n16 /2.24%) 2.91 (1.24 to 6.85) ≥ 75 and < 80 (n21 /5.08%) 6.81 (2.99 to 15.5) ≥ 80 (n13/ 5.58%) 7.51 (3.08 to 18.34) MV FS: Model 1 interval as categorical Age (years), < 55 (ref) ≥ 55 and < 60 0.20 (0.02 to 1.61)	UV HR (95% CI): (n=11944) (vs<55 n23/2122) 55-64 years (n39/3179) 1·33 (0·79–2·23) ; 65-74 years (n84/3957) 2·87 (1·80–4·57) p<0·0001 =/+75(n64/2686) years 4·72 (2·90–7·67) p<0·0001 Mulitvariate HR (95% CI):(vs<55) 55-64 years 1·28 (0·77–2·15); 65-74 years 2·66 (1·66–4·24) p<0·0001 =/+75 years 3·82 (2·33–6·27) p<0·0001		Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
				≥ 70 and < 75 1.74 (1.30 to 2.35) ≥ 75 and < 80 1.81 (1.28 to 2.54) ≥ 80 1.81 (1.21 to 2.70) MV Effects of age as a risk factor on AA incidence at FS : Model 2 interval as continuous Age (years) < 55 (Ref) ≥ 55 and < 60 1.57 (1.15 to 2.15) ≥ 60 and < 65 1.37 (1.01 to 1.86) ≥ 65 and < 70 1.24 (0.92 to 1.68) ≥ 70 and < 75 1.75 (1.30 to 2.35) ≥ 75 and < 80 1.81 (1.28 to 2.54) ≥ 80 1.81 (1.21 to 2.71)	≥ 60 and < 65 1.18 (0.44 to 3.18) ≥ 65 and < 70 1.86 (0.76 to 4.55) ≥ 70 and < 75 2.11 (0.86 to 5.19) ≥ 75 and < 80 5.92 (2.56 to 13.71) ≥ 80 4.68 (1.81 to 12.07) MV FS: Model 2 interval as continuous Age (years), < 55 (ref) ≥ 55 and < 60 0.20 (0.02 to 1.57) ≥ 60 and < 65 1.16 (0.43 to 3.12) ≥ 65 and < 70 1.86 (0.76 to 4.56) ≥ 70 and < 75 2.18 (0.89 to 5.35) ≥ 75 and < 80 6.21 (2.69 to 14.35) ≥ 80 5.03 (1.96 to 12.94)			
Coleman 2015	Retrospective cohort with nested case control	N= 6972 Age = 62.3 (13.1) Sex =54.7 Male	Study conducted over a 6 year time period		MV HR vs <50(1,237/18): 50–<60 1.27 (1609/29 1.8%) (0.71–2.29) 60–<70 1.99 (1916/51 2.7%) (1.16–3.41) 70–<80 (1613/60 3.7%) 3.10 (1.83–5.26) 80 or older (597/35 5.9%) 6.16 (3.48–10.91)			Low risk of bias
Cottet 2012	Retrospective cohort study	N= 5779 Age = 61.1 (12.9) years in men; 62.2 (13.6) years in women (p<0.001). <60 years: 41% 60-79: 50.8%	FS Median follow up 7.7 year (IQR -5.2-10.5)		AA at index: SIR (95% CI) Age (years) <60 3.65 1.88 to 6.37 60-79 1.75 1.18 to 2.50 =/>80 3.32 1.66 to 5.95			Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
		=/+80 8.2% Sex = 58.4% Male			Non AA at index <60 0.39 0.08 to 1.13 60-79 0.74 0.45 to 1.15 =/>80 0.84 0.17 to 2.44			
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Age%: 50-59yr 13.3 (11.5-15) 60-69 yr 14.1 (12.6-15.6) OR 1.0 (0.8-1.2).				High risk of bias
Emilsson 2017 (and Loberg 2014)	Retrospective cohort	N= 90,864 Age = median 67.7yr) 40–49 (7.9%) 50–59 (19.7%) 60–69 (29.4%) 70–79 (29.3%) =/+ 80 (13.7%) Sex = 51.5% Male	Long term follow up - Median follow-up was 7.2 years				UV analysis: Ref 40-49yr HR(95%CI):50–59 yr 2.20 (1.43, 3.38) <.01 MV: 2.13 (1.38, 3.27) <.01 UV HR (95%CI):60–69 yr 3.55 (2.35, 5.36) <.01 MV: 3.50 (2.31, 5.29) <.01 UV HR (95%CI):70–79 yr 6.37 (4.21, 9.63) <.01 MV: 6.10 (4.03, 9.22) <.01	Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
							UV HR (95%CI):≥80 yr 16.07 (10.47 24.66)<.01 MV:14.97 (9.74, 23.01) <.01	
Huang 2012	Retrospective cohort – data for the sub cohort with baseline adenomas	N = 197 Age = 52 +/- 6.4 Sex = NR for sub cohort	FS- 5 years	Reference is 50-60 years. >60 years: 16 (27.6%) RR 3.91 (2.48-7.52) p<0.001				Low risk of bias
Huang 2012a	Retrospective cohort	N= 1794 Age = Mean NR <50: 40% 50-60: 29% >60 years: 30% Sex = 64% Male	FS combined (had "at least one surveillance"), 2.67 years		Interval CRC <50: 1(reference) (n2) 50-60: (n3) 0.26 (0.05 - 1.26) p=0.094 ≥60: (n9) 1.34 (1.08 - 1.92), p=0.030			Low risk of bias
Huang 2010	Retrospective cohort	N= 1356 Age = 52.4 (±12.5) (range 20– 84 years) Sex = 63.6% male	FS SS subsequent - data on cummulative recurrence 1 – 20 years.	Age vs <50yr(n20/3.6%)s: 50-60yrs (n43/10.9%) (HR1.81 (1.05–3.12) p=0.03 >60yrs (n60/14.7%) (HR 4.81 (2.80–8.25) p=<0.001				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	n/s p=0.059				Low risk of bias
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	HR (95%CI). *Age 1.02 (1.01-1.03).				Moderate risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo	Prospective cohort (from thePPT)	N = 1905 Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Per 1-year increase AA v NAA RR 1.04 (1.02-1.06); AA v No A RR 1.05 (1.03-1.07)				Low to moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
2012; Laiyamo 2013; Leung 2010)								
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): Age continuous 1.045 (0.995-1.096)P=0.076. MV analysis: 1.062 (1.008–1.118) P=0.024) independent risk factor for AA in MV analysis.				Low risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR (95%CI) *Age: 50-59 is reference (AA 8.6 (7.5–9.8) CRC 0.3 (0.1–0.6). <40 (AA 3.9% (95%CI 0.8–7.0) CRC 0.0) OR 0.41 (0.18-0.94); 40-49 (AA 6.3 (4.7–8.0) CRC 0.1 (0.0–0.4)) OR 0.67 (0.48-0.93); 60-69 (AA 12.2 (11.1–13.2) CRC 0.6 (0.3–0.8)) OR 1.39 (1.16-1.68); 70-79 (AA 14.5 (13.0–16.0) CRC 1.3 (0.8–1.7)) OR 1.72 (1.40-2.11); 80+ (AA 17.7 (8.2–27.3) CRC 1.6 (0.0–4.7)) OR 2.79 (1.31-5.57)				Low risk of bias
Morelli 2013 (Imperiale, 2014)	Retrospective cohort	N = 965 Age = 57.8 (9.8) Sex = 62% Male	Mean (median) SD interval between index and first surveillance colonoscopies was 33.9 (36.3) 20.2 months; and 44.1 (38.5) 18.6 months	Age (increase of 10 yr) MV OR (95%CI): FS 1.47 (1.16-1.87)				

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
			between first and second surveillance.					
*Park 2016	Retrospective cohort study	N = 1479 (high-risk adenoma at index and last surveillance ≥ 2.5 years after index). Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): *Age <50yrs as ref: 50-70yrs: 1.61 (0.96-2.71) >=70yrs: 2.56 (1.43-4.59)				Moderate risk of bias
Solakoglu 2017	Prospective Cohort	N = 47 Age =55.81 ±10.84 Sex = 72.3%	3 years	Age (per 10-year increase) MV OR: 1.984, 95%CI: 0.845, 1.150.				High risk of bias
Tae 2017	Retrospective cohort study	N = 2904 Age = 57.5 ± 9.0 Sex = 71.3% Male	FS - Mean follow up period 3 years, patients underwent 1.3 surveillance colonoscopies	The mean (SD) Age (years), was higher in patients who had recurrent AAs compared to those who did not: UV: 58.4 ± 9.1 v 59.5 ± 8.8 p=0.002 MV: OR (95%CI) 1.02 (1.01-1.04) p=0.027				Moderate risk of bias.
Van Enckevort 2014	Retrospective cohort	N= 433 Age = 55 (range 24-82) Sex = 41% Male	Median follow-up period was 85 months (range 9-260).	Age (continuous) (HR=1.05; 95% CI 1.03-1.07; p<0.001)				Moderate risk of bias
*Vemulapalli 2014	Retrospective cohort study	N=1414 Age = (split by 5 groups increasing in risk) Grp 1: 56.7 (10.4); Grp 2: 60.6 (9.4); Grp 3: 62.3 (9.4); Grp 4: 61.3 (11.3); Grp 5: 64.7 (10.2). Sex = Male Grp 1: 51.4%; Grp 2: 64.4%; Grp 3: 67.7%; Grp 4: 52.7%; Grp 5: 62.6%.	FS >200 days and less than 3 years.	*UV OR(95% CI) Age (yearly increments): 1.04 (1.01-1.07).				Moderate risk of bias
CQ1.10 Patient: Older age (e.g. <75 vs 75+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Older age range								

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
All evidence uses a reference of younger age so is included in CQ1.9								
CQ1.11 Patient: Smoking (variants: current, ex, never) N/a								
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	*HR (95%CI) Current or ex smoker 1.04 (0.78-1.37).				Moderate risk of bias
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): Smoking 2.409 (0.928–6.254)P=0.071. MV analysis: 2.969 (0.911–9.672) P=0.071.				Low risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR (95%CI) *Smoking Never is reference (AA 11.1% (95%CI 9.9–12.2) CRC 0.5 (0.2–0.8). Former (AA 12.1 (11.1–13.1) CRC 0.9 (0.6–1.2)) OR 1.08 (0.92-1.27); Current (AA 11.8% (10.0–13.5) CRC 0.2 (0.0–0.5)) OR 1.13 (0.90-42)				Low risk of bias
*Park 2016	Retrospective cohort study	N = 1479 patients with high-risk adenoma detected at index colonoscopy who underwent their last colonoscopic surveillance ≥ 2.5 years after index colonoscopy were identified. Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): Current or ex smoker 1.07 (0.77–1.47)				Moderate risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
Tae 2017	Retrospective cohort	N = 2904 Age = 57.5 ± 9.0 Sex = 71.3% Male	FS - Mean follow up period 3 years, patients underwent 1.3 surveillance colonoscopies	Current smoker MV: OR (95% CI) 0.69 (0.45-1.05) p=0.086				Moderate risk of bias.
CQ1.12 Patient: High body mass index (e.g. BMI>25)? Patient: NOT High body mass index								
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	n/s p=0.183				Low risk of bias
*Jung 2016	Retrospective cohort study	N = 1646 Age = HRF =>3: 61.7 (10.4); HRF =<2: 59.3 (9.7) years. Sex = Male HRF =>3: 340 (73.4%); HRF =<2: 876 (74%)	FS: HRF =>3: 4.0 years (range 2.5-11); HRF =<2: 4.1 years (range 2.5-10.9)	*HR (95%CI) BMI >25. 0.92 (0.71-1.19).				Moderate risk of bias
Laiyamo 2008 (Laiyamo 2011; Laiyamo 2012; Laiyamo 2013; Leung 2010)	Prospective cohort (from thePPT)	N = 1905 (only data for 1826 patients for weight and height) Age = 61.1 (9.9) Sex = 64.5% Male	4 years (end of trial). (follow up data at 6.2 years after the end of the trial)	Reference is <25kg/m2. 25-29 kg/m2 AA v NAA RR 0.99 (0.61-1.62), AA v No A RR 1.10 (0.69-1.77); 30-38.8 kg/m2 AA v NAA RR 1.58 (0.95-2.60), AA v No A RR 1.69 (1.04-2.75). Obesity was associated with an increased risk of advanced adenoma recurrence RR 1.62, 1.01-2.57.				Low to moderate risk of bias
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison)	UV analysis OR (95%CI): BMI (=/+25) 1.391 (0.475-4.075)P=0.554.				Low risk of bias
*Martinez 2009	Pooled analysis of 8 restrospective studies	N = 9167 Age = Mean 62.0 Sex = 71.2% male	Median follow-up was 47.2 months, range 36.9 to 59.0	MV OR (95%CI) *BMI <25 is reference (AA 11.7% (95%CI 10.4–13.1) CRC 0.5 (0.2–0.8)). 25-<30 AA 11.6 (10.6–12.7) CRC 0.7 (0.4–1.0)) (OR 1.00 (0.84-1.19);				Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
				30+ (AA 11.6 (10.2–12.9) CRC 0.8 (0.4–1.2)) 1.13 (0.93-1.38)				
*Park 2016	Retrospective cohort study	N = 1479 patients with high-risk adenoma detected at index colonoscopy who underwent their last colonoscopic surveillance ≥ 2.5 years after index colonoscopy were identified. Age = Group 1, < 50 years (n = 233) Group 2, 50–69 years (n = 1000) Group 3, ≥70 years (n = 246) Sex = Group 1 75.1% Male, Group 274.6% Male, Group 3 69.5% Male.	Mean time to the last colonoscopic surveillance was about 4 years. Groups 1, 2, and 3 (4.1 ± 1.4, 4.0 ± 1.4, and 4.0 ± 1.5, respectively).	*HR (95% CI): BMI 0.89 (0.62–1.27)				Moderate risk of bias
Tae 2017	Retrospective cohort study	N = 2904 Age = 57.5 ± 9.0 Sex = 71.3% Male	FS - Mean follow up period 3 years, patients underwent 1.3 surveillance colonoscopies	BMI MV: OR (95%CI) < 25 vs 25-29: 0.89 (0.64-1.23) p=0.481 Vs ≥ 30: 1.04 (0.46-2.35) p=0.935				Moderate risk of bias.
CQ1.13 Index colonoscopy Bowel prep quality (variants: good, adequate, inadequate/poor) Inadequate/poor bowel prep								
Atkin 2017	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	UV Ref Excellent/good OR (95%)(n=4608) Satisfactory 1.19 (0.89 - 1.59) Poor 1.54 (1.04 - 2.28) Unknown 1.39 (1.16 - 1.68)	UV Ref Excellent/good OR (95%)(n=4608) Satisfactory 0.66 (0.27 - 1.61) Poor 2.87 (1.36 - 6.06) Unknown 0.89 (0.55 - 1.46) MV FS: Model 1 interval as categorical Best bowel preparation, Excellent/good/satisfactory/unknown (ref) Poor 3.80 (1.79 to 8.05)	UV HR (95% CI): (n=11944) (vs Excellent or good) Satisfactory 1·41 (0·90–2·22) ; Poor 2·32 (1·33–4·06); Unknown 1·37 (0·99–1·91) p= 0·0299 Mulitvariate HR (95% CI):(vsExcellent or good) Satisfactory 1·51 (0·95–2·39); Poor 2·09 (1·19–3·67); Unknown 1·39 (1·00–1·94) p=0·0452		Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
					MV FS: Model 2 interval as continuous Best bowel preparation, Excellent/good/satisfactory/unknown (ref) Poor 3.30 (1.54 to 7.07)			
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Bowel prep%: Inadequate 21.4 (-0.1-42.9) Adequate 13.7 (12.6-14.9) OR 0.6 (0.2-2.4)				High risk of bias
Faccioruss o 2016a & b [sub sample]	Retrospective cohort	n = 746 Age: Median 58 (Range 36-81) Sex: 62.7% Male	FS at 3 years.	UV Split by local recurrence of ACAs and metachronous distant polyp occurrence (reference poor): All ns Local: Excellent 0.96 (0.75-1.32) Good 0.92 (0.81-1.13) Fair 1.03 (0.76-1.25) Met dist: Excellent 0.71 (0.55-0.92) Good 0.88 (0.73-1.04) Fair 0.93 (0.81-1.11)				Low risk of bias
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	Bowel preparation good or fair v poor OR 2.208 (1.238-4.662)				Low risk of bias
*Van Heijninge n 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	*MV OR (95%CI) Bowel prep (ref good) (AA 152 (5.6%); CRC 31 (1.1%) Moderate (AA 5 (2.2%); CRC 6 (2.6%) OR 0.8 (0.4-1.5) Insufficient (AA 8 (17.7%); CRC 1 (2.2%) OR 3.4 (1.6-7.4)				Moderate risk of bias
CQ1.14 Index colonoscopy complete to caecum incomplete colonoscopy								
Atkin 2017	Retrospective,	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance	FS or more (All surveillance intervals, 0, 1, 2 3+,	UV Ref Complete OR (95%)(n=4608) Unknown 1.78 (1.49 - 3.13)	UV Ref Complete OR (95%)(n=4608)	UV HR (95% CI): (n=11944) (vs Complete) Incomplete		Low risk of bias.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv (*indicates AN)	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Level of evidence (QUIPS)
				Absolute values (where available) and OR/HR/RR				
	multicentre, cohort study	visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	Incomplete 1.57 (1.22 - 2.02) MV FS: Model 1 interval as categorical Most complete colonoscopy, Complete (ref) Incomplete/unknown 1.92 (1.58 to 2.33) MV FS: Model 2 interval as continuous Most complete colonoscopy, Complete (ref) Incomplete/unknown 1.92 (1.58 to 2.33)	Unknown 1.00 (0.56 - 1.79) Incomplete 4.28 (2.61 - 7.03)	or not known 1·64 (1·24–2·16) p= 0·0007 Mulitvariate HR (95% CI):(vsComplete) Incomplete or not known 1·80 (1·34–2·41) p= 0·0001		
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	*Complete to caecum%: No 11.5 (-0.7-23.8); Yes 13.8 (12.6-14.9). OR 1.1 (0.3 -3.7)				High risk of bias
*Van Heijninge n 2013	Retrospective cohort study	N=2990 Age = 61.3 Sex = 1647 (55%) Male.	FS Median 24 months (IQR 12-40m) Mean number of surveillances 1.7 (range 1-5)	*MV OR (95%CI) Complete (yes ref) (AA 156 (5.6%); CRC 35 (1.2%) Proximal (AA 5 (2.8%); CRC 2 (1.1%) OR 0.6 (0.3-1.3) Distal (AA 4 (12%); CRC 1 (3%) OR 3.2 (1.2-8.5).				Moderate risk of bias
CQ1.15 Index colonoscopy by high-quality colonoscopist NOT high quality colonoscopist								
Jang 2015	Retrospective cohort	N = 434 Age = 61.0 +/- 8.6 Sex = 77.4% Male	FS more than 1 year since index	Endoscopist n/s p=0.135				Low risk of bias
CQ1.16 Index colonoscopy using high-adenoma-detecting technologies (variants: HD scope, chromoendoscopy) no high-adenoma-detecting technologies								
No evidence identified.								

UV Univariate; MV Multivariate (adjusted); OR Odds ratio; HR Hazard ratio; RR Risk Ratio; SIR standardised incidence ratio; AA Advanced Adenoma; CRC colorectal cancer; *Advanced Neoplasia (AN) a composite measure of AA and CRC. Green highlight indicates statistically significant positive associations. Red highlight indicates non significant findings. Pink highlight indicates statistically significant negative associations. Absolute values reported where available in the paper.

