Review of the lower age limit and frequency of early-detection colonoscopy in the colorectal cancer screening programme[1]

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This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

According to §139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose 'all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received'. The Institute received the completed 'Form for disclosure of potential conflicts of interest' from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Chapter A14 of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

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IQWiG thanks the external experts for their collaboration in the project.

Patient and family involvement

Patients or family members were consulted during the preparation of the report.

One person participated in the discussion.

The aim of the discussion was to obtain information on the following topics: expectations regarding the early detection examination and motivation to take part, experiences with the examination, consequences of results and concerns regarding the screening examination.

IQWiG would like to thank the participant for taking part in the discussion. This person was not involved in the actual writing of the report.

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Key statement

Research question

The aim of this investigation was to

- assess the benefit of CRC screening using colonoscopy or iFOBT compared with no CRC screening in people under the age of 50 years (research question 1: review of the lower age limit),
- assess the benefit of CRC screening using
  - 3 colonoscopies, each carried out at intervals of 10 years, or
  - 3 colonoscopies, each carried out at intervals of more than 10 years, or
  - 2 colonoscopies, carried out at an interval of more than 10 years,

  compared with the current CRC screening programme of colonoscopy with a maximum of 2 examinations with an interval of 10 years, for people aged 45 years and older (research question 2: review of the intervals between and number of colonoscopies).

Both research questions relate to individuals with no suspected CRC and no specific increased risk of CRC, and examine the benefits in terms of patient-relevant outcomes.

Conclusion

Benefit assessment

In the benefit assessment, no relevant studies were identified for either of the 2 research questions. It is therefore not proven whether people under the age of 50 with no suspected CRC and no specific increased risk of CRC can benefit from CRC screening. It also remains unproven whether people aged 45 and over, with no suspected CRC and no specific increased risk of CRC, would benefit from a colonoscopy screening programme with modifications in terms of the number of screenings and the intervals between them. Overall, therefore, in the absence of direct evidence, no benefit can be derived.

Modelling

In addition to the benefit assessment, decision-analytic modelling was therefore conducted to obtain information on different options for CRC screening. It should be noted that the results were determined from the perspective of participants who attend the screening regularly and fully (100%) and who fully adhere to any clarification tests for positive findings and surveillance procedures.

The key findings of the modelling show the ratio of additional colonoscopies (disadvantage) for one additional case of CRC prevented and, furthermore, for one life year gained (both advantages). These are calculated as the difference in the total number of colonoscopies (incremental colonoscopies) divided by the difference in the respective outcome (incremental cases of CRC prevented or life years gained) when comparing 2 undominated screening strategies. Strategies that involve, for example, fewer colonoscopies whilst at the same time being associated with more cases of CRC or more years of life gained, compared with other strategies, lie on what is known as the efficiency frontier. All undominated strategies lie on the efficiency frontier and represent screening alternatives from which the optimal strategy can be selected, depending on a threshold value. It should be noted, however, that recommending specific screening strategies based on the modelling results requires the establishment of a threshold value for an acceptable ratio (e.g. measured in terms of the number of additional colonoscopies per life year gained). Setting such a threshold value would involve a value judgement and is therefore not undertaken in this report.

For screening using iFOBT, for example, a strategy involving tests every 2 years from the age of 45, rather than from the current age of 50, could potentially offer an advantage. However, when varying the probability of participation, this finding was only partially confirmed in men, and was not confirmed in women. Modelling showed that shortening the interval to an annual iFOBT resulted in a further increase in effectiveness, i.e. a slightly higher number of CRC cases prevented and life years gained; however, this was associated with a substantially greater number of colonoscopies.

In the case of colonoscopy-based screening, it would seem more advantageous to conduct CRC screening over a longer period than to start it earlier. One way to achieve this would be to adopt a strategy involving 3 colonoscopies instead of the current 2, whilst maintaining the current lower age limit of 50 years for starting screening. This finding was confirmed when varying the reduction in the probability of participation. If the maximum possible number of 2 colonoscopies in the current CRC screening programme is not to be exceeded, extending the screening interval to 15 years, for example, would potentially be superior to the current screening programme. However, when varying the reduction in the probability of participation, this finding was not confirmed. For women, CRC screening is potentially advantageous even in later life, whereas for men, starting screening at an earlier age is likely to offer a greater advantage compared with the current screening programme. If the lower age limit is to be reduced, then CRC screening starting at the age of 45 would also be a potentially advantageous option (compared with younger lower age limits, it would be at least as effective whilst requiring substantially fewer colonoscopies). However, if the lower age limit for starting screening were to be reduced, the screening interval would need to be extended to 20 years, or the maximum possible number of colonoscopies would need to be increased, as otherwise the overall screening period would be too short.

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List of abbreviations

Abbreviation	Meaning
ACG	American College of Gastroenterology
CRC	colorectal cancer
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
iFOBT	immunological faecal occult blood test
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
SR	systematic review
SSL	sessile serrated lesion
USPSTF	U.S. Preventive Services Task Force

1 Background

Colorectal cancer (CRC) or bowel/colon cancer refers to malignant neoplasms of colon (ICD-10 C18), rectosigmoid junction (ICD-10 C19) and rectum (ICD-10 C20) [1]. In Germany, CRC is the second most common cancer among all new cancer cases in women and the third most common in men. For both women and men, CRC is estimated to be the third most common cause of cancer death [2].

In around three-quarters of cases, CRC develops from slow-growing, initially benign neoplasms (adenomas) that form in the mucosa of the colon and rectum and are often polypoid [3,4]. According to the adenoma-carcinoma sequence model [5], adenomas can grow through various stages, invade the deeper layers of the intestinal wall and become malignant. Approximately one-quarter of CRCs develop on the base of serrated polyps (which include, among others, sessile serrated lesions [SSLs]) [4]. Screening tests for CRC have 2 objectives: One is to detect and remove precancerous lesions before they become malignant. Secondly, carcinomas should be identified before they become symptomatic and metastasize. The ultimate aim is to reduce morbidity, in particular the rate of new cases of CRC, and (CRC-specific) mortality [6].

Under the regulations governing organized CRC screening set out in the Directive for Organized Cancer Screening Programmes (oKFE-RL), people covered by statutory health insurance in Germany are entitled to CRC screening from the age of 50 [6]. Until March 2025, the screening programme differed for men and women aged between 50 and 54: From the age of 50, men could choose between 2 colonoscopies 10 years apart or an immunological faecal occult blood test (iFOBT), which was offered annually between the ages of