Synthesis of evidence for CQ1

CQ1.1
Thirteen studies reported evidence relating to risks at first surveillance associated with the presence of high grade dysplasia at index colonoscopy. There was fairly consistent evidence, with generally low to moderate risk of bias, for the risk of advanced adenoma (AA) with five studies (Atkin 2017; Facciorusso 2016; Van Enckevort 2014; Fairley 2014; Huang 2010) reporting statistically significantly increased odds of AA at first surveillance if HDG was present at index. Atkin (2017) reported an incidence of AA of 19.06% (OR 1.44 95%CI 1.18 - 1.75), and Huang (2010) reported an incidence of 27.7% (HR 1.61 95%CI 1.07–2.42). Odds ratios only were reported by Facciorusso (2016) and Fairley (2014), respectively, as 4.25 (95%CI 2.11-7.5) and 4.3 (95%CI 2.2 - 8.4), and Van Enckevort reported a hazard ratio of 1.73 (95% CI 1.13-2.64; p=0.012) . Five studies (Park 2016; Lee 2013; Martinez 2009; Cubiella 2016; Van Heijningen 2013) only reported statistical analyses on advanced neoplasia (AN) with four reporting no significant association between HDG at index and risk of AN at first surveillance, and the fifth study (Cubiella 2016) reporting an OR 0.7 (95%CI 0.5-0.98), showing significantly reduced risk associated with HGD. Again risk of bias was generally rated as moderate to low. Across these studies, where reported, incidence ranged from 12.1% (Cubiella 2016) for AN up to 16% for AA and CRC 1.3% (Martinez 2009). The risk of CRC at next surveillance was reported on in three studies all rated as having a low risk of bias (Atkin 2017; Fairley 2014; Huang 2012) and demonstrated consistent statistically significant associations between HDG at index and CRC incidence, although as the number of events was very small. One of these studies reported on the incidence of CRC as 3.06% (n26) (OR 2.09 95%CI 1.29 - 3.37) (Atkin, 2017; Huang 2012) respectively. The two other studies reported an odds ratio of 13.2 (95%CI 2.8 - 62.1) for incidence of CRC (Fairley 2014), and an odds ratio of 1.61 (95%CI 1.07 - 2.42) for interval CRC (Huang 2012). Only one study reported evidence for long term CRC incidence (Atkin 2017) demonstrating a significant association with HDG at index (OR 1·85 95%CI 1·34–2·55). Although this study was large scale and was rated as having a low risk of bias the number of events were very small. No studies reported evidence for CRC mortality. GRADE of recommendation MODERATE.

CQ1.2
Sixteen studies reported evidence relating to risks at first surveillance associated with the presence tubulovillous or villous histology at index colonoscopy. Overall the evidence suggests that risk for AA at first surveillance was increased if tubulovillous or villous components (rather than tubular) were identified at index with consistent statistically significant associations reported across four studies (Atkin 2017; Huang 2010; Fairley 2014; Laiyamo 2008) rated as low to moderate risk of bias, and in one study (Nusko 2008) rated as having a high risk of bias. Incidence of AA when tubulovillous components identified at index was 17.51% (OR 1.93 95%CI 1.59 to 2.34) and 25.05% (OR 3.03 (2.33 to 3.95) when villous components were identified (Atkin 2017). The incidence for AA when villous components were reported at index was reported as 21.2% in Nusko (2008). Incidence for tubulovillous and villous histology combined was reported

as 26.1% (HR 2.57; 95%CI 1.24–5.32) in Huang (2010), and Fairley (2014) reported an odds ratio for villous histology of 3.7 (95%CI 2.9, 4.7). Laiyamo (2008) presented data on risk ratios comparing AA with no AA at first surveillance and AA with no adenoma at first surveillance, reporting statistically significant risk ratios of 2.38 (95%CI 1.56-3.64) and 2.25 (95%CI 1.49-3.39), respectively. A further study, Laish (2017), reported no significant association when the index tubulovillous adenoma was small (OR 0.63 (0.36-1.12), but the association was statistically significant when it was large (OR 2.11 95%CI 1.40-3.19). Two further studies (Facciorusso 2016; Solakoglu 2017) did not report statistically significant associations. When the outcome measure was AN (advanced neoplasia) the findings were similar to those reported for AA with five studies rated as low to moderate risk of bias (Park 2016; Lee 2013; Martinez 2009; Cubiella 2016; Van Heijningen 2013) reporting evidence. Four of the five studies reported significant associations, showing increased risk for AN at first surveillance if tubulovillous or villous components (rather than tubular) were identified at index. Incidence of AN when villous components were identified at index was reported as 15.5% (OR 1.4 95%CI 1.1-1.7) (Cubiella 2016), 11.9% (Lee 2013), and Van Heijningen (2013) reported an odds ratio of 2.0 (95%CI 1.2-3.2) with incidence of AA 13% and for CRC 3.8%. Where findings were reported for tubulovillous and villous components combined Martinez (2009) reported an odds ratio of 1.28 (95%CI 1.07-1.52) with incidence of AA as 16.8%, and CRC as 0.9%. In the final study (Park 2016) although the hazard ratio (HR 1.29 95%CI 0.92–1.81), indicated increased risk, it was not statistically significant. It should be noted that a number of studies did not include data relating to the number of events. The risk for CRC at first surveillance was reported on in five studies rated as low risk of bias (Atkin 2017; Huang 2012a; Coleman 2015; Fairley 2014; Laish 2017) with all five reporting statistically significant findings, showing that risk for CRC was increased at first surveillance if tubulovillous or villous histology (rather than tubular) was present at index. Atkin (2017) reported an incidence of CRC of 1.83% (OR 1.76 95%CI 1.00 to 3.09) if tubulovillous components were identified at index and 4.14% (OR 4.09 95%CI 2.13 to 7.86) if villous components were identified. Fairley (2014) reported a statistically significant odds ratio of 7.4 (95%CI 2.5 - 21.5) for the risk of CRC if villous components were present at index. The incidence of CRC was reported as 2.9% (HR 1.51 (1.02-2.23) (Coleman, 2015) and the odds for interval CRC was 1.38 (1.03-1.85) (Huang 2012a) if tubulovillous or villous components were present at index. Laish (2017) reported the incidence of CRC at first surveillance if small tubulovillous adenomas (TVA) were present at index as 1.5%, and as 1.3% large TVA. One study, rated as having a low risk of bias, presented evidence on long term CRC incidence (Atkin 2017) showing, in univariate analyses, a statistically significant increased risk for long term CRC (vs tubular) if tubulovillous components were present at index (HR 1·36 95%CI 1·00–1·87) and if villous components were present (HR 1·65 95%CI 1·03–2·64). There wasno statistically significant increased risk for long term CRC if tubulovillous or villous histology was present at index in multivariate analyses, although it should be noted that not all studies presented multivariate analyses, therefore confounding factors may be present in these analyses. One other study on long term CRC mortality (HR 1.30 95%CI 1.13-1.50) (Emillsson 2017; Loberg 2014) with reported tubulovillous or villous histology as a statistically significant risk factor for CRC. There is fairly

consistent moderate to high quality evidence suggesting that tubulovillous or villous histology at index is associated with an increased risk for AA or AN and CRC at the next surveillance. Findings were reported across a number of studies although there is some uncertainly due to the lack of absolute values available in some studies, the evidence was, however, consistent with a number of large studies rated as having a low risk of bias. Evidence for long term CRC incidence and mortality was limited being presented in only one study for each outcome, however each was a large scale study rated as either low or moderate risk of bias. GRADE of recommendation: MODERATE

CQ1.3
Fifteen studies reported evidence relating to polyp size, and were rated as having a moderate to low risk of bias. Risk for AA at first surveillance was increased if the size of the adenoma at index was equal to or greater than 20mm, this association was statistically significant in three studies (Atkin 2017; Facciorusso 2016a&b; Huang 2010), reporting incidence of AA ranging from 21.35% (Atkin 2017) to 81.1% (Huang 2010). In one study, reporting the outcome AN in statistical analyses, (Martinez 2009) the incidence of AA was 19.3% and 1.2% for CRC. One study reporting the outcome AA (Fairley 2014) and three studies reporting the outcome AN (Park 2016; Martinez 2009; Van Heijningen 2013) demonstrated significant associations if the size of the adenoma was between 10mm and 20mm at index, with incidence rates of 15.9% for AA, and 0.8% for CRC (Martinez 2009), and in a second study 7.5% for AA and 1.7% for CRC (Van Heijningen 2013). One study reported an odds ratio of 3.6 (95%CI 2.8-4.5) (Fairley 2014) and one study reported a hazard ratio of 1.81 (1.28-2.55) (Park 2016). No other associations relating to adenomas at smaller sizes were statistically significant for the outcome AA or AN. Two studies (Atkin 2017; and Fairley 2014), both rated as having a low risk of basis reported on the outcome CRC incidence at next surveillance, and one study on interval CRC (Huang 2012a). Risk for CRC at first surveillance was statistically significantly associated with size of the adenoma at index equal to or greater than 20mm in one large study with a low risk of bias, with incidence of AA reported as 2.2% (Atkin 2017), and with size of adenoma at index equal to or greater than 10mm in a second study the odds ratio was reported as 5.2 (95%CI 1.8-15.1)(Fairley 2014). There was no statistically significant association reported for interval CRC (Huang 2012) when size of adenoma at index was equal to or greater than 10mm, although uncertainty is expected as there were a small number of patients with the prognostic factor at index and the point estimate suggests there may be some increased risk. Only one study rated as low risk of bias presented evidence for the outcome long term CRC incidence (Atkin 2017). Consistent with findings for other outcomes, statistically significant associations were reported for adenomas 10-19mm in size with incidence reported as 2.1% and for those equal to or greater than 20mm in size with incidence reported as 1.7%. There was no evidence reported for the outcome long term CRC mortality. GRADE of recommendation: MODERATE.

CQ1.4
Twenty one studies presented evidence on risk associated with number of adenomas at index. The evidence was not consistently statistically significant

across the included studies and the quality of the studies ranged from low to high risk of bias. Having two adenomas (compared to one) at index was reported to be a statistically significant risk factor for AA at next surveillance in two studies with the incidence of AA reported as 18.33% (Atkin 2017) and 6.1% (Huang 2010). When assessing the evidence relating to any number more than one (e.g two or more) adenomas at index the evidence was mixed, probably due to the small numbers of patients with these risk factors at baseline. Compared to 1 or 2 adenomas there was a statistically significant increased risk for AA reported in three studies (Huang 2010; Huang 2012; Fairley 2014) with incidence of AA if 3 or more adenomas were present at index, reported as 23% (Huang 2010) and 33.3% (Huang 2012) and Fairley reported a significant odds ratio of 2.4 (95%CI 1.9-3.0). Facciorusso (2016) reported significantly increased risk for AA if patients had more than one advanced colorectal adenoma at index (OR 3.22 95%CI 2.19-5.39), Laish (2017) reported (compared to 1 or 2 non advanced adenomas) statistically significantly increased risk for AA at first surveillance if three or more non advanced adenomas were present at index (OR 2.32 95%CI 1.63-3.54) and also if three or if multiple AAs were present at index (OR 3.11 95%CI 1.90-5.09). Further, Jang (2015) reported the odds of AA at first surveillance to be statistically significantly increased as number of adenomas at baseline increased. Atkin (2017) reported no significant association when comparing one adenoma to three or four adenomas, and three studies reported no significant associations for any comparisons (Lee 2017; Laiyamo 2008; Solakoglu 2017). Six studies, rated as having low to moderate risk of bias, reported evidence for the outcome AN. Four studies presented findings showing significantly increased risks for AN with increasing numbers of adenomas at index (Martinez 2009; Cubiella 2016; Vemulapalli 2014; Van Heijningen 2013). With one adenoma as reference, both Martinez (2009) and Van Heijningen (2013) reported statistically increased risk for AN if two, three, and five or more adenomas were present at index, Martinez also reported significantly increased risk for four adenomas at index, although this comparison was not statistically significant in the analyses reported in Van Heijningen (2013). Incidence rates for AA reported across these two studies ranged from 12.7% for two adenomas to 24.1% for five or more adenomas. With less than three adenomas as reference, Cubiella (2016), reported statistically increased risk for AN with incidence of AA when three or four adenomas were present at index as 14.8%, and when five to nine adenomas as 18.4%. Vemulapalli (2014) reported odds ratios for risk for AN at first surveillance, with 1-2 adenomas smaller than 10mm as reference. Findings showed that there was no significantly increased risk if 3 or 4 adenomas less than 10mm were present at index, but there was statistically significant increased risk for AN if five or more adenomas less than 10mm (OR 3.1 95%CI 1.2-8.2), three or four with one 10mm or more (OR 5.6 95%CI 2.1-15.1), and five or more with one 10mm or more (OR 10.8 95%CI 4.5-25.7) at index. Two studies did not find any significantly increased risk for AN associated with number of adenomas present at index (Lee 2013; Jung 2016). Six studies rated as having low to moderate risk of bias (Atkin 2017; Huang 2012a; Cottett 2012; Colemen 2015; Fairley 2014; Laish 2017) reported evidence for the outcome CRC at next surveillance, with two reporting statistically significantly increased risks for CRC at next surveillance with increased numbers of adenomas at index. Cottet (2012) reported significantly increased risks for CRC

at first surveillance if one advanced adenoma (SIR 2.32 95%CI 1.62-3.21) and two or more advanced adenomas (SIR 2.07 95%CI 1.21 to 3.32) were present at index. Whereas if the index adenomas were non advanced there was no increased risk of CRC for either one or two or more adenomas. Fairley (2014) reported a statistically significant increased risk for CRC when three or more adenomas (compared to one or two) were present at index (OR 4.3 95%CI 1.4-12.9). Laish (2017) reported incidence rates without statistical analyses for CRC of 1.1% when 1-2 non advanced adenomas (NAA) were present at index, 2.7% when 3 or more NAAs were present at index, and 3.7% when multiple advanced adenomas were present at index. Three studies reported no statistically significant increased risk for CRC incidence (Atkin 2017; Coleman 2015) and interval CRC (Huang 2012a), with increasing numbers of adenomas. Although, it should be noted that the number of events, particularly in the CRC analyses are very small therefore the findings are very uncertain. One study rated as having a low risk of bias (Atkin 2017) reported evidence on long term CRC incidence and did not demonstrate a statistically significant association. Again, uncertainty is expected where there are a small number of patients with the prognostic factor at index. One further large scale study (Emilsson 2017) presented evidence on CRC mortality reporting statistically significantly increased risk if more than one adenoma was present at index (HR 1.30 95%CI 1.10-1.55). GRADE of recommendation: LOW to MODERATE

CQ1.5

Twelve studies, rated as having low to high risk of bias, presented evidence on the risk associated with the presence of proximal adenoma at index. Across the 12 studies the findings did not consistently report statistically significant increased risk for proximal adenomas at index. Seven studies presented evidence relating to the risk of AA at first surveillance (Atkin 2017; Huang 2012; Huang 2010; Lee 2017; Jang 2015; Laiyamo 2008; Solakoglu 2017) with only one (Laiyamo 2008) reporting statistically significant associations between proximal adenomas at baseline and risk for AA at first surveillance, when compared to both non advanced adenoma or no adenoma (AA vs Non AA at first surveillance: RR 1.58 95%CI 1.11-2.25; AA vs no adenoma at first surveillance: RR 1.84 95%CI 1.31-2.59). Of those who had a proximal adenoma at baseline 9% had an AA at first surveillance, whereas 5% of those with a distal adenoma at baseline had an AA at first surveillance. Three studies presented data on the outcome AN (Lee 2013; Martinez, 2009; Van Heijningen 2013) with all three reporting statistically significant associations between proximal adenomas at baseline and risk for AN at first surveillance, incidence of AN in those with a proximal adenoma at baseline ranged from 7.7% for AN (Lee, 2013) to 11.8% for AA, and 0.8% for CRC (Martinez 2009). There was no evidence for a statistically significant association for CRC incidence at next surveillance (Atkin 2017; Cottet 2012), although one study (Atkin 2017) did present a statistically significant association between proximal adenoma at index and the risk for long term CRC (HR 1.76 95%CI 1.30-2.38) with a 2% incidence rate. One further large scale study (Emilsson 2017) presented evidence on CRC mortality reporting no association between proximal adenomas at index and long CRC mortality. GRADE of recommendation: LOW

CQ1.6

Four studies (Facciourusso 2016; Huang 2012; Huang 2010; Cubiella 2016) presented evidence on the risk associated with adenoma morphology at index, three of these studies were rated as having a low risk of bias, whilst the fourth was rated as having a high risk of bias (Cubiella 2016). Three studies presented evidence on the risks for AA (Facciourusso 2016; Huang 2012; Huang 2010) and only one reported a statistically significant association (Facciourusso 2016) demonstrating an increased risk of AA in patients with sessile (OR 1.96 95%CI 1.12-2.43) or nonpolypoid adenomas (OR 2.43 95%CI 1.14-3.26) at index, relative to those with pedunclulated adenomas at index. For the two remaining studies, although increased risk was reported it was not statistically significant. One final study presented evidence relating to the outcome AN (Cubiella 2016) showing no statistically significant increased risk relating to adenoma morphology at index. No evidence relating to CRC at the next surveillance, long term CRC incidence, or long term CRC mortality was identified. GRADE of recommendation: VERY LOW

CQ1.7
Twenty studies, of generally low risk of bias, presented evidence on the risk associated with male sex. Eleven studies presented evidence relating to AA (Atkin 2017; Facciourusso 2016; Lee 2017; Huang 2010; Huang 2012; Tae 2017; Jang 2015; Laiyamo 2008; Pinksy 2009; Solakoglu 2017; Imperiale 2014). Of these, four studies presented evidence showing a statistically significant increased risk of AA at first surveillance if the patient was male (Huang 2019, Huang 2012, Tae 2017 and Jang 2015), with incidence rates where reported ranging from 12.2% (Huang 2010) to 17.6% (Huang 2012). Five studies presented evidence on the outcome AN (Park 2016; Martinez 2009; Cubiella 2016; Jung 2016; Vemulapalli 2014) with one study (Martinez 2009) reporting a statistically significant increased risk of AN at first surveillance in males (OR 1.40 95%CI 1.19-1.69), with incidence rates of 11.7% for AA and 0.8% for CRC. Four studies presented evidence on CRC incidence at next surveillance with only one study (Coleman 2015) reporting male sex as a statistically significant risk factor (HR 1.69 95%CI 1.26-2.27) with an incidence of 3.2%. However, it should be noted some studies reported a reduction in risk for AA and CRC incidence at next surveillance in females, although at a level that was not statistically significant (Atkin 2017 Huang 2012a). One study reported an association for the risk of long term CRC (Atkin 2017) and a further study for the risk of long term CRC mortality (Emilsson 2017), however, neither were statistically significant. GRADE of recommendation: VERY LOW.

CQ1.8
Seven studies, rated as moderate to low risk of bias, (Cottet 2012; Jang 2015; Jung 2016; Laiyamo 2008; Martinez 2009; Park 2016; Tae 2017) reported evidence on the risks associated with a family history of CRC. Two studies reported on the outcome AA (Tae 2017; Jang 2015), and three on the outcome AN (Park 2016; Martinez 2009; Jung 2016). There was no statistically significant increased risk of either AA or AN at first surveillance for patients with a family history of CRC. One study reported on incidence of CRC at first surveillance (Cottet 2012) and again there was no evidence for increased risk associated with a family history of CRC. Cottett (2012) presented evidence separately for those

with AA at index, and for those with non AA at index. In those with an AA at index both those with a family history (SIR 3.76 95%CI 1.51-7.75) and those without (SIR 2.10 95%CI 1.54 – 2.81) were at statistically significantly increased risk for CRC at first surveillance. A formal statistical test for difference between those with or without family history was not performed. Whereas in the non AA group neither those with or without a family history of CRC were at increased risk of CRC, although as for the analysis above a formal statistical test for difference between those with or without family history was not performed. Only one study reported on the long term incidence of CRC (Laiyamo 2008) reporting that of new CRC cases diagnosed during follow up 44% (4/9) had a family history of CRC, however no statistical analyses were presented. No evidence on long term CRC mortality was identified. GRADE of recommendation: MODERATE

CQ1.9

Nineteen studies, generally rated as low risk of bias (Atkin 2017; Huang 2012; Huang 2012a; Huang 2010; Cottet 2012; Lee 2017; Van Enckevort 2014; Emilsson 2017; Tae 2017; Coleman 2015; Jang 2015; Laiyamo 2008; Solakoglu 2017; Imperiale, 2014; Park 2016; Martinez 2009; Cubiella 2016 Jung 2016; Vemulapalli 2014) presented evidence on the risks associated with increasing age, and demonstrated that there is relatively consistent evidence suggesting increasing age as a risk factor. Ten studies (Atkin 2017; Huang 2012; Huang 2010; Lee 2017; Van Enckevort 2014; Tae 2017; Jang (2015); Laiyamo 2008; Solakoglu 2017; Imperiale, 2014) reported on AA. Studies used a younger age group as the reference (e.g <55yrs; 50-60years) and reported risks for a range of different older age groups, or presented the findings as the risk associated with increasing age (e.g 1 or 10 year increase/continuous). Two studies reported increased risk for AA at first surveillance associated with older age but this was not statistically significant (Solakoglu 2017; Jang 2015). Although in one of these studies this finding was close to significance (Jang, 2015) and may have become statistically significant if age was categorised. Of the remaining eight studies, Atkin (2017), Huang (2012) and Huang (2010) presented evidence for different age groups compared to a younger age group, showing that compared to the younger age group risk for AA at first surveillance was statistically significantly increased for those aged from 55 years to those over 80 years with incidence, with the exception of the age group 65-69 in one study (Atkin 2017) who did not have a statistically significant increased risk for AA relative to the younger group with an incidence of AA of 14.51%, although this still shows the same overall trend. The incidence of AA at first surveillance across the two studies ranged from 10.9% for the 50-60 year age group (Huang, 2010) to 22.75% in the 80 years or older age group (Atkin, 2017), although it should be noted that the trend was not linear, with Huang (2012) reporting an incidence of 27.6% for an older than 60 years age group. Five further studies presented evidence showing statistically significant increased risk for AA at first surveillance with increasing age presented as a continuous variable (Lee 2017; Enckevort 2014; Tae 2017; Laiyamo 2008; Imperiale, 2014) with odds ratios ranging from 1.02 (95%CI 1.01-1.04) (Tae 2017) to 1.47 (95%CI 1.16-1.87) (Imperiale 2014). Five studies reported on AN (Park 2016; Martinez 2009; Cubiella 2016 Jung 2016; Vemulapalli 2014) with findings more mixed. Three studies presented evidence

per age group relative to the younger age group. Martinez (2009) reported statistically significant increased risks for AN across three age groups (60-69; 70-70; 80+) compared to the younger age group (50-59) with incidence of AA at first surveillance as 12.2%, 14.5%, and 17.7% respectively. Furthermore, Martinez (2009) presented evidence on the younger than 40 age group, and the 40-49 age group relative to the 50-59 age group. For both of these age groups the odds ratio and confidence intervals were below one, suggesting that younger age has a protective effect. Park (2016) reported only the 70 year or older age group had statistically significantly increased risk for AN (HR 2.56 95%CI 1.43-4.59), whilst for the 50-70 year age group there was no statistically significant association. The association reported in Cubiella (2016) for the 60-69 year age group relative to the 50-59 year age group was not statistically significant. Two studies reported statistically significant increased risk for AN with increasing age, with age as a continuous variable the hazard ratio was 1.02 (95%CI 1.01-1.03) (Jung 2016) and with age increasing with yearly increments the odds ratio was 1.04 (95%CI 1.01-1.07) (Vempulapalli, 2014). Four studies (Atkin 2017; Cottet 2012; Huang 2012a; Coleman 2015) reported evidence on incidence of CRC at first surveillance. All four studies reported statistically significant associations between risk of CRC and increasing age, although it should be noted that there are a small number of events across each age group. All four studies used a younger age group as the reference (e.g <55yrs; 50-60years) and reported risks for a range of different older age groups. Relative to patients younger than 55 years, Atkin (2017) reported only those 75 years or older had statistically significant increased risk for CRC at first surveillance with incidence reported as 5.08% and 5.58% respectively. Coleman (2015) reported, relative to the under 50 year group, significantly increased risks for CRC for the 60-69 group, the 70-79 group, and the 80 years or older group, with incidence of CRC at first surveillance reported as 2.7%, 3.7% 5.9% respectively, whereas there was no significantly increased risk in the 50-59 age group. Huang (2012a) reported on interval CRC showing a statistically significant increased risk for the 60 years or older age group (OR 1.34 95%CI 1.08-1.92) relative to the under 50 year age group, but this comparison was not significant for the 50-60 year age group. Cottet (2012) reported on the risk of CRC at first surveillance associated with increasing age groups for those with AA and those with non AA at index separately. For each of the age groups the standardised incidence ratio was statistically significant for those with AA at index (<60 years: SIR 3.65 95%CI 1.88 to 6.37; 60-79 years SIR 1.75 95%CI 1.18 to 2.50; =/>80 years SIR 3.32 95%CI 1.66 to 5.95). However, there was no increased risk associated with any of the three age groups when patients had a non AA at index. Long term CRC incidence was reported on in one study (Atkin 2017) reporting statistically significant increased risk relative to those younger than 55 years for those in the age range 65-74years (2.1%) and those 75 years and older (2.4%), but there was no statistically significant increased risk for long term CRC in the 55-64 age group. One study (Emilsson 2017) reported on long term CRC mortality relative to a 40-49 years age group, all older age groups up to those 80 years and older had a statistically significant increased risk (50-59 years HR 2.13 95%CI 1.38-3.27; 60-69 years HR 3.50 95%CI 2.31-5.29; 70-79 years HR 6.10 95%CI 4.03-9.22; 80 or older HR 14.97 95%CI 9.74-23.01). GRADE of recommendation: MODERATE

CQ1.10
All studies assessing age as a prognostic risk factor use a younger age group as reference and is therefore included in CQ1.9, although it can be noted that those studies that did compare to cohorts older than 75 years did demonstrate a similar pattern in that there were statistically significant increased risks in these older cohorts compared to younger reference cohorts (<55 years), for AA (Atkin 2017) and AN (Martinez 2009) at first surveillance, for CRC incidence at first surveillance in two studies (Atkin 2017; Coleman 2015), yet only for those with an AA at index in a further study (Cottet 2012), for long term CRC incidence (Atkin 2017) and for long term CRC mortality (Emilsson 2017). GRADE of recommendation: MODERATE

CQ1.11
Five studies, rated as low to moderate risk of bias (Lee 2017; Tae 2017; Park 2016; Jung 2016; Martinez 2009), presented evidence relating to the risks associated with smoking status. Two studies presented evidence on the risk for AA at first surveillance associated with being a smoker (Lee 2017; Tae 2017) reporting no statistically significantly increased risk. Three studies presented evidence on the risk of AN at first surveillance associated with being a smoker (Park 2016; Jung 2016; Martinez 2009), again no statistically significantly increased risk was reported. No studies presented evidence on CRC at next surveillance, long term CRC incidence, or long term CRC mortality. GRADE of recommendation: LOW.

CQ1.12
Eight studies, rated as having a low to moderate risk of bias, provided evidence on the risks associated with high BMI (Kim 2012; Lee 2017; Tae 2017; Jang 2015; Laiyemo 2008; Park 2016; Jung 2016; Martinez 2009). Five studies reported evidence on the risk for AA at first surveillance associated with a high BMI (Kim 2012; Lee 2017; Tae 2017; Jang 2015; Laiyemo 2008). One study reported a statistically significantly increased risk of AA if patients had a BMI of 25 or above (HR 2.69 95%CI 1.64-4.42) (Kim 2012), and a second study (Laiyemo 2008) presented evidence that those with AA at index together with a high BMI were at increased risk of AA at first surveillance (RR 1.62 95%CI 1.01-2.57). The remaining three studies did not report statistically significant associations between the risk for AA at first surveillance and high BMI (Lee 2017; Tae 2017; Jang 2015). Three studies reported evidence on the risk for AN at first surveillance associated with a high BMI (Park 2016; Jung 2016; Martinez 2009) with none of these studies reporting a statistically significant association. No studies presented evidence on CRC at the next surveillance, long term CRC incidence or long term CRC mortality. GRADE of recommendation: LOW.

CQ1.13
Five studies, ranging from low to high risk of bias, reported on the risks associated with different levels of bowel preparation quality (Atkin 2017; Facciorusso 2016; Jang 2015; Cubiella 2016; Van Heijningen 2013). Three studies reported evidence on the risks for AA at first surveillance (Atkin 2017; Facciorusso 2016; Jang 2015). Relative to excellent or good bowel preparation

there were statistically significant associations between poor bowel preparation and the risk for AA in two studies (Atkin 2017 [OR 1.54 95%CI 1.04-2.28]; Jang, 2015 [OR 2.208 95%CI 1.238-4.662]). There were no statistically significant associations between adequate, moderate, or satisfactory bowel preparation (relative to excellent) and the risk for AA. Two studies reported evidenc on the risks for AN at first surveillance (Cubiella 2016; Van Heijningen 2013), with only one (Van Heijingen 2013) reporting a statistically significant increased risk for AN associated with insufficient bowel preparation relative to good bowel preparation with an incidence of AA of 17.7% and of CRC 2.2%. There was no increased risk when bowel preparation was reported as moderate in the same study, and also when bowel preparation was reported as adequate (relative to inadequate) in a the second study (Cubiella 2016). One study (Atkin 2017) reported on incidence of CRC at first surveillance and presented similar findings in that there was only statistically significantly increased risk for CRC if bowel preparation was poor (OR 3.80 95%CI 1.79-8.05) and not if it were satisfactory. The same study (Atkin 2017) reported on long term CRC incidence and again the associations were only statistically significant for poor bowel preparation (HR 2.09 95%CI 1.19-3.67) and not for satisfactory bowel preparation. No studies were identified which presented evidence on long term CRC mortality. GRADE of recommendation: LOW.

CQ1.14
Three studies, ranging from low to high risk of bias, presented evidence on the risks associated with completeness of colonoscopy (Atkin 2017; Cubiella 2016; Van Heijningen 2013). Only one study (Atkin 2017) reported on the risks for AA at first surveillance associated with incomplete colonoscopy at index, reporting a statistically significant increased risk for AA (OR 1.92 95%CI 1.58-2.33). Two studies reported on the risk for AN at first surveillance and found no statistically significant association incomplete colonoscopy and the risk for AN. One study (Atkin 2017) presented evidence on the risk for CRC at first surveillance and found it statistically significantly increased if colonoscopy was incomplete at index (OR 4.28 95%CI 2.61-7.03), and the same study (Atkin 2017) presented evidence on long term CRC incidence, similarly finding statistically significantly increased risk if colonoscopy was incomplete at index (HR 1.80 95%CI 1.34-2.41). No studies were identified which presented evidence on long term CRC mortality. GRADE of recommendation: VERY LOW.

CQ1.15
One study (Jang 2015) reported on the risk for AA associated with a low quality colonoscopist at index, reporting no statistically significant association. Absolute values were not available for this risk factor, therefore, there is considerable uncertainty in the evidence. GRADE of recommendation: VERY LOW.

CQ1.16
There is no evidence to make an assessment of whether using high-adenoma-detecting technologies at index reduces risk for AA or CRC at first surveillance.

Results relating to CQ2

No studies were included for CQ2, therefore was no evidence on which to make an assessment on whether 1st surveillance (as opposed to index colonoscopy polyp clearance) reduces future CRC risk, across any of the sixteen prognostic factors.

Results relating to CQ3

8 citations relating to 6 studies were included at full text (Atkin 2017; Atkin 2017a; Pinsky 2009; Lee 2017; Chung 2011; Cubiella 2016; Winawer 1993; Winawer 1993a). The evidence relating to each of the prognostic factors is presented in Table 7.

Table 7. Findings from studies included for CQ3 for each of the prognostic factors.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv Incidence CRC at next surv Long term CRC incidence Long term CRC mortality Other results	Level of evidence. (QUIPS / ROBINS-I)
Atkin 2017 (& Atkin, 2017)	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	Advanced adenoma: Interval between index and first surveillance < 18 months (reference)(n (n=4318) 2 years - UV 1.13 (0.92 to 1.40); MV 1.05 (0.83 to 1.33) 3 years - UV 0.93 (0.75 to 1.15); MV 1.06 (0.83 to 1.34) 4 years – UV 1.04 (0.76 to 1.43); MV 1.10 (0.78 to 1.55) 5 years – UV 1.03 (0.70 to 1.53); MV 1.24 (0.81 to 1.91) 6 years – UV 0.95 (0.57 to 1.60); MV 0.90 (0.51 to 1.61) ≥ 6.5 years – UV 1.94 (1.26 to 2.98); MV 1.52 (0.90 to 2.57) Per year increase UV 1.04 (0.99 to 1.09) p 0.1103 MV interval as continuous 1.03 (0.98 to 1.09) p 0.2513 (no absolute values available) There was little evidence of a relationship between interval and AA at first surveillance, both before and after adjusting for other factors; the test statistics were non-significant and all but one 95% CI included 1, although there was a tendency towards increasing odds with increasing interval. CRC: : Interval between index and first surveillance < 18 months (reference)(n (n=4318) 2 years - UV 1.57 (0.91 to 2.69); MV 1.69 (0.94 to 3.03) 3 years - UV 0.34 (0.14 to 0.82); MV 0.53 (0.22 to 1.31) 4 years - UV 1.55 (0.73 to 3.31); MV 2.46 (1.12 to 5.44) 5 years - UV 1.12 (0.39 to 3.22); MV 2.08 (0.70 to 6.18) 6 years - UV 2.53 (0.96 to 6.65); MV 3.02 (1.00 to 9.10) ≥ 6.5 years - UV 3.14 (1.28 to 7.72); MV 4.12 (1.37 to 12.41) Per year increase UV 1.13 (1.03 to 1.25) p 0.0232 n/a; MV interval as continuous 1.21 (1.08 to 1.37) 0.0040 A longer interval was significantly associated with increased odds of CRC detection at first surveillance, both before and after adjustment, regardless of whether interval was modelled as a continuous or categorical variable. After adjustment for covariates there was 21% greater odds of finding CRC per year increase in interval (OR 1.21, 95% CI 1.08 to 1.37; p = 0.0040). There was evidence of weak negative confounding as the effect of interval became stronger after adjusting for other factors.	Low risk of bias
Chung 2011	Prospective cohort	671 low risk group (1 or 2 adenomas <10 mm) ; 539 high risk group(an advanced adenoma or>3 adenomas) Age = LR 57.8 + 8.3; HR 59.8 + 8.4	Median time between Index and FS 32.6m (range 11-78) and between 2nd and 3rd 37.6m(range 11-102m).	Advanced Adenoma incidence at interval between index and first surveillance <3yrs v 3-5 years Low Risk group = n 6/355 (7.1%) v n 7/316 (2.2%); High Risk group = n 52/516 (10.1%) v n 2/23 (8.7%) (only absolute values available, no statistical analyses)	Low risk of bias

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv Incidence CRC at next surv Long term CRC incidence Long term CRC mortality Other results	Level of evidence. (QUIPS / ROBINS-I)
		Sex = LR Male 68.3%; HR Male 73.3%			
Winawer 1993 (and Winawer 1993a)	RCT (sub cohort)	N = 1418 Age = 61.2 (9.8) Sex = 70% Male	1&3 vs 3 years follow-up: 3 years (Winnawer 1993); 6 years (Winnawer 1993a)	1st surveillance @1 yr versus 3 yrs Group A data @1 year: 0 CRC Group B data @3 years: 2CRC Surveillance at 1 yr + 3 yr versus only at 3 yrs 3- year follow-up Group A: 1 CRC Group B: 2 CRC 7 year follow-up (1993a) Group A: 2 CRC Group B: 3 CRC (only absolute values available, no statistical analyses)	High risk of bias.
Lee 2017	Retrospective cohort	N= 399 Age = 56.6±9.3 Sex = 69.7% Male	FS at 3 or 5 years (comparison) (data split by LRA and HRA)	Advanced adenoma: MV analysis ≥3year surveillance interval independent risk factor for AA. UV analysis OR (95%CI): ≥3year surveillance interval (LRA 5/221; HRA 3/178) 2.204 (0.866-5.607)P=0.097. MV analysis: 2.972 (1.114–7.928) P=0.030. UV analysis OR (95%CI): ≥5year surveillance interval(LRA 7/221; HRA 7/178) 2.304 (0.796-6.669)P=0.124. MV analysis: NR.	Low risk of bias
Pinksy 2009	Retrospective cohort study	N = 2607 Age = 63 years Sex = 60% Male	FS mean 3.4 - 4.3 yrs (depending on index adenoma)	Advanced adenoma: MV OR Ref: Interval from baseline to FS, less than or equal to 4 years (incidence of AA was 9.6% when surveillance was performed at 4 or less years after index) (incidence of AA was 8% when surveillance was performed at more than 4 years after index) Interval > 4 years, 0.86 (0.6 to 1.2)	Low risk of bias.
*Cubiella 2016	Retrospective cohort study	N = 5401 (2022 HR group; 3379 IR group) Age = 60-69yr; HR 842 (60%); IR 1241 (58.2%); 50-59yrs; HR 562 (40%) IR 891 (41.8%). Sex = Male HR 74.9%; IR 67.4%.	Mean follow up 2.8 years (SD 1 yr) for 65% of study population	Advanced neoplasia: Time to 1st surv <3yrs 14.4% (12.6-16.2) =>3yrs 13.3 (11.8-14.7) OR 1.0 (0.8-1.2).	High risk of bias.

OR=Odds ratios calculated using Logistic regression, and HR = Hazard ratios calculated using cox proportional hazards models unless otherwise stated. Absolute rates presented where available in the paper. *Indicates the outcome measure is neoplasia rather than AA, = AA+CRC. MV= Multivariate; UV=Univariate

Synthesis of evidence for CQ3

Six studies reported evidence relating to the surveillance interval for first surveillance (Atkin 2017; Atkin 2017a; Pinsky 2009; Lee 2017; Chung 2011; Cubiella 2016; Winawer 1993; Winawer 1993a). Although only four of these studies reported statistical analyses (Atkin 2017; Atkin 2017a; Pinsky 2009; Lee 2017; Cubiella 2016). The evidence demonstrated fairly consistently, although across a relatively small number of studies with the quality varying from high to low risk of bias, no statistically significant increased risk for AA, AN or CRC with increasing time interval between index and first surveillance, for intervals less than 3 years. Two studies (Atkin 2017; 2017a; Pinsky 2009) reported non significant associations between risk for AA and increasing interval between index and first surveillance. Atkin (2017; 2017a) reported a non significant but positive association, for the per year increase in risk for AA (OR 1.04 (0.99 to 1.09), this was also non significant in the multivariate analysis (OR 1.03 (0.98 to 1.09). Again, when comparing the interval of less than 18 months to each time interval there was no statistically significant association (2 years: OR 1.05 (0.83 to 1.33); 3 years OR 1.06 (0.83 to 1.34); 4 years OR 1.10 (0.78 to 1.55); 5 years OR 1.24 (0.81 to 1.91); 6 years OR 0.90 (0.51 to 1.61)) until the comparision with 6.5 years or more where the unadjusted odds were 1.94 (1.26 to 2.98), although this association did not remain significant when adjusted for covariates. Pinsky (2009) also reported no significantly association for advanced adenoma when they compared incidence at first surveillance of 4 years or less to incidence after a 4 year interval. They showed that incidence of AA was 9.6% when surveillance was performed at 4 or fewer years after index, and incidence of AA was 8% when surveillance was performed at more than 4 years after index, with the associated odds of 0.86 (0.6 to 1.2). Chung (2011) reported on incidence of AA for the interval between index and first surveillance of less then 3 years compared to 3-5 years, for low risk (n6/355 (7.1%) v n7/316 (2.2%)) and high risk groups (n52/516 (10.1%) v n2/23 (8.7%)) but did not present statistical analyses. Contrary to these findings one study (Lee 2017) reported that an interval between index and first surveillance of 3 or more years was an independent risk factor for advanced adenoma, reporting an adjusted odds ratio of 2.972 (1.114–7.928 P=0.030), but there was no statistically significant association when the interval was 5 years or more (OR 2.304 (0.796-6.669)P=0.124.) One study only looked at advanced neoplasia (Cubiella 2016) and showed no significant association when comparing first surveillance at less than 3 years (14.4% (12.6-16.2)) to 3 or more years (13.3% (11.8-14.7)), with an associated odds ratio of 1.0 (0.8-1.2). Two studies reported on CRC incidence at next surveillance (Atkin 2017; Atkin 2017a; Winawer 1993; Winawer 1993a), although only Atkin (2017; 2017a) presented statistical analyses which showed that a longer interval was significantly associated with increased odds of CRC at first surveillance, both before and after adjustment.. They reported that after adjustment for covariates there was 21% greater odds of CRC incidence per year increase in interval (OR 1.21, 95% CI 1.08 to 1.37; p = 0.0040). When comparing the interval between index and first surveillance, relative to an interval of less than 18 months, the odds of finding CRC at 2, 3 or 5 years was not statistically significant, although there was a significant association at 4 years with an adjusted odds ratio of 2.46 (1.12 to 5.44); at 6 years 2.08 (0.70 to 6.18), and at 6.5 or more years 4.12 (1.37 to 12.41). There was no evidence relating to long term CRC incidence and long term CRC mortality. GRADE of recommendation: LOW

Results relating to CQ4

Two citations relating to 1 study were included at full text (Atkin et al., 2017; Atkin et al 2017a). Evidence was reported in one large study with a low risk of bias. Although some statistically significant associations between risk of advanced adenoma or colorectal cancer at

second surveillance and prognostic factors identified at first surveillance were reported, for some prognostic factors the number of patients was small, and the reported associations were not statistically significant. The evidence relating to each of the prognostic factors is presented in Tables 8 and 9.

Table 8. Study Characteristics for the one study included for CQ4.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Level of evidence (QUIPS).
Atkin 2017 (Atkin et al., 2017a)	Retrospective, multicentre, cohort study	N = 11 944 (5019; 42% did not attend surveillance; 6925; 58% attended one or more surveillance visits. N= 1635 for 2nd surveillance analyses. Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%)	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	Low risk of bias

Table 9. Findings from studies included for CQ4 for each of the prognostic factors.

Incidence of AA at next surveillance	Incidence CRC at next surveillance
CQ4.1 High grade dysplasia v low grade	
Worst dysplasia:UV ref no adenoma (n:75/1010) Low grade (n=61/508) OR:1.70 (1.19 to 2.43) High grade (n=4/46) OR 1.19 (0.41 to 3.40) Unknown (n=6/71) OR:1.15 (0.48 to 2.74)	Worst dysplasia:UV ref no adenoma (n=6/1010) Low grade (n=3/508)OR: 0.99 (0.25 to 3.99) High grade n=(0/46)OR: n/a Unknown (n=0/46)OR: n/a
CQ4.2 Polyp: Villous component ≥25% (tubulovillous or villous histology) Polyp: NO Villous component ≥25% (tubulovillous or	
Worst histology: UV ref No adenomas (n=75/1010) OR:1 Tubular (n=33/340) OR: 1.34 (0.87 to 2.06) Tubulovillous (n=19/156) OR:1.73 (1.01 to 2.95) Villous (n=10/66) OR:2.23 (1.09 to 4.54) Unknown (n=9/63) OR=2.08 (0.99 to 4.37)	Worst histology: UV ref No adenomas (n6/1010) Tubular (n2/340) 0.99 (0.20 to 4.93) Tubulovillous 0 Villous (n=1/66) 2.57 (0.31 to 21.70) Unknown 0
CQ4.3 Polyp: Size of largest adenoma (variants: ≥10mm, or ≥20mm) Polyp: Size of largest adenoma NOT greater than (variants: ≥10mm, or ≥20mm)	
UV Largest size (mm) ref No adenomas (n75/1010) < 10 (n36/379) 1.31 (0.86 to 1.98) 10–14 (n8/95) 1.15 (0.54 to 2.45) 15–19 (n7/52) 1.94 (0.85 to 4.45) ≥ 20 (n15/75) 3.12 (1.69 to 5.75) Unknown (n5/24) 3.28 (1.19 to 9.03)	UV Largest size (mm) ref No adenomas (n6/1010) < 10 (n2/340) 1.34 (0.33 to 5.37) 10-14 0 15-19 0 ≥20 0 Unknown 0
CQ4.4 Polyp: Number of adenomas (variants: 1,2,3,4,5-9,10+; the main categories may be 1-2, 3-4 and 5+ but we would like to capture all reported variations) N/a	
UV OR: Number ref 0 (n75/1010) 1 (n39/429) 1.25 (0.83 to 1.87) 2 (n20/117) 2.57 (1.50 to 4.39) 3 (n4/37) 1.51 (0.52 to 4.38) 4 (n4/21) 2.93 (0.96 to 8.94) 5+ (4/21) 2.93 (0.96 to 8.94)	UV Number ref 0 (n6/1010) 1 (n2/429) 0.78 (0.16 to 3.90) 2 (n1/117) 1.44 (0.17 to 12.09) 3 0 4 0 5+ 0
CQ4.5 Polyp: Presence of adenoma in proximal colon Polyp: Absence of adenoma in proximal colon	
UV OR Proximal adenomas ref No adenomas (n75/1010) No (n31/319) 1.34 (0.87 to 2.08) Yes (n40/306) 1.87 (1.25 to 2.82)	UV OR Proximal adenomas ref No adenomas (n6/1010) No 0 Yes (n3/306) 1.66 (0.41 to 6.66)

Incidence of AA at next surveillance	**Incidence CRC at next surveillance**
Proximal polyps ref No polyps (n44/667) No (n40/499) 1.23 (0.79 to 1.93) Yes (n62/469) 2.16 (1.44 to 3.24)	Proximal polyps ref No polyps (n5/667) No (n1/499)0.27 (0.03 to 2.28) Yes (n3/469)0.85 (0.20 to 3.58)
CQ4.6 Polyp: Adenoma morphology (variants: pedunculated, sessile, flat) N/a	
CQ4.7 Patient: Male gender Patient: Female gender Low risk of bias	
UV OR Gender Male ref (n90/956) Female (n56/679) 0.86 (0.61 to 1.23)	UV OR Gender Male ref (n5/956) Female (n4/679) 1.13 (0.30 to 4.21)
CQ4.8 Patient: Family history of CRC Patient: NO Family history of CRC	
CQ4.9 Patient: Younger age (e.g. <55 vs 55+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Younger age range	
Age (years) at first follow-up ref < 55 (n25/329) ≥ 55 and < 60 (n21/256) 1.09 (0.59 to 1.99) ≥ 60 and < 65 (n30/279) 1.47 (0.84 to 2.56) ≥ 65 and < 70 (n31/305) 1.38 (0.79 to 2.39) ≥ 70 and < 75 (n19/253) 0.99 (0.53 to 1.84) ≥ 75 and < 80 (n13/142) 1.23 (0.61 to 2.47) ≥ 80 (n7/71) 1.33 (0.55 to 3.21)	Age (years) at first follow-up ref < 55 (n2/329) ≥ 55 and < 60 0 ≥ 60 and < 65 (n2/279)1.18 (0.17 to 8.44) ≥ 65 and < 70 (n1/305) 0.54 (0.05 to 5.96) ≥ 70 and < 75 (n1/253) 0.65 (0.06 to 7.20) ≥ 75 and < 80 (2/142) 2.34 (0.33 to 16.75) ≥ 80 (n1/71) 2.34 (0.21 to 26.12)
CQ4.10 Patient: Older age (e.g. <75 vs 75+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Older age range	
CQ4.11 Patient: Smoking (variants: current, ex, never) N/a	
CQ4.12 Patient: High body mass index (e.g. BMI>25)? Patient: NOT High body mass index	
CQ4.13 Index colonoscopy Bowel prep quality (variants: good, adequate, inadequate/poor) Inadequate/poor bowel prep	
UV OR Best bowel preparation at colonoscopy, Excellent/good ref (n31/464) Satisfactory (n27/169) 2.66 (1.53 to 4.60) Poor (n5/68)1.11 (0.42 to 2.96) Unknown (n58/661) 1.34 (0.85 to 2.11)	UV OR Best bowel preparation at colonoscopy, Excellent/good ref (n2/464) Satisfactory (1/169) 1.38 (0.12 to 15.26) Poor (n1/68) 3.45 (0.31 to 38.54) Unknown (n4/661) 1.41 (0.26 to 7.71)
CQ4.14 Index colonoscopy complete to caecum incomplete colonoscopy	
UV OR Most complete examination, ref Complete colonoscopy (n101/1087) Colonoscopy of unknown completeness (n8/130) 0.64 (0.30 to 1.35) Incomplete colonoscopy (n12/145) 0.88 (0.47 to 1.65)	UV OR Most complete examination, ref Complete colonoscopy (n4/1087) Colonoscopy of unknown completeness (n1/130) 2.10 (0.23 to 18.92) Incomplete colonoscopy (n3/145) 5.72 (1.27 to 25.87)
CQ4.15 Index colonoscopy by high-quality colonoscopist NOT high quality colonoscopist	
CQ4.16 Index colonoscopy using high-adenoma-detecting technologies (variants: HD scope, chromoendoscopy) no high-adenoma-detecting technologies	

Odds ratios (OR) calculated using Logistic regression, and Hazard ratios (HR) calculated using cox proportional hazards models unless otherwise stated. Absolute values presented where available. N = total number of patients; n = number of patients with outcome at second surveillance of total with prognostic factor at first surveillance. UV = Univariate (unadjusted). IQR = Interquartile range.

Synthesis of evidence for CQ4

CQ4.1
One study rated as having a low risk of bias reported findings regarding high grade dysplasia. When the reference was no adenoma at first surveillance, there was no statistically significant association between high grade dysplasia at first surveillance colonoscopy and risk for AA at second surveillance (OR 1.19, 95% CI: 0.48 to 2.74) (Atkin 2017; Atkin 2017a). Although this result was not statistically significant, uncertainty is expected due to the small number of patients with high grade dysplasia at first surveillance (n=46) and the point estimate suggests that patients with high grade dysplasia may be at increased risk. A greater number of patients had low grade dysplasia (n=508) and there was a statistically significant association of low grade adenoma and AA at second surveillance (OR 1.70, 95%CI: 1.19 to 2.43) (Atkin 2017; Atkin 2017a). There were no CRC events at second surveillance for patients with high grade dysplasia (unadjusted OR: n/a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.2
One study rated as having a low risk of bias reported findings regarding the risk of AA or CRC associated with different types of histology at first surveillance with the reference as no adenoma. Risk for AA at second surveillance was increased if tubulovillous (OR 1.73, 95%CI: 1.01 to 2.93) or villous components (OR 2.23, 95%CI: 1.09 to 4.54) were identified at first surveillance (Atkin 2017; Atkin 2017a). There were no CRC events at second surveillance for patients with tubulovillous components (unadjusted OR: n/a). For Villous components, the magnitude of the OR suggests an increased CRC risk however the number of events were small and the result is not statistically significant (OR 2.57, 95%CI: 0.31 to 21.70) (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.3
Only one study rated as having a low risk of bias reported evidence on risk for AA and CRC at second surveillance, with the reference as no adenomas at first surveillance. Risk for AA at second surveillance was statistically significantly increased if the size of the adenoma at first surveillance was equal to or greater than 20mm (OR 3.12, 95%CI: 1.69 to 5.75) (Atkin 2017; Atkin 2017a).For adenomas of a smaller size the magnitude of the ORs suggests an increased CRC risk however the result are not statistically significant. There were no CRC events at second surveillance for patients with adenomas >10mm. For patients with adenomas <10 there was an increased risk of CRC, however the result was not statistically significant (OR 1.34, 95%CI: 0.33 to 5.37) (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW.

CQ4.4
Only one study rated as having a low risk of bias reported evidence on risk for AA and CRC at second surveillance, with the reference as no adenomas at first surveillance. Risk for AA at second surveillance was statistically significantly increased if the number of adenomas at first surveillance was two (OR 2.57 95%CI 1.50 to 4.39), although there was no statistically significant increased risk for AA for if patients had one, three, four or five (or more) adenomas at first surveillance. There was no statistically significant association for any number of adenomas at first surveillance and risk of CRC at second surveillance (Atkin 2017; Atkin 2017a). Although it should be noted that as the number of events in each category was small

the findings are uncertain. There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.5
Only one study rated as having a low risk of bias reported evidence on risk for AA and CRC at second surveillance, with the reference as no adenomas at first surveillance. Risk for AA at second surveillance was increased if an adenoma or polyp was identified at a proximal location at first surveillance (OR 1.87 95%CI 1.25 to 2.82). There was no such association for CRC (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.6
There is no evidence on which to make an assessment of whether adenoma morphology at first surveillance has a significant impact on findings at second surveillance.

CQ4.7
There was no statistically significant association between male gender at first surveillance colonoscopy and risk for AA and CRC at second surveillance (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.8
There is no evidence on which to make an assessment of whether a family history of CRC at first surveillance has a significant impact on findings at second surveillance.

CQ4.9
There were no statistically significant associations between age at first surveillance colonoscopy and risk for AA and CRC at second surveillance, although the general trend was for increased risk in most age groups compared to the reference category (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.10
There were no statistically significant associations between older age at first surveillance colonoscopy and risk for AA and CRC at second surveillance, although the general trend was for increased risk in most age groups compared to the reference category (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.11
There is no evidence on which to make an assessment of whether being a smoker at first surveillance has a significant impact on findings at second surveillance.

CQ4.12
There is no evidence on which to make an assessment of whether having a high BMI at first surveillance has a significant impact on findings at second surveillance.

CQ4.13
Only one study rated as having a low risk of bias reported evidence on risk for AA and CRC at second surveillance, with the reference as excellent or good bowel preparation at first

surveillance. There is little evidence for an association between bowel preparation quality at first surveillance and the risk of AA or CRC at second surveillance. There was only one statistically significant association reported showing the risk for AA was increased if bowel preparation quality was satisfactory (OR 2.66 95%CI 1.53 to 4.60), all other associations were not statistically significant for AA or CRC incidence (Atkin 2017; Atkin 2017a). There is no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.14
Only one study rated as having a low risk of bias reported evidence on risk for AA and CRC at second surveillance, with the reference complete colonoscopy at first surveillance. There was no evidence for a statistically significant association between the risk of AA at second surveillance and completeness of the colonoscopy at first surveillance, however there was a significant association between the risk of CRC at second surveillance where the colonoscopy at first surveillance was reported as incomplete (OR 5.72 95%CI 1.27 to 25.87)(Atkin 2017; Atkin 2017a). There was no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ4.15
There is no evidence on which to make an assessment of whether the colonoscopy is performed by a high quality colonoscopist at first surveillance has a significant impact on findings at second surveillance.

CQ4.16
There is no evidence on which to make an assessment of whether the colonoscopy is performed using high-adenoma-detecting technologies at first surveillance has a significant impact on findings at second surveillance.

Results relating to CQ5

Three citations relating to 2 retrospective cohort studies were included at full text (Chung et al., 2013; Morelli et al., 2013; Imperiale et al., 2014). Each study examined different prognostic predictors for advanced colorectal adenomas (AA) after first surveillance but did not report evidence on colorectal cancer (CRC) risk. The studies were rated as having a moderate to low risk of bias. Evidence was only reported for CQ5.7, CQ5.9, and CQ5.12, and is shown in table 10.

Table 10. Findings from studies included for CQ5 for each of the prognostic factors.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Other results	Level of evidence.
CQ5.1 High grade dysplasia v low grade									
CQ5.2 Polyp: Villous component ≥25% (tubulovillous or villous histology) Polyp: NO Villous component ≥25% (tubulovillous or									
CQ5.3 Polyp: Size of largest adenoma (variants: ≥10mm, or ≥20mm) Polyp: Size of largest adenoma NOT greater than (variants: ≥10mm, or ≥20mm)									
CQ5.4 Polyp: Number of adenomas (variants: 1,2,3,4,5-9,10+; the main categories may be 1-2, 3-4 and 5+ but we would like to capture all reported variations) N/a									
CQ5.5 Polyp: Presence of adenoma in proximal colon Polyp: Absence of adenoma in proximal colon									
CQ5.6 Polyp: Adenoma morphology (variants: pedunculated, sessile, flat) N/a									
CQ5.7 Patient: Male gender Patient: Female gender									
Chung 2013 Predictors of a 'high risk adenoma' at 2nd surveillance – by characteristics at index or 1st surveillance	Retrospective cohort	N = 131 Age = 65.5 ± 8.5 Sex = 82.4% Male	The median interval (min-max) between the first and second colonoscopy was 17 (6-101) months, while the median interval (min-max) between the second and third colonoscopy was 24 (6-90) months.	UV HR: 0.46 (0.11-1.93) MV 0.00					Low risk of bias.
Imperiale, 2014(Morelli 2013)	Retrospective cohort	N = 965 Age = 57.8 (9.8) Sex = 62% Male	Mean (median) SD interval between index and first surveillance colonoscopies was 33.9 (36.3) 20.2 months; and 44.1 (38.5) 18.6 months between first and second surveillance.	Men v women: MV OR (95% CI) 0.81 (0.46-1.44)					Low risk of bias.
CQ5.8 Patient: Family history of CRC Patient: NO Family history of CRC									
CQ5.9 Patient: Younger age (e.g. <55 vs 55+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Younger age range									
Chung 2013				UV HR: 1.02 (0.97-1.07) MV HR: 1.02 (0.93-1.12)					Low risk of bias.
Imperiale, 2014(Morelli 2013)				Age (increase of 10 yr) MV OR (95%CI): 1.30 (0.97-1.75)					Low risk of bias
CQ5.10 Patient: Older age (e.g. <75 vs 75+; there will be other variants of age cut-off and we would like to capture these too) Patient: NOT in Older age range									
CQ5.11 Patient: Smoking (variants: current, ex, never) N/a									
CQ5.12 Patient: High body mass index (e.g. BMI>25)? Patient: NOT High body mass index									

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv	Incidence CRC at next surv	Long term CRC incidence	Long term CRC mortality	Other results	Level of evidence.
Chung 2013				UV HR: 0.75 (0.58-0.98) MV HR: 0.71 (0.50-1.01)					Low risk of bias.
CQ5.13 Index colonoscopy Bowel prep quality (variants: good, adequate, inadequate/poor) Inadequate/poor bowel prep									
CQ5.14 Index colonoscopy complete to caecum incomplete colonoscopy									
CQ5.15 Index colonoscopy by high-quality colonoscopist NOT high quality colonoscopist									
CQ5.16 Index colonoscopy using high-adenoma-detecting technologies (variants: HD scope, chromoendoscopy) no high-adenoma-detecting technologies									

Odds ratios (OR) calculated using Logistic regression, and Hazard ratios (HR) calculated using cox proportional hazards models unless otherwise stated. Absolute values presented where available. UV Univariate; MV Multivariate.

Synthesis of evidence for CQ5

CQ5.7
Two studies (Chung 2013; Morelli 2014; Imperiale 2013) reported no significant association between male gender at first surveillance colonoscopy and risk for advanced adenoma at second surveillance. There was no evidence for CRC at second surveillance, long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

CQ5.9
Two studies reported on an association between increasing age and the risk of advanced adenoma at second surveillance (Chung et al., 2013; Morelli et al., 2014; Imperiale et al., 2013). Morelli et al. (2013) reported a statistically significant association between increasing age (increase of 10 years) and risk of AA at second surveillance (OR 1.30 95%CI 0.97-1.75) whereas the similar analyses in Chung et al. were not statistically significant, although the association was still positive and the lack of statistical significance may have been due to the difference in the analyses, with Chung et al., analysing a 1 year increase. There was no evidence for CRC at second surveillance, long term CRC incidence or CRC mortality. GRADE of recommendation: LOW.

CQ5.12
One study reported evidence relating to BMI at index and first surveillance and the risk for AA or CRC (high risk adenomas) at second surveillance (Chung, 2013). Although increasing BMI at index and first surveillance was not associated with increased risk for AA or CRC at second surveillance, a statistically significant reduced risk for AA or CRC with increasing BMI was reported in in univariate analysis (HR 0.75 95%CI 0.58-0.98) and this finding was close to significance in the multivariate analysis. There was no evidence for CRC at second surveillance, long term CRC incidence or CRC mortality. GRADE of recommendation: LOW.

Results relating to CQ6

No studies were included for CQ6, therefore there was no evidence on which to make an assessment on whether 2nd (and subsequent) surveillance reduces future CRC risk, across any of the sixteen prognostic factors.

Results relating to CQ7

Three citations relating to 2 studies were included at full text (Atkin 2017; Atkin 2017a; Miller 2011). The evidence relating to this question is presented in Table 11.

Table 11. Findings from studies included for CQ7 for each of the prognostic factors.

First author, year	Study design	Participants Age (M, SD unless otherwise specified) and Sex	Follow up times	Incidence of AA at next surv Incidence CRC at next surv Long term CRC incidence Long term CRC mortality Other results	Level of evidence.
Atkin 2017*	Retrospective, multicentre, cohort study	N = **11 944** patients with data available for analysis; **4608** attended one or more surveillance visits and **7336** patients did not attend surveillance.Age = Median age 66·7 years (IQR 58·4–74·0) <55yrs 2122 (18%); 55-64yrs 3179 (27%); 65-74yrs 3957 (33%); 75+ys 2686 (22%) Sex = 55.47 Male	FS or more (All surveillance intervals, 0, 1, 2 3+, plus comparisons of no surveillance v surveillance)Median follow up time 7·9 years, (IQR 5·6–11·1),	New advanced neoplasia Interval between first and second surveillance < 18 months (reference) (n29/387) (n=1635) 2 years (n35/376) - UV 1.30 (0.78 to 2.18); MV 1.62 (0.93 to 2.81) 3 years (n52/518) - UV 1.42 (0.88 to 2.28); MV 2.02 (1.19 to 3.42) 4 years (n15/152) - UV 1.39 (0.72 to 2.67); MV 2.45 (1.20 to 5.00) 5 years (n11/131) – UV 1.16 (0.56 to 2.40); MV 2.01 (0.91 to 4.44) 6 years (n4/31) – UV 1.18 (0.62 to 5.74); MV 2.76 (0.84 to 9.12) ≥ 6.5 years (n7/30) – UV 3.86 (1.53 to 9.76); MV 5.95 (2.15 to 16.46) Per year increase UV 1.11 (1 to 1.24) p 0.0501 MV interval as continuous 1.22 (1.09 to 1.36) p 0.0010 (As so few CRCs were found at 2nd surveillance, new AA and CRC were combined and new AN was treated as the outcome measure instead.	Low risk of bias
Miller 2011	Retrospective cohort	N = 88 Age = 61.2 +/- 8.2 years (range 49-85) Sex = 59.1% Male	Median time between Index and FS 32.6m (range 11-78) and between 2nd and 3rd 37.6m(range 11-102m).	Interval between FS and SS (=/>3 Years) OR 0.95 (0.37,2.49) for AA	Moderate risk of bias.

Odds ratios calculated using Logistic regression, and Hazard ratios calculated using cox proportional hazards models unless otherwise stated. Absolute rates presented where available in the paper. *Indicates the outcome measure is neoplasia rather than AA, = AA+CRC. UV Univariate; MV Multivariate

Synthesis of evidence for CQ7

Two studies examined the interval between first and second surveillance (Atkin 2017; Atkin 2017a; Miller 2011). One study rated as having a low risk of bias (Atkin 2017; 2017a) was only able to report on advanced neoplasia (AN) (a composite of AA and CRC) due to a very small number of CRC events occurring. This study demonstrated statistically significant increased odds of AN per year increase (OR 1.11 95%CI 1 to 1.24), this was also significant in multivariate analysis (OR 1.22 95%CI 1.09 to 1.36). Although when comparing the interval of less than 18 months to a 2 year interval the multivariate association was not statistically significant, but did show increased risk, this association was statistically significant when comparing less than 18 months and 3 years (OR 2.02 95%CI 1.19 to 3.42) , and less than 18 months and 4 years (OR 2.45 95%CI 1.20 to 5.00), and less than 18 months and more than 6.5 years (OR 5.95 95%CI 2.15 to 16.46) (comparisons of less than 18 months and 5 or 6 years were not significant). The second study rated as having a moderate risk of bias (Miller 2011) did not find a statistically significant positive association between risk for advanced adenoma and interval between first and second surveillance when the interval was 3 or more years. There was no evidence for long term CRC incidence or CRC mortality. GRADE of recommendation: LOW

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Appendix 1

Table 1.1. Additional questions ScHARR was asked to synthesise the evidence for.

CQ8	Stop surveillance criteria	At what age can surveillance be stopped without increasing the risk of CRC development?	Adults >75 years (or other older age cohort) who have been diagnosed with at least one colorectal adenoma and all detected adenomas have been resected completely at baseline; and adults >75 years (or other older age cohort) who have undergone potentially curative treatment for primary CRC and have had a baseline clearance colonoscopy.	endoscopic surveillance	No surveillance	Subsequent CRC incidence, CRC mortality, all cause mortality
CQ9	Stop surveillance criteria	At what estimate of life expectancy can surveillance be stopped without increasing the risk of CRC development?	Adults age >65 who have a life expectancy at 5 years of <60% (e.g. By Schonberg Index)	endoscopic surveillance	No surveillance	Subsequent CRC incidence, CRC mortality, all cause mortality
CQ10	Stop surveillance criteria	What is the risk of colonoscopy in adults >75 years (or other older age cohort)	Adults >75 who have undergone colonoscopy for any indication	colonoscopy	No colonoscopy	Subsequent mortality or significant morbidity
CQ11	Stop surveillance criteria	When (and in whom) can surveillance be stopped, relating to colonoscopy findings?	No PICO			
CQ16	Quality of procedure	Does a high quality colonoscopy have a significant impact on findings (outcomes) at surveillance colonoscopy	Adults undergoing colonoscopy	High quality colonoscopy () **see excel sheet**	"Standard colonoscopy" (minimum standard) and low quality colonoscopy **see excel sheet**	Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality

CQ8

Statement/question

Q8: At what age can surveillance be stopped without increasing the risk of CRC development?

S: There is no evidence on which to make an assessment of what age can surveillance be stopped without increasing the risk of CRC development

PICO table

P: Adults >75 years (or other older age cohort) who have been diagnosed with at least one colorectal adenoma and all detected adenomas have been resected completely at baseline; and adults >75 years (or other older age cohort) who have undergone potentially curative treatment for primary CRC and have had a baseline clearance colonoscopy.

I: endoscopic surveillance

C: no surveillance

O: Subsequent CRC incidence, CRC mortality, all cause mortality

Results

Results of the bibliographic searches

After removing duplicates, 5334 articles were found. 198 were considered potentially relevant and acquired in full text. (See flow chart).

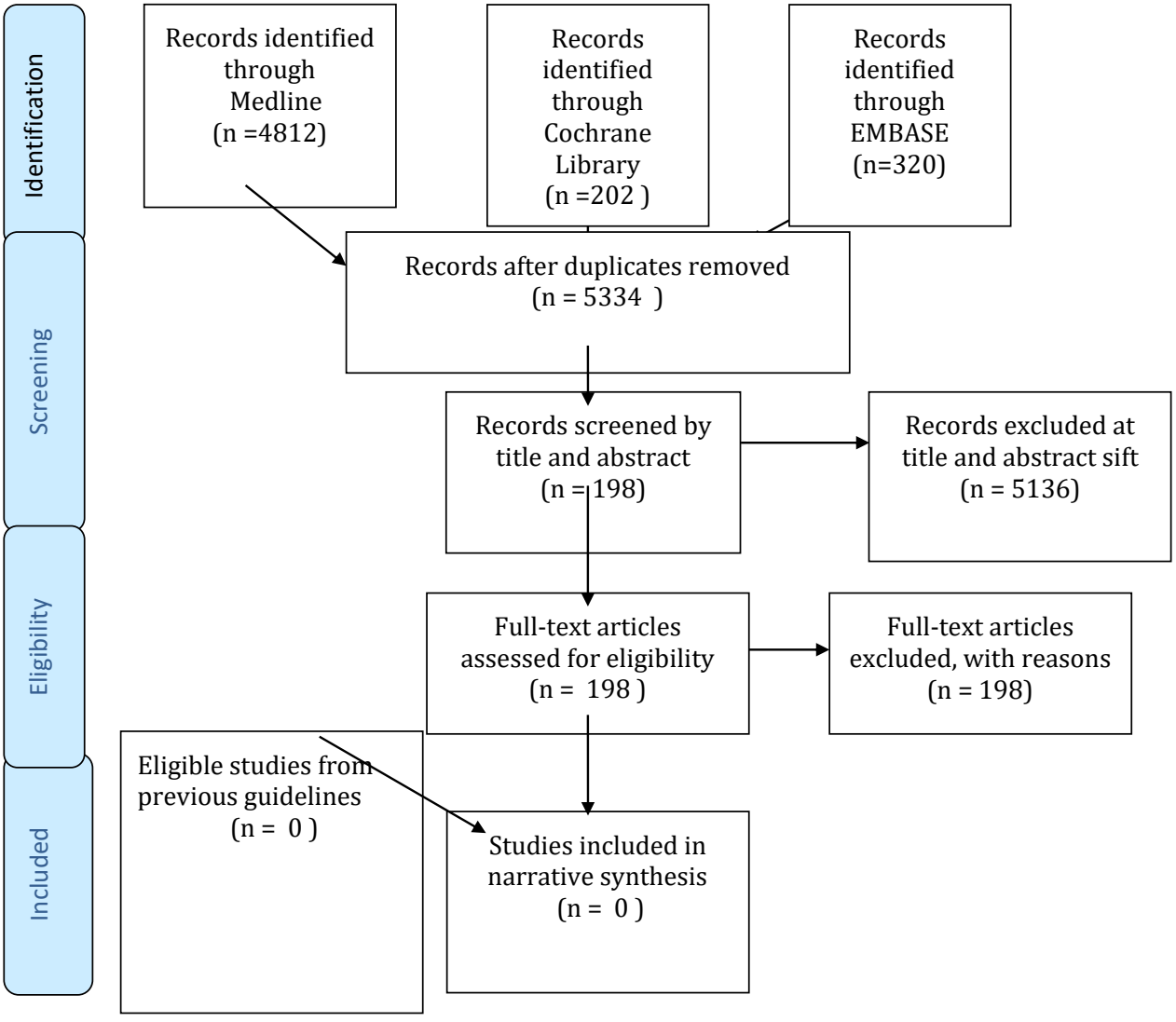
Excluded studies

198 studies were excluded because they did not meet the inclusion criteria.

Included studies

No studies were included.

PRISMA Flow Diagram



CQ9

Statement/question

Q9: At what estimate of life expectancy can surveillance be stopped without increasing the risk of CRC development?
S: There is no evidence on which to make an assessment of what estimate of life expectancy can surveillance be stopped without increasing the risk of CRC development

PICO table

P: Adults age >65 who have a life expectancy at 5 years of <60% (e.g. By Schonberg Index)
I: endoscopic surveillance
C: No surveillance
O: Subsequent CRC incidence, CRC mortality, all cause mortality

Results

Results of the bibliographic searches

After removing duplicates, 5334 articles were found. No systematic reviews were found as potentially relevant. 198 were considered potentially relevant and acquired in full text. (See flow chart).

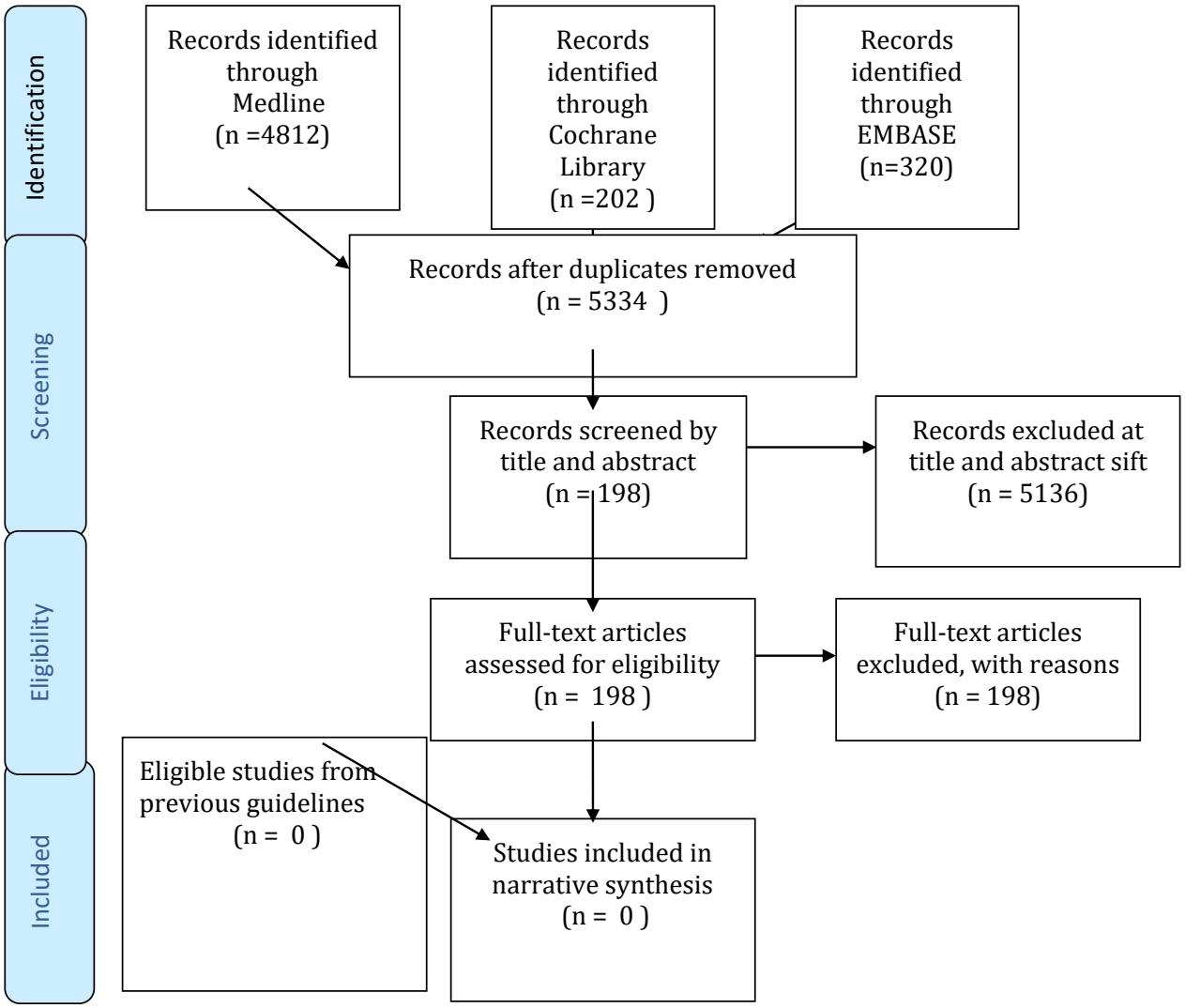
Excluded studies

198 studies (refs) were excluded because they did not meet the inclusion criteria.

Included studies

No studies were included.

PRISMA Flow Diagram



CQ10

Statement/question

Q10: What is the risk of colonoscopy in adults >75 years (or other older age cohort)?
S: Use of colonoscopy in elderly patients reduces the risk of CRC but is associated with adverse gastrointesinal events.

PICO table

P: Adults >75 who have undergone colonoscopy for any indication
I: Colonoscopy
C: No colonoscopy
O: Subsequent mortality or significant morbidity

Results

Results of the bibliographic searches

After removing duplicates, 5334 articles were found. No systematic reviews were found as potentially relevant. 198 were considered potentially relevant and acquired in full text. (See flow chart).

Excluded studies

195 studies were excluded because they did not meet the inclusion criteria.

Included studies

3 studies were included at full text (Wang et al., 2016; Garicia-Albeniz et al., 2017; Warren et al., 2009).

Evidence based discussion text

What is the risk of colonoscopy in adults >75 years (or other older age cohort)? (compared to no colonoscopy)

Three studies were identified comparing patients in older age cohorts who had undergone colonoscopy screening with those who had not. Two studies assessed incidence of colorectal cancer in elderly patients comparing those who had had colonoscopy compared to those that had not (Wang et al., 2016; Garcia-Albeniz et al., 2017). Wang et al (2016) reported significantly fewer CRCs were diagnosed in the colonoscopy group. 379 (1.55%) CRCs diagnosed in the control group, 37 (0.65%) diagnosed in the colonoscopy group (p<0.001). This finding remained for distal and proximal CRCs with significantly fewer distal CRCs in the colonoscopy group (175 (0.72%) control group, 12 (0.21%) in the colonoscopy group (p<0.001)), and significantly fewer proximal CRCs in the colonoscopy group (187 (0.77%) control group, 25 (0.44%) in the colonoscopy group (p<0.01). Compared with the control group, the cumulative incidence of CRC was significantly lower in the colonoscopy group. Subgroup analyses by CRC location showed a similar reduction in the cumulative incidence of both distal CRC (p<0.001) and proximal CRC (p<0.05) in the colonoscopy group (5-year distal CRC: 0.26 vs 0.77%; 5 year proximal CRC: 0.43 vs 0.79%, both p<0.05.) Compared with the control group, colonoscopy was associated with a lower risk of all CRC (HR 0.42, 95% CI 0.28-0.65, p<0.001), distal CRC (HR 0.36, 95% CI 0.18-0.70, p<0.01), and proximal CRC (HR 0.53, 95% CI 0.30-0.92, p<0.05). Garcia-Albeniz et al reported a modest benefit of screening colonoscopy for the prevention of CRC in people aged 70-74 years, and a smaller benefit in those aged 75-79 with the standardized 8-year risk of CRC (95% CI) 2.84% (2.54, 3.13) in the colonoscopy screening arm and 2.97% (2.92, 3.03) in the no screening arm; risk difference −0.14% (−0.41, 0.16). Whilst the risk of adverse events was low, it was greater for older individuals.

Warren et al reported that risk for adverse events among persons undergoing colonoscopy increased with age. Relative to persons age 66 to 69 years, the adjusted predictive risk for adverse gastrointestinal events was significantly higher for patients age 80 years or older (risk per 1000 procedures in persons 80 to 84 years of age vs. those 66 to 69 years of age: 8.8 [CI, 6.9 to 10.7] vs. 5.0 [CI, 3.8 to 6.2] for serious gastrointestinal events and 15.9 [CI, 13.5 to 18.3] vs. 6.9 [CI, 5.6 to 8.2] for other gastrointestinal events). Persons in the colonoscopy group were significantly more likely

than their age-equivalent matched group to have adverse gastrointestinal events. The risk for adverse cardiovascular events increased with age among persons undergoing colonoscopy, but these rates did not significantly differ from those in the age-equivalent matched group.

In conclusion: Elderly patients who had colonoscopy screening appeared to have a lower risk for CRC, but were more likely to have adverse gastrointestinal events compared to those who did not. The risk for adverse gastrointestinal events in the colonoscopy group increases with age, and is significantly higher patients 80 years or older compared to those 66 to 69 years.

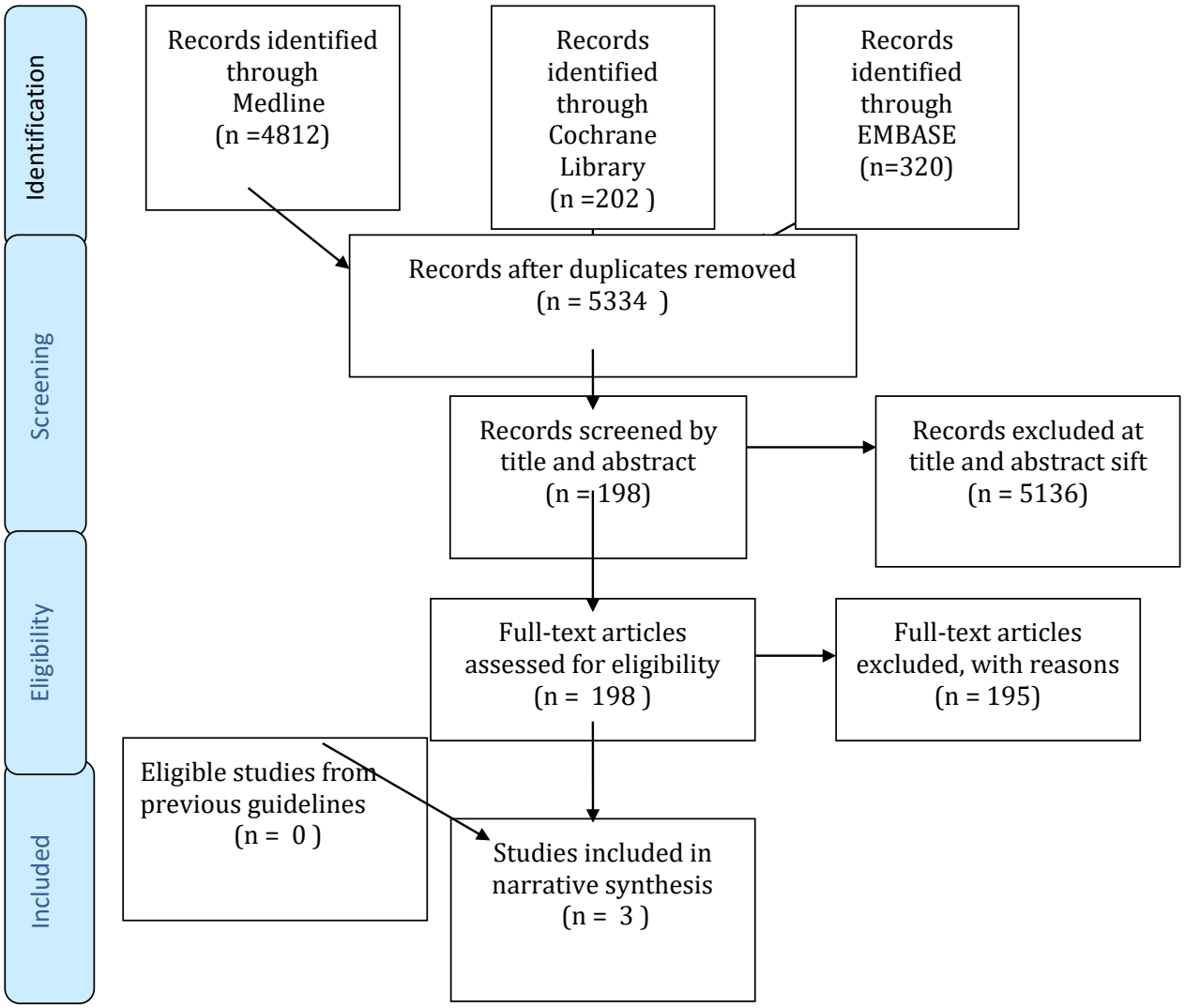
GARCIA-ALBENIZ, X., HSU, J., BRETTHAUER, M. & HERNAN, M. A. 2017. Effectiveness of Screening Colonoscopy to Prevent Colorectal Cancer Among Medicare Beneficiaries Aged 70 to 79 Years: A Prospective Observational Study. *Annals of Internal Medicine,* 166**,** 18-26.

WANG, Y. R., CANGEMI, J. R., LOFTUS, E. V., JR. & PICCO, M. F. 2016. Decreased Risk of Colorectal Cancer after Colonoscopy in Patients 76-85 Years Old in the United States. *Digestion,* 93**,** 132-8.

WARREN, J. L., KLABUNDE, C. N., MARIOTTO, A. B., MEEKINS, A., TOPOR, M., BROWN, M. L. & RANSOHOFF, D. F. 2009. Adverse events after outpatient colonoscopy in the Medicare population. *Annals of Internal Medicine,* 150**,** 849-57, W152.

Author, publication year	Study Objective	Participants/ Setting	Intervention	Outcome	Comparisons	Results	Conclusion
Garcia Albeniz 2017	Population based prospective study. To evaluate the effectiveness and safety of screening colonoscopy to prevent cancer in individuals aged 70-74 and 75-79.	Individuals aged 70–79 without history of prior colorectal cancer who, in the five years before baseline, no history of adenoma, inflammatory bowel disease or colectomy, had not received a colonoscopy, sigmoidoscopy or FOBT.	Observational data used to emulate a target trial with 2 arms: colonoscopy screening and no screening. Using the SEER-medicare linked database.	Primary outcome was CRC incidence. Secondary, adverse events	Colonoscopy screening versus no screening	70–74 age group, the standardized 8-year risk of CRC (95% CI) was 2.19% (2.00, 2.37) in the colonoscopy screening arm and 2.62% (2.56, 2.67) in the no screening arm; risk difference −0.42% (−0.24, −0.63). 75–79 age group, the standardized 8-year risk of CRC (95% CI) was 2.84% (2.54, 3.13) in the colonoscopy screening arm and 2.97% (2.92, 3.03) in the no screening arm; risk difference −0.14% (−0.41, 0.16).	The findings suggest a modest benefit of screening colonoscopy for the prevention of CRC in people aged 70-74 years, and a smaller benefit in older people. The risk of adverse events was low, but greater for older individuals.
Wang 2016	Population based retrospective cohort study.To evaluate whether colonoscopy use is associated with reduced risk of both distal and proximal CRC in this age group.	The colonoscopy group included patients 75-86 years old who were free of cancer on the date of their out patient colonoscopy. Control group included all patients aged 76-85, were not in the study group, and did not have cancer.	SEER-Medicare linked database was used to provide data on both groups.	CRC incidence	NA	Compared with the control group, colonoscopy was associated with a lower risk of all CRC.	Among elderly patients (76-85 years old) risks of both distal and proximal CRC decreased after colonscopy. Screening colonscopy could be considered for healthy elderly patients with no major comorbidities and long life expectancy.
Warren 2009	Population based matched cohort study. To determine risk for adverse events after outpatient colonoscopy in elderly patients.	Persons age 66 to 95 years at the time of their procedure, who had two or fewer colonoscopies during the study period.	SEER-Medicare linked database was used to provide data on both groups.	Adverse events occurring within 30 days after outpatient colonoscopy that were severe enough to require an emergency department visit or hospitalization.	NA	Risk for an adverse event increased with age. Persons undergoing colonoscopy at age 75 years or older were at increased risk for other gastrointestinal adverse events. The risk for serious gastrointestinal adverse events was 75% higher for persons age 80 to 84 years compared with persons age 66 to 69 years. Although the risk for adverse cardiovascular events increased with age among persons undergoing colonoscopy, the rate of events in the colonoscopy group did not significantly differ from that in the age-equivalent matched group, suggesting that the events were more related to age than colonoscopy.	The risk for adverse events after outpatient colonoscopy among elderly patients is strongly related to the type of procedure performed, patient age, and comorbid conditions.

PRISMA Flow Diagram



CQ16

Statement/question

Q16: Does a high quality colonoscopy have a significant impact on findings (outcomes) at surveillance colonoscopy?

PICO table

P: Adults undergoing colonoscopy
I: High quality colonoscopy
C: "Standard colonoscopy" (minimum standard) and low quality colonoscopy
O: Advanced adenoma incidence at next surveillance (diameter ≥10mm or HGD or villous component ≥25%); CRC incidence at next surveillance (includes interval CRCs as well if reported); Long-term CRC incidence; Long-term CRC mortality

Results

Results of the bibliographic searches

After removing duplicates, 5334 articles were found. No systematic reviews were found as potentially relevant. 198 were considered potentially relevant and acquired in full text. (See flow chart).

Excluded studies

198 studies (refs) were excluded because they did not meet the inclusion criteria.

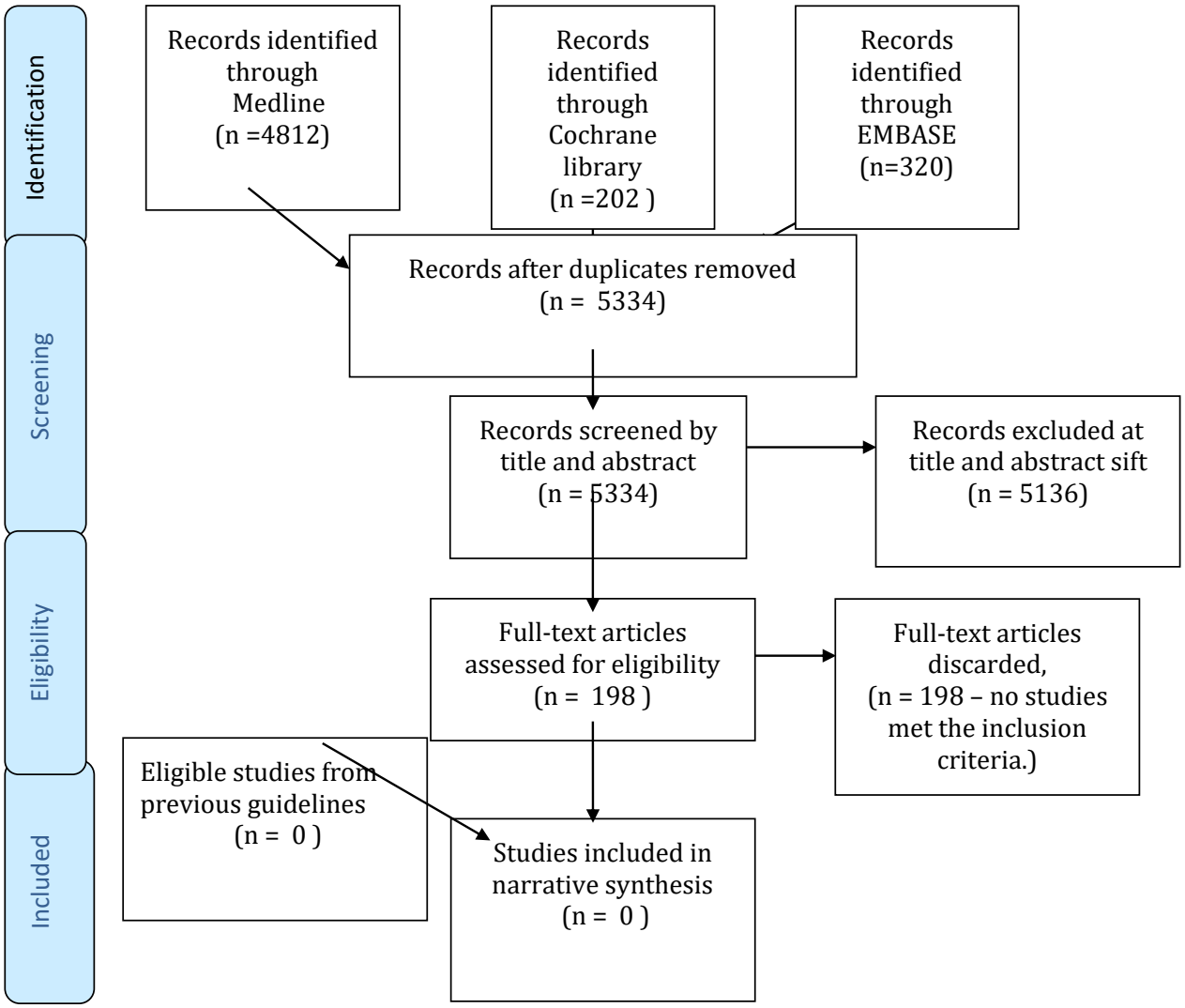
Included studies

No studies were included at full text.

STATEMENT: There is no evidence on which to make an assessment of whether a high quality colonoscopy has a significant impact on findings at surveillance colonoscopy.

Evaluative text: There is no evidence on which to make an assessment of whether a high quality colonoscopy has a significant impact on findings at surveillance colonoscopy.

PRISMA Flow Diagram



Appendix 2

Table 2.1. Search terms for CQ1 – Q16

Medline search terms
26th January 2018

#	Searches
1	exp *Colorectal Neoplasms/
2	((colorect* or colo rect* or colon or bowel* or intestine*) adj3 (cancer* or neoplas* or oncolog* or malignan* or tumo?r* or carcinoma* or adeno*)).tw.
3	*Adenoma/
4	(adenoma* or neoplasia).tw.
5	*Intestinal Polyps/
6	(polyp* or postpolyp* or lesion*).tw.
7	*Colonoscopy/
8	(colonoscop* or postcolonoscop*).tw.
9	(surveillance or ((screening or rescreening) adj2 colonoscop*)).tw.
10	1 or 2
11	or/3-6
12	or/7-9
13	10 and 11 and 12
14	exp *Incidence/
15	exp *Prevalence/
16	incidence.tw.
17	prevalence.tw.
18	*Risk/
19	risk.tw.
20	or/14-19
21	13 and 20
22	(1 or 2) and (3 or 4 or 5 or 6)
23	7 or 8
24	(22 or 23) and 9
25	21 or 24
26	limit 25 to (english language and yr="2007 -Current")
27	letter/
28	editorial/
29	news/
30	exp historical article/
31	anecdotes as topic/
32	comment/
33	case report/
34	(letter or comment*).ti.
35	or/27-34
36	randomized controlled trial/ or random*.ti,ab.

37	35 not 36
38	animals/ not humans/
39	exp animals, laboratory/
40	exp animal experimentation/
41	exp models, animal/
42	exp rodentia/
43	(rat or rats or mouse or mice).ti.
44	or/37-43
45	26 not 44

Embase search terms
26th January 2018

#	Searches
1	exp *colorectal tumor/
2	((colorect* or colo rect* or colon or bowel* or intestine*) adj3 (cancer* or neoplas* or oncolog* or malignan* or tumo?r* or carcinoma* or adeno*)).tw.
3	*adenoma/
4	(adenoma* or neoplasia).tw.
5	*intestine polyp/
6	(polyp* or postpolyp* or lesion*).tw.
7	*colonoscopy/
8	(colonoscop* or postcolonoscop*).tw.
9	(surveillance or ((screening or rescreening) adj2 colonoscop*)).tw.
10	1 or 2
11	or/3-6
12	or/7-9
13	10 and 11 and 12
14	exp *incidence/
15	exp *prevalence/
16	incidence.tw.
17	prevalence.tw.
18	*risk/
19	risk.tw.
20	or/14-19
21	13 and 20
22	(1 or 2) and (3 or 4 or 5 or 6)
23	7 or 8
24	(22 or 23) and 9
25	21 or 24
26	limit 25 to (english language and yr="2007 -Current")
27	letter.pt. or letter/
28	note.pt.
29	editorial.pt.
30	case report/ or case study/
31	(letter or comment*).ti.

32	or/27-31
33	randomized controlled trial/ or random*.ti,ab.
34	32 not 33
35	animal/ not human/
36	nonhuman/
37	exp animal experiment/
38	exp experimental animal/
39	animal model/
40	exp rodent/
41	(rat or rats or mouse or mice).ti.
42	or/34-41
43	26 not 42
44	limit 43 to conference abstract status
45	43 not 44

Cochrane search terms
26th January 2018

#	Searches
#1	MeSH descriptor: [Colorectal Neoplasms] explode all trees
#2	((colorect* or colo rect* or colon or bowel* or intestine*) near/3 (cancer* or neoplas* or oncolog* or malignan* or tumo*r* or carcinoma* or adeno*)):ti,ab
#3	MeSH descriptor: [Adenoma] explode all trees
#4	(adenoma* or neoplasia):ti,ab
#5	MeSH descriptor: [Intestinal Polyps] explode all trees
#6	(polyp* or postpolyp* or lesion*):ti,ab
#7	MeSH descriptor: [Colonoscopy] explode all trees
#8	(colonoscop* or postcolonoscop*):ti,ab
#9	(surveillance or ((screening or rescreening) near/2 colonoscop*)):ti,ab
#10	#1 or #2
#11	{or #3-#6}
#12	{or #7-#9}
#13	#10 and #11 and #12
#14	MeSH descriptor: [Incidence] this term only
#15	MeSH descriptor: [Prevalence] this term only
#16	incidence:ti,ab
#17	prevalence:ti,ab
#18	MeSH descriptor: [Risk] this term only
#19	risk:ti,ab
#20	{or #14-#19}
#21	#13 and #20
#22	surveillance:ti,ab
#23	(#1 or #2) and (#3 or #4 or #5 or #6)
#24	#7 or #8
#25	(#23 or #24) and #22
#26	#21 or #25 Publication Year from 2007

Appendix 3

Table3.1. List of studies excluded at full text sift.

Reference	Reason
ADLER, S. N. 2012. Beat colon cancer mortality? Yes we can! Annals of Gastroenterology, 25, 368.	Opinion
ANDERSON, J., MOTT, L., COLE, B., BARON, J. & ROBERTSON, D. 2015. Surveillance of low risk adenomas at 3 versus 5 year intervals: data to support current surveillance guidelines. Gastroenterology. [Online], 148. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/156/CN-01089156/frame.html.	Abstract only
ANONYMOUS 2014. Millions of data from screening colonoscopy evaluated. Best Practice Onkologie, 9, 4.	Non English Language
ATES, O., SIVRI, B. & KILICKAP, S. 2017. Evaluation of risk factors for the recurrence of colorectal polyps and colorectal cancer. Turkish Journal of Medical Sciences, 47, 1370-1376.	Patients with CRC at baseline not separated in the analysis
BAIK, S. J., PARK, H., PARK, J. J., LEE, H. J., JO, S. Y., PARK, Y. M. & LEE, H. S. 2017. Advanced Colonic Neoplasia at Follow-up Colonoscopy According to Risk Components and Adenoma Location at Index Colonoscopy: A Retrospective Study of 1,974 Asymptomatic Koreans. Gut & Liver, 11, 667-673.	No relevant outcome measures
BAXTER, N. N., WARREN, J. L., BARRETT, M. J., STUKEL, T. A. & DORIA-ROSE, V. P. 2012. Association between colonoscopy and colorectal cancer mortality in a US cohort according to site of cancer and colonoscopist specialty. Journal of Clinical Oncology, 30, 2664-9.	Not about risk of colonoscopy
BECKER, F., NUSKO, G., WELKE, J., HAHN, E. G. & MANSMANN, U. 2007. Benefit-risk analysis of different risk-related surveillance schedules following colorectal polypectomy. Hepato-Gastroenterology, 54, 2249-58.	No original data
BECKER, F., NUSKO, G., WELKE, J., HAHN, E. G. & MANSMANN, U. 2007. Follow-up after colorectal polypectomy: a benefit-risk analysis of German surveillance recommendations. International Journal of Colorectal Disease, 22, 929-39.	No original data
BJERRUM, A., MILTER, M. C., ANDERSEN, O., FISCHER, A. & LYNGE, E. 2015. Risk stratification and detection of new colorectal neoplasms after colorectal cancer screening with faecal occult blood test: experiences from a Danish screening cohort. European Journal of Gastroenterology & Hepatology, 27, 1433-7.	No relevant outcomes reported
BOTTERI, E., CROSTA, C., BAGNARDI, V., TAMAYO, D., SONZOGNI, A. M., DE ROBERTO, G., DE LEONE, A., LOWENFELS, A. & MAISONNEUVE, P. 2016. Predictors of advanced colorectal neoplasia at initial and surveillance colonoscopy after positive screening immunochemical faecal occult blood test. Digestive & Liver Disease, 48, 321-6.	No relevant outcomes
BRAWARSKY, P., NEVILLE, B. A., FITZMAURICE, G. M., EARLE, C. & HAAS, J. S. 2013. Surveillance after resection for colorectal cancer. Cancer, 119, 1235-42.	No relevant outcomes
BRENNER, H., ALTENHOFEN, L. & HOFFMEISTER, M. 2010. Estimated long-term effects of the initial 6 years of the German screening colonoscopy program. Gastrointestinal Endoscopy, 72, 784-9.	Not about surveillance
BRENNER, H., ALTENHOFEN, L., STOCK, C. & HOFFMEISTER, M. 2015. Prevention, early detection, and overdiagnosis of colorectal cancer within 10 years of screening colonoscopy in Germany. Clinical Gastroenterology & Hepatology, 13, 717-23.	Not about surveillance
BRENNER, H., CHANG-CLAUDE, J., JANSEN, L., SEILER, C. M. & HOFFMEISTER, M. 2012. Role of colonoscopy and polyp characteristics in colorectal cancer after colonoscopic polyp detection: a population-based case-control study. Annals of Internal Medicine, 157, 225-32.	Includes patients with remaining polyps

CAFFERTY, F. H., WONG, J. M., YEN, A. M., DUFFY, S. W., ATKIN, W. S. & CHEN, T. H. 2007. Findings at follow-up endoscopies in subjects with suspected colorectal abnormalities: effects of baseline findings and time to follow-up. Cancer Journal, 13, 263-70.	No relevant outcomes
CHA, J. M., KOZAREK, R. A., LA SELVA, D., GLUCK, M., ROSS, A., CHIOREAN, M., KOCH, J. & LIN, O. S. 2016. Risks and Benefits of Colonoscopy in Patients 90 Years or Older, Compared With Younger Patients. Clinical Gastroenterology & Hepatology, 14, 80-6.e1.	Elderly
CHIU, H. M., LEE, Y. C., TU, C. H., CHANG, L. C., HSU, W. F., CHOU, C. K., TSAI, K. F., LIANG, J. T., SHUN, C. T. & WU, M. S. 2015. Effects of metabolic syndrome and findings from baseline colonoscopies on occurrence of colorectal neoplasms. Clinical Gastroenterology & Hepatology, 13, 1134-42.e8.	No relevant analyses
CHOKSHI, R. V., HOVIS, C. E., HOLLANDER, T., EARLY, D. S. & WANG, J. S. 2012. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. Gastrointestinal Endoscopy, 75, 1197-203.	No relevant outcome
COOPER, G. S., KOU, T. D., BARNHOLTZ SLOAN, J. S., KOROUKIAN, S. M. & SCHLUCHTER, M. D. 2013. Use of colonoscopy for polyp surveillance in Medicare beneficiaries. Cancer, 119, 1800-7.	No relevant outcome
COOPER, G. S., XU, F., BARNHOLTZ SLOAN, J. S., SCHLUCHTER, M. D. & KOROUKIAN, S. M. 2012. Prevalence and predictors of interval colorectal cancers in medicare beneficiaries. Cancer, 118, 3044-52.	Not relevant population
CRISPIN, A., MANSMANN, U., MUNTE, A., OP DEN WINKEL, M., GOKE, B. & KOLLIGS, F. T. 2013. A direct comparison of the prevalence of advanced adenoma and cancer between surveillance and screening colonoscopies. Digestion, 87, 170-5.	No comparison data incidence only
CURRIE, A. C., ASKARI, A., RAO, C., SAUNDERS, B. P., ATHANASIOU, T., FAIZ, O. D. & KENNEDY, R. H. 2016. The potential impact of local excision for T1 colonic cancer in elderly and comorbid populations: a decision analysis. Gastrointestinal Endoscopy, 84, 986-994.	No relevant outcomes
DOUBENI, C. A., CORLEY, D. A., QUINN, V. P., JENSEN, C. D., ZAUBER, A. G., GOODMAN, M., JOHNSON, J. R., MEHTA, S. J., BECERRA, T. A., ZHAO, W. K., SCHOTTINGER, J., DORIA-ROSE, V. P., LEVIN, T. R., WEISS, N. S. & FLETCHER, R. H. 2016. Effectiveness of screening colonoscopy in reducing the risk of death from right and left colon cancer: a large community-based study. Gut, 12, 12.	Not age / study design
FIGUEIREDO, J. C., CROCKETT, S. D., SNOVER, D. C., MORRIS, C. B., MCKEOWN-EYSSEN, G., SANDLER, R. S., AHNEN, D. J., ROBERTSON, D. J., BURKE, C. A., BRESALIER, R. S., CHURCH, J. M., CHURCH, T. R. & BARON, J. A. 2015. Smoking-associated risks of conventional adenomas and serrated polyps in the colorectum. Cancer Causes & Control, 26, 377-86.	Outcome not relevant
FORSBERG, A., HAMMAR, U., EKBOM, A. & HULTCRANTZ, R. 2017. Post-colonoscopy colorectal cancers in Sweden: room for quality improvement. European Journal of Gastroenterology & Hepatology, 29, 855-860.	Not a surveillance populations
GOOD, N. M., MACRAE, F. A., YOUNG, G. P., O'DYWER, J., SLATTERY, M., VENABLES, W., LOCKETT, T. J. & O'DWYER, M. 2015. Ideal colonoscopic surveillance intervals to reduce incidence of advanced adenoma and colorectal cancer. Journal of Gastroenterology & Hepatology, 30, 1147-54.	Personal or family history of CRC
GROSS, C. P., SOULOS, P. R., ROSS, J. S., CRAMER, L. D., GUERRERO, C., TINETTI, M. E. & BRAITHWAITE, R. S. 2011. Assessing the impact of screening colonoscopy on mortality in the medicare population. Journal of General Internal Medicine, 26, 1441-9.	Elderly - No relevant outcomes
GUPTA, S., JACOBS, E. T., BARON, J. A., LIEBERMAN, D. A., MURPHY, G., LADABAUM, U., CROSS, A. J., JOVER, R., LIU, L. & MARTINEZ, M. E. 2017. Risk stratification of individuals with low-risk colorectal adenomas using clinical characteristics: a pooled analysis. Gut, 66, 446-453.	Same studies as Martinez but restricts to low risk excluded as doesn't add new data

HAN, M. S., LEE, H. J., PARK, S. J., HONG, S. P., CHEON, J. H., KIM, W. H. & KIM, T. I. 2017. The effect of metformin on the recurrence of colorectal adenoma in diabetic patients with previous colorectal adenoma. International Journal of Colorectal Disease, 32, 1223-1226.	No relevant outcomes
HASSAN, C., PICKHARDT, P. J., DI GIULIO, E., KIM, D. H., ZULLO, A. & MORINI, S. 2009. Cost-effectiveness of early one-year colonoscopy surveillance after polypectomy. Diseases of the Colon & Rectum, 52, 964-71; discussion 971.	Not split by prog factors
HEINE-BRORING, R. C., WINKELS, R. M., BOTMA, A., WAHAB, P. J., TAN, A. C. I. T. L., NAGENGAST, F. M., WITTEMAN, B. J. M. & KAMPMAN, E. 2013. Dietary supplement use is not associated with recurrence of colorectal adenomas: A prospective cohort study. International Journal of Cancer, 132, 666-675.	Did not fit pop inclusion criteria adenoma at any point in their life
HENNINK, S. D., VAN DER MEULEN-DE JONG, A. E., WOLTERBEEK, R., CROBACH, A. S., BECX, M. C., CROBACH, W. F., VAN HAASTERT, M., TEN HOVE, W. R., KLEIBEUKER, J. H., MEIJSSEN, M. A., NAGENGAST, F. M., RIJK, M. C., SALEMANS, J. M., STRONKHORST, A., TUYNMAN, H. A., VECHT, J., VERHULST, M. L., DE VOS TOT NEDERVEEN CAPPEL, W. H., WALINGA, H., WEINHARDT, O. K., WESTERVELD, D., WITTE, A. M., WOLTERS, H. J., CATS, A., VEENENDAAL, R. A., MORREAU, H. & VASEN, H. F. 2015. Randomized Comparison of Surveillance Intervals in Familial Colorectal Cancer. Journal of Clinical Oncology, 33, 4188-93.	Includes patients with zero adenomas at baseline no separate data
HIGURASHI, T., HOSONO, K., TAKAHASHI, H., KOMIYA, Y., UMEZAWA, S., SAKAI, E., UCHIYAMA, T., TANIGUCHI, L., HATA, Y., UCHIYAMA, S., HATTORI, A., NAGASE, H., KESSOKU, T., ARIMOTO, J., MATSUHASHI, N., INAYAMA, Y., YAMANAKA, S., TAGURI, M. & NAKAJIMA, A. 2016. Metformin for chemoprevention of metachronous colorectal adenoma or polyps in post-polypectomy patients without diabetes: a multicentre double-blind, placebo-controlled, randomised phase 3 trial. Lancet Oncology, 17, 475-83.	Some patients had cancer at baseline
HORNUNG, T. A., BEVAN, R., MUMTAZ, S., HORNUNG, B. R. & RUTTER, M. D. 2015. Surveillance colonoscopy in low-risk postpolypectomy patients: Is it necessary? Frontline Gastroenterology, 6, 77-84.	No relevant analyses
HOTTA, K., FUJII, T., SAITO, Y. & MATSUDA, T. 2009. Local recurrence after endoscopic resection of colorectal tumors. International Journal of Colorectal Disease, 24, 225-30.	Only local recurrence no relevant outcomes
HOUISSA, F., KCHIR, H., BOUZAIDI, S., SALEM, M., DEBBECHE, R., TRABELSI, S., MOUSSA, A., SAID, Y. & NAJJAR, T. 2011. Colonoscopy in elderly: feasibility, tolerance and indications: about 901 cases. Tunisie Medicale, 89, 848-52.	Elderly No relevant outcomes
IACOPINI, F. 2015. The post-polypectomy surveillance. Giornale Italiano di Endoscopia Digestiva, 38, 61-65.	Non English
ISOHATA, N., YAMADA, R., MIYAKURA, Y., UTANO, K., ENDO, S., KUMAMOTO, K., AIZAWA, M., NEMOTO, D., KATO, H. & TOGASHI, K. 2016. Validity and safety of colonoscopy in the very elderly: multicenter study in Japan. Journal of gastroenterology and hepatology (australia). Conference: asia pacific digestive week, APDW 2016. Japan. Conference start: 20161102. Conference end: 20161105 [Online], 31. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/915/CN-01252915/frame.html	Elderly No relevant outcomes
JACOBS, E. T., MARTINEZ, M. E., ALBERTS, D. S., JIANG, R., LANCE, P., LOWE, K. A. & THOMPSON, P. A. 2007. Association between body size and colorectal adenoma recurrence. Clinical Gastroenterology & Hepatology, 5, 982-90.	pooled data already included in Martinez
JANG, E. S., KIM, J. W., JUNG, Y. J., JEONG, J. B., KIM, B. G., LEE, K. L., KIM, J. S., JUNG, H. C. & SONG, I. S. 2013. Clinical and endoscopic predictors of colorectal adenoma recurrence after colon polypectomy. Turkish Journal of Gastroenterology, 24, 476-82.	No relevant outcomes
JOHN, B. J., IRUKULLA, S., PILGRIM, G., SWIFT, I. & ABULAFI, A. M. 2008. Surveillance colonoscopies for colorectal polyps--too often, too many! An Audit at a Large District General Hospital. Colorectal Disease, 10, 898-900.	Adherence to guidelines only

JORGENSEN, O. D., KRONBORG, O., FENGER, C. & RASMUSSEN, M. 2007. Influence of long-term colonoscopic surveillance on incidence of colorectal cancer and death from the disease in patients with precursors (adenomas). Acta Oncologica, 46, 355-60.	Barium enema
KAHI, C. J., AZZOUZ, F., JULIAR, B. E. & IMPERIALE, T. F. 2007. Survival of elderly persons undergoing colonoscopy: implications for colorectal cancer screening and surveillance. Gastrointestinal Endoscopy, 66, 544-50.	Elderly – no relevant outcomes
KAWAMURA, T., ODA, Y., MURAKAMI, Y., KOBAYASHI, K., MATSUDA, K., KIDA, M., TANAKA, K., KAWAHARA, Y., KOIZUMI, W., YASUDA, K. & TAJIRI, H. 2014. Relationship between frequency of surveillance colonoscopy and colorectal cancer prevention. Digestive Endoscopy, 26, 409-16.	Incorrect population various numbers of colonoscopies in the past
KEREN, D., RAINIS, T., GOLDSTEIN, O., STERMER, E. & LAVY, A. 2008. Significant colonic neoplasia prevalence and ASGE recommendations: is it time for a change? Journal of Clinical Gastroenterology, 42, 886-91.	No relevant analyses
KIM, B., CHOI, A. R., PARK, S. J., CHEON, J. H., KIM, T. I., KIM, W. H. & HONG, S. P. 2016. Long-Term Outcome and Surveillance Colonoscopy after Successful Endoscopic Treatment of Large Sessile Colorectal Polyps. Yonsei Medical Journal, 57, 1106-14.	No relevant outcomes only local recurrence
KIM, B., KIM, B. C., NAM, S. Y., NAM, J. H., RYU, K. H., PARK, B. J., SOHN, D. K., HONG, C. W., HAN, K. S. & KIM, H. B. 2017. Visceral Adipose Tissue Volume and the Occurrence of Colorectal Adenoma in Follow-up Colonoscopy for Screening and Surveillance. Nutrition & Cancer, 69, 739-745.	CT colonoscopy
KIM, B. C. 2015. Surveillance Colonoscopy After a Resection of Colorectal Cancer. Annals of Coloproctology, 31, 170-1.	Editorial
KIM, H. G., CHO, Y. S., CHA, J. M., SHIN, J. E., KIM, K. O., YANG, H. J., KOO, H. S., JOO, Y. E. & BOO, S. J. 2017. Risk of metachronous neoplasia on surveillance colonoscopy in young patients with colorectal neoplasia. Gastrointestinal Endoscopy, 12, 12.	Screening population not all with adenomas at index
KIM, H. G., LEE, S. H., JEON, S. R., LEE, T. H., KO, B. M., KIM, J. O., CHO, J. Y. & LEE, J. S. 2013. Clinical significance of the first surveillance colonoscopy after endoscopic early colorectal cancer removal. Hepato-Gastroenterology, 60, 1047-52.	Cancer at index
KIM, K. O. 2014. Surveillance colonoscopy after polypectomy: actual practice in Korea. Intestinal Research, 12, 83-4.	Letter
KIM, M. C., JUNG, S. W., KIM, C. S., CHUNG, T. H., YOO, C. I. & PARK, N. H. 2012. Metabolic syndrome is associated with increased risk of recurrent colorectal adenomas in Korean men. International Journal of Obesity, 36, 1007-11.	Outcome AA includes cancer / small sample size
KIM, N. H., PARK, J. H., PARK, D. I., SOHN, C. I., CHOI, K. & JUNG, Y. S. 2016. Metabolic syndrome is a risk factor for adenoma occurrence at surveillance colonoscopy: A single-center experience in Korea. Medicine, 95, e4454.	no relevant outcomes only local recurrence
KIM, Y., KIM, Y. & LEE, S. 2009. An association between colonic adenoma and abdominal obesity: a cross-sectional study. BMC Gastroenterology, 9, 4.	Compares patients with and without adenomas
KNABE, M., POHL, J., GERGES, C., ELL, C., NEUHAUS, H. & SCHUMACHER, B. 2014. Standardized long-term follow-up after endoscopic resection of large, nonpedunculated colorectal lesions: a prospective two-center study. American Journal of Gastroenterology, 109, 183-9.	No relevant outcomes
KOBAYASHI, N., MATSUDA, T., FUJII, T., SANO, Y., KUDO, S.-E., ODA, Y., KANEKO, K., HOTTA, K., SHIMODA, T., SAITO, Y., KONISHI, K., IKEMATSU, H., IISHI, H., KOBAYASHI, K., YAMAGUCHI, Y., HASUDA, K., SHINOHARA, T., ISHIKAWA, H., MURAKAMI, Y., TANIGUCHI, H. & YOSHIDA, S. 2015. Predictive factors of high-risk adenomas at surveillance colonoscopy based on the findings of two-times baseline colonoscopies: results from the Japan polyp study. Gastroenterology. [Online], 148. Available:	Abstract only

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KUSHNIR, V. M., NALBANTOGLU, I., WATSON, R., GOODWIN, J., SAFAR, E., CHOKSHI, R. V., AZAR, R. R. & DAVIDSON, N. O. 2014. Advanced colorectal adenomas in patients under 45 years of age are mostly sporadic. Digestive Diseases & Sciences, 59, 2757-64.	No relevant outcomes
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LAISH, I., SEREGEEV, I., NAFTALI, T. & KONIKOFF, F. M. 2017. Surveillance after positive colonoscopy based on adenoma characteristics. Digestive & Liver Disease, 49, 1115-1120.	No relevant outcome measures
LAIYEMO, A., DOUBENI, C., BRIM, H., ASHKTORAB, H., SCHOEN, R., LANZA, E., PLATZ, E. & CROSS, A. 2012. Race and colon cancer disparity: a comparison of the prevalence and recurrence of adenoma in the polyp prevention trial. Gastroenterology. [Online], 142. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/400/CN-01007400/frame.html.	Abstract only
LAIYEMO, A. O., DOUBENI, C., BRIM, H., ASHKTORAB, H., SCHOEN, R. E., GUPTA, S., CHARABATY, A., LANZA, E., SMOOT, D. T., PLATZ, E. & CROSS, A. J. 2013. Short- and long-term risk of colorectal adenoma recurrence among whites and blacks. Gastrointestinal Endoscopy, 77, 447-54.	Analyses with race as the covariate
LAIYEMO, A. O., PINSKY, P. F., MARCUS, P. M., LANZA, E., CROSS, A. J., SCHATZKIN, A. & SCHOEN, R. E. 2009. Utilization and yield of surveillance colonoscopy in the continued follow-up study of the polyp prevention trial. Clinical Gastroenterology & Hepatology, 7, 562-7; quiz 497.	No relevant outcomes
LANSDORP-VOGELAAR, I., FEDEWA, S., LIN, C. C., VIRGO, K. S. & JEMAL, A. 2014. Utilization of surveillance after polypectomy in the medicare population--a cohort study. PLoS ONE [Electronic Resource], 9, e110937.	No relevant outcomes
LEE, H. S., PARK, H. W., LEE, J. S., KIM, J. C., CHOE, J., SOH, J. S., LEE, S., BAE, J. H., LEE, H. J., YANG, D. H., MYUNG, S. J., YANG, S. K., CHANG, H. S. & BYEON, J. S. 2017. Treatment outcomes and recurrence following standard cold forceps polypectomy for diminutive polyps. Surgical Endoscopy, 31, 159-169.	Advanced adenoma not separated in the model
LEE, J., PARK, S. W., KIM, Y. S., LEE, K. J., SUNG, H., SONG, P. H., YOON, W. J. & MOON, J. S. 2017. Risk factors of missed colorectal lesions after colonoscopy. Medicine, 96, e7468.	Does not compare high and low quality interventions
LEE, J. Y., PARK, H. W., KIM, M. J., LEE, J. S., LEE, H. S., CHANG, H. S., CHOE, J., HWANG, S. W., YANG, D. H., MYUNG, S. J., YANG, S. K. & BYEON, J. S. 2016. Prediction of the Risk of a Metachronous Advanced Colorectal Neoplasm Using a Novel Scoring System. Digestive Diseases & Sciences, 61, 3016-3025.	Not all polypectomy patients
LEE, S. M., KIM, J. H., SUNG, I. K. & HONG, S. N. 2015. The Risk of Metachronous Advanced Colorectal Neoplasia Rises in Parallel with an Increasing Number of High-Risk Findings at Baseline. Gut & Liver, 9, 741-9.	No relevant outcomes
LIEBERMAN, D. A., WEISS, D. G., HARFORD, W. V., AHNEN, D. J., PROVENZALE, D., SONTAG, S. J., SCHNELL, T. G., CHEJFEC, G., CAMPBELL, D. R., KIDAO, J., BOND, J. H., NELSON, D. B., TRIADAFILOPOULOS, G., RAMIREZ, F. C., COLLINS, J. F., JOHNSTON, T. K., MCQUAID, K. R., GAREWAL, H., SAMPLINER, R. E., ESQUIVEL, R. & ROBERTSON, D. 2007. Five-year colon surveillance after screening colonoscopy. Gastroenterology, 133, 1077-85.	No relevant analyses or outcomes
LIM, D. N. F., ROBINSON, R., WURM, P., DECAESTECKER, J. & MOORE, A. 2017. Outcome of an endoscopic mucosal resection service for large sessile colonic polyps (>= 20 mm) over A	No relevant outcomes

9-Year period: A single centre experience and analysis of change over time in a university teaching hospital. Journal of Gastroenterology and Hepatology Research, 6, 2318-2323.	
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LIN, O. S. 2014. Performing colonoscopy in elderly and very elderly patients: Risks, costs and benefits. World Journal of Gastrointestinal Endoscopy, 6, 220-6	Elderly – no relevant outcomes
LIU, L., MESSER, K., BARON, J. A., LIEBERMAN, D. A., JACOBS, E. T., CROSS, A. J., MURPHY, G., MARTINEZ, M. E. & GUPTA, S. 2016. A prognostic model for advanced colorectal neoplasia recurrence. Cancer Causes & Control, 27, 1175-85.	Pooled data from PPT
LOFFELD, R. J. 2014. Development of polyps and cancer in patients with a negative colonoscopy: a follow-up study of more than 20 years. Isrn Gastroenterology Print, 2014, 261302.	Does not compare high and low quality interventions
LORENZO-ZUNIGA, V., MORENO DE VEGA, V., DOMENECH, E., MANOSA, M., CABRE, E., PLANAS, R. & BOIX, J. 2011. High-definition colonoscopy and risk factors for recurrence of advanced adenomas in patients with a personal history of polyps. European Journal of Gastroenterology & Hepatology, 23, 425-30.	Population excluded some had invasive neoplasia at baseline
MARKS, A. R., PIETROFESA, R. A., JENSEN, C. D., ZEBROWSKI, A., CORLEY, D. A. & DOUBENI, C. A. 2015. Metformin use and risk of colorectal adenoma after polypectomy in patients with type 2 diabetes mellitus. Cancer Epidemiology, Biomarkers & Prevention, 24, 1692-8.	Exposure metformin use only
MARTINEZ, M. E., THOMPSON, P., MESSER, K., ASHBECK, E. L., LIEBERMAN, D. A., BARON, J. A., AHNEN, D. J., ROBERTSON, D. J., JACOBS, E. T., GREENBERG, E. R., CROSS, A. J. & ATKIN, W. 2012. One-year risk for advanced colorectal neoplasia: U.S. versus U.K. risk-stratification guidelines. Annals of Internal Medicine, 157, 856-64.	Pooled analysis
MATARESE, V. G., FEO, C. V., LANZA, G., FUSETTI, N., CARPANELLI, M. C., CATALDO, S., CIFALA, V., FERRETTI, S., GAFA, R., MARZOLA, M., MONTANARI, E., PALMONARI, C., SIMONE, L., TREVISANI, L., STOCKBRUGGER, R. & GULLINI, S. 2011. The first 2 years of colorectal cancer screening in Ferrara, Italy. European Journal of Cancer Prevention, 20, 166-8.	No surveillance
MATSUDA, T., FUJII, T., SANO, Y., KUDO, S. E., ODA, Y., IGARASHI, M., IISHI, H., MURAKAMI, Y., ISHIKAWA, H., SHIMODA, T., KANEKO, K. & YOSHIDA, S. 2009. Five-year incidence of advanced neoplasia after initial colonoscopy in Japan: a multicenter retrospective cohort study. Japanese Journal of Clinical Oncology, 39, 435-42.	Not relevant population
MATSUDA, T., FUJII, T., SANO, Y., KUDO, S.-E., ODA, Y., KANEKO, K., HOTTA, K., SHIMODA, T., SAITO, Y., KOBAYASHI, N., KONISHI, K., IKEMATSU, H., IISHI, H., KOBAYASHI, K., YAMAGUCHI, Y., HASUDA, K., SHINOHARA, T., ISHIKAWA, H., MURAKAMI, Y., TANIGUCHI, H., FUJIMORI, T., AJIOKA, Y., SAITO, D. & YOSHIDA, S. 2014. Randomized comparison of surveillance intervals after colonoscopic removal of adenomatous polyps: results from the Japan polyp study. Gastroenterology. [Online], 146. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/250/CN-01061250/frame.html.	Abstract
MATTAR, W. & REX, D. K. 2008. Large sessile adenomas are associated with a high prevalence of synchronous advanced adenomas. Clinical Gastroenterology & Hepatology, 6, 877-9.	Not surveillance
MCGILL, S. K., SOETIKNO, R., ROUSE, R. V., LAI, H. & KALTENBACH, T. 2017. Patients with Nonpolypoid (Flat and Depressed) Colorectal Neoplasms at Increased Risk for Advanced Neoplasias, Compared with Patients with Polypoid Neoplasms. Clinical Gastroenterology & Hepatology, 15, 249-256.e1.	Group comparison no relevant data
MELSON, J., MA, K., ARSHAD, S., GREENSPAN, M., KAMINSKY, T., MELVANI, V., BISHEHSARI, F., MAHON, B. & JAKATE, S. 2016. Presence of small sessile serrated polyps increases rate	No relevant outcome data

of advanced neoplasia upon surveillance compared with isolated low-risk tubular adenomas. Gastrointestinal Endoscopy, 84, 307-14.	
MESHER, D., DOVE-EDWIN, I., SASIENI, P., VASEN, H., BERNSTEIN, I., ROYER-POKORA, B., HOLINSKI-FEDER, E., LALLOO, F., EVANS, D. G., FORSBERG, A., LINDBLOM, A. & THOMAS, H. 2014. A pooled analysis of the outcome of prospective colonoscopic surveillance for familial colorectal cancer. International Journal of Cancer, 134, 939-47.	Cancer at baseline
MILLER, H. L., MUKHERJEE, R., TIAN, J. & NAGAR, A. B. 2010. Colonoscopy surveillance after polypectomy may be extended beyond five years. Journal of Clinical Gastroenterology, 44, e162-6.	No relevant outcomes
MILSOM, J. W. & SHUKLA, P. 2011. Should intraoperative colonoscopy play a role in the surveillance for colorectal cancer? Diseases of the Colon & Rectum, 54, 504-6.	Editorial
MITTAL, S., LIN, Y. L., TAN, A., KUO, Y. F., EL-SERAG, H. B. & GOODWIN, J. S. 2014. Limited life expectancy among a subgroup of medicare beneficiaries receiving screening colonoscopies. Clinical Gastroenterology & Hepatology, 12, 443-450.e1.	Not about risk
MIZUNO, K., SUZUKI, Y., TAKEUCHI, M., KOBAYASHI, M. & AOYAGI, Y. 2014. Natural history of diminutive colorectal polyps: long-term prospective observation by colonoscopy. Digestive Endoscopy, 26 Suppl 2, 84-9.	Not a relevant population
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MUNOZ GARCIA-BORRUEL, M., HERVAS MOLINA, A. J., RODRIGUEZ PERALVAREZ, M. L., MORENO RINCON, E., PEREZ MEDRANO, I., SERRANO RUIZ, F. J., CASAIS JUANENA, L. L., PLEGUEZUELO NAVARRO, M., NARANJO RODRIGUEZ, A. & VILLAR PASTOR, C. 2017. Post-colonoscopy colorectal cancer: Characteristics and predictive factors. Medicina Clinica, 10, 10.	Non English
NAGPAL, S. J. S., MUKHIJA, D., SANAKA, M., LOPEZ, R. & BURKE, C. A. 2017. Metachronous colon polyps in younger versus older adults: a case-control study. Gastrointestinal Endoscopy, 23, 23.	No relevant outcomes
NAKADA, A., NIIKURA, R., YAMADA, A., YOSHIDA, S., HIRATA, Y. & KOIKE, K. 2017. The incidence of post-colonoscopy colorectal cancer: a retrospective long-term cohort study using a colonoscopy database. International Journal of Colorectal Disease, 32, 839-845.	Population includes those without polypectomy
NAYOR, J., SALTZMAN, J. R., CAMPBELL, E. J., PERENCEVICH, M. L., JAJOO, K. & RICHTER, J. M. 2017. Impact of physician compliance with colonoscopy surveillance guidelines on interval colorectal cancer. Gastrointestinal Endoscopy, 85, 1263-1270.	Not a relevant population
NCT. 2014. A Prospective Randomized Controlled Trial of an Endoscopic Quality Improvement Project-2 (EQUIP-2) to Improve Adenoma Detection in Screening and Surveillance Colonoscopy. Clinicaltrials.gov [www.clinicaltrials.gov] [Online]. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/705/CN-01050705/frame.html.	Clinical trials . gov entry only
NISHIHARA, R., WU, K., LOCHHEAD, P., MORIKAWA, T., LIAO, X., QIAN, Z. R., INAMURA, K., KIM, S. A., KUCHIBA, A., YAMAUCHI, M., IMAMURA, Y., WILLETT, W. C., ROSNER, B. A., FUCHS, C. S., GIOVANNUCCI, E., OGINO, S. & CHAN, A. T. 2013. Long-term colorectal-cancer incidence and mortality after lower endoscopy. New England Journal of Medicine, 369, 1095-105.	Not a polypectomy population

OH, D. M., LEE, J. K., KIM, H., PARK, C. K., JUNG, J. K., KIM, D. J., CHUNG, Y. J., KIM, T. H., PARK, M. I. & PARK, J. P. 2017. Local Recurrence and Its Risk Factor after Incomplete Resection of Colorectal Advanced Adenomas: A Single Center, Retrospective Study. Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi, 70, 33-38.	Not relevant population incomplete resection
OKA, S., TANAKA, S., SAITO, Y., IISHI, H., KUDO, S. E., IKEMATSU, H., IGARASHI, M., SAITOH, Y., INOUE, Y., KOBAYASHI, K., HISABE, T., TSURUTA, O., SANO, Y., YAMANO, H., SHIMIZU, S., YAHAGI, N., WATANABE, T., NAKAMURA, H., FUJII, T., ISHIKAWA, H., SUGIHARA, K., COLORECTAL ENDOSCOPIC RESECTION STANDARDIZATION IMPLEMENTATION WORKING GROUP OF THE JAPANESE SOCIETY FOR CANCER OF THE, C. & RECTUM, T. J. 2015. Local recurrence after endoscopic resection for large colorectal neoplasia: a multi-center prospective study in Japan. American Journal of Gastroenterology, 110, 697-707.	Not relevant population incomplete resection
PARK, H. W., HAN, S., LEE, J. Y., CHANG, H. S., CHOE, J., CHOI, Y., SO, H., YANG, D. H., MYUNG, S. J., YANG, S. K., KIM, J. H. & BYEON, J. S. 2015. Probability of high-risk colorectal neoplasm recurrence based on the results of two previous colonoscopies. Digestive Diseases & Sciences, 60, 226-33.	Not relevant population not all polypectomy
PARK, S. K., HWANG, S. W., KIM, K. O., CHA, J. M., BOO, S. J., SHIN, J. E., JOO, Y. E., JUNG, Y., LEE, J., YANG, H. J., PARK, D. I. & INTESTINAL CANCER STUDY GROUP OF THE KOREAN ASSOCIATION FOR THE STUDY OF INTESTINAL, D. 2017. Risk of advanced colorectal neoplasm in patients with more than 10 adenomas on index colonoscopy: A Korean Association for the Study of Intestinal Diseases (KASID) study. Journal of Gastroenterology & Hepatology, 32, 803-808.	Neoplasia and small scale
PARK, S. K., KIM, J. W., PARK, S. H., YANG, D. H., JUNG, K. W., KIM, K. J., YE, B. D., MYUNG, S. J., YANG, S. K., KIM, J. H. & BYEON, J. S. 2014. Risk of developing metachronous colon neoplasm after polypectomy: comparison of one-stage versus two-stage polypectomy. Surgical Endoscopy, 28, 1634-40.	population unclear if polypectomy at index only
PARK, S. K., SONG, Y. S., JUNG, Y. S., KIM, W. H., SOO EUN, C., KO, B. M., SEO, G. S., CHA, J. M., PARK, J. J., MO MOON, C., JUNG, Y., JEON, S. R. & PARK, D. I. 2017. Do surveillance intervals in patients with more than five adenomas at index colonoscopy be shorter than those in patients with three to four adenomas? A Korean Association for the Study of Intestinal Disease study. Journal of Gastroenterology & Hepatology, 32, 1026-1031.	No relevant outcomes.
PARKER-RAY, N., BARAKAT, J., ROY, P. K., WHITE, R. E., SCHRADER, R. M. & HOFFMAN, R. M. 2010. Statin use does not prevent recurrent adenomatous polyp formation in a VA population. Indian Journal of Gastroenterology, 29, 106-11.	Exposure statin use no separate data
PELLISE, M., BURGESS, N. G., TUTTICCI, N., HOURIGAN, L. F., ZANATI, S. A., BROWN, G. J., SINGH, R., WILLIAMS, S. J., RAFTOPOULOS, S. C., ORMONDE, D., MOSS, A., BYTH, K., P'NG, H., MAHAJAN, H., MCLEOD, D. & BOURKE, M. J. 2017. Endoscopic mucosal resection for large serrated lesions in comparison with adenomas: a prospective multicentre study of 2000 lesions. Gut, 66, 644-653.	Not relevant population no relevant outcomes
POHL, H., ROBERTSON, D. J., MOTT, L. A., AHNEN, D. J., BURKE, C. A., BARRY, E. L., BRESALIER, R. S., FIGUEIREDO, J. C., SHAUKAT, A., SANDLER, R. S. & BARON, J. A. 2016. Association between adenoma location and risk of recurrence. Gastrointestinal Endoscopy, 84, 709-16.	Outcome not relevant neoplasia
PULLENS, H. J., LEENDERS, M., SCHIPPER, M. E., VAN OIJEN, M. G. & SIERSEMA, P. D. 2015. No decrease in the rate of early or missed colorectal cancers after colonoscopy with polypectomy over a 10-year period: a population-based analysis. Clinical Gastroenterology & Hepatology, 13, 140-7.	Not relevant population
QASIM, A., MULDOON, C. & MCKIERNAN, S. 2009. Colonic adenoma patients have higher incidence of hyperplastic polyps on surveillance colonoscopy. European Journal of Gastroenterology & Hepatology, 21, 877-81.	No relevant outcomes in the relevant group
RAJU, G. S., LUM, P. J., ROSS, W. A., THIRUMURTHI, S., MILLER, E., LYNCH, P. M., LEE, J. H., BHUTANI, M. S., SHAFI, M. A., WESTON, B. R., PANDE, M., BRESALIER, R. S., RASHID, A.,	Local recurrence no relevant outcome

MISHRA, L., DAVILA, M. L. & STROEHLEIN, J. R. 2016. Outcome of EMR as an alternative to surgery in patients with complex colon polyps. Gastrointestinal Endoscopy, 84, 315-25.	
RAMSEY, S. D., HOWLADER, N., ETZIONI, R., BROWN, M. L., WARREN, J. L. & NEWCOMB, P. 2007. Surveillance endoscopy does not improve survival for patients with local and regional stage colorectal cancer. Cancer, 109, 2222-8.	Cancer population
RANDALL, J. K., GOOD, C. S. & GILBERT, J. M. 2013. 22-year longitudinal study of repetitive colonoscopy in patients with a family history of colorectal cancer. Annals of the Royal College of Surgeons of England, 95, 586-90.	Not relevant population at index (mixed, no separate data)
REN, J., KIRKNESS, C. S., KIM, M., ASCHE, C. V. & PULI, S. 2016. Long-term risk of colorectal cancer by gender after positive colonoscopy: population-based cohort study. Current Medical Research & Opinion, 32, 1367-74.	Not relevant population (no separate data for polypectomy subgroup)
ROBERTSON, D. J., BURKE, C. A., WELCH, H. G., HAILE, R. W., SANDLER, R. S., GREENBERG, E. R., AHNEN, D. J., BRESALIER, R. S., ROTHSTEIN, R. I., COLE, B., MOTT, L. A. & BARON, J. A. 2009. Using the results of a baseline and a surveillance colonoscopy to predict recurrent adenomas with high-risk characteristics. Annals of Internal Medicine, 151, 103-9.	No relevant outcome data
ROBERTSON, D. J., LIEBERMAN, D. A., WINAWER, S. J., AHNEN, D. J., BARON, J. A., SCHATZKIN, A., CROSS, A. J., ZAUBER, A. G., CHURCH, T. R., LANCE, P., GREENBERG, E. R. & MARTINEZ, M. E. 2014. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut, 63, 949-56.	Pooled analysis
ROSA, I., FIDALGO, P., SOARES, J., VINGA, S., OLIVEIRA, C., SILVA, J. P., FERRO, S. M., CHAVES, P., OLIVEIRA, A. G. & LEITAO, C. N. 2012. Adenoma incidence decreases under the effect of polypectomy. World Journal of Gastroenterology, 18, 1243-8.	No relevant outcomes
ROZEN, P., SHABTAI, E. I., LIPHSHITZ, I. & BARCHANA, M. 2011. Risk for colorectal cancer in elderly persons and possible methodologies for their screening. European Journal of Gastroenterology & Hepatology, 23, 431-7.	Elderly – no relevant outcomes
SAINI, S., SCHOENFELD, P. & VIJAN, S. 2010. Surveillance colonoscopy is cost-effective for patients with adenomas who are at high risk of colorectal cancer (Provisional abstract). Gastroenterology [Online], 138. Available: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22010001139/frame.html https://www.sciencedirect.com/science/article/pii/S0016508510003392?via%3Dihub.	Population - polyps remained
SAINI, S. D., SCHOENFELD, P. & VIJAN, S. 2010. Surveillance colonoscopy is cost-effective for patients with adenomas who are at high risk of colorectal cancer. Gastroenterology, 138, 2292-9, 2299.e1.	Duplicate
SAKAMOTO, T., MATSUDA, T., OTAKE, Y., NAKAJIMA, T. & SAITO, Y. 2012. Predictive factors of local recurrence after endoscopic piecemeal mucosal resection. Journal of Gastroenterology, 47, 635-40.	Not relevant outcome
SAMADDER, N. J., CURTIN, K., TUOHY, T. M., PAPPAS, L., BOUCHER, K., PROVENZALE, D., ROWE, K. G., MINEAU, G. P., SMITH, K., PIMENTEL, R., KIRCHHOFF, A. C. & BURT, R. W. 2014. Characteristics of missed or interval colorectal cancer and patient survival: a population-based study. Gastroenterology, 146, 950-60.	CRC population and adenoma at index a risk factor
SANO, Y., FUJII, T., MATSUDA, T., ODA, Y., KUDO, S., IGARASHI, M., IISHI, H., KANEKO, K., HOTTA, K., KOBAYASHI, N., YAMAGUCHI, Y., KOBAYASHI, K., ISHIKAWA, H., MURAKAMI, Y., SHIMODA, T., FUJIMORI, T., AJIOKA, Y., TANIGUCHI, H., IKEMATSU, H., KONISHI, K., SAITO, Y. & YOSHIDA, S. 2014. Study design and patient recruitment for the Japan Polyp Study. Open Access Journal of Clinical Trials, 6, 37-44.	Methodological study

SCHEER, A. & AUER, R. A. 2009. Surveillance after curative resection of colorectal cancer. Clinics in Colon & Rectal Surgery, 22, 242-50.	Cancer
SEO, G. J., SOHN, D. K., HAN, K. S., HONG, C. W., KIM, B. C., PARK, J. W., CHOI, H. S., CHANG, H. J. & OH, J. H. 2010. Recurrence after endoscopic piecemeal mucosal resection for large sessile colorectal polyps. World Journal of Gastroenterology, 16, 2806-11.	No relevant outcomes recurrence
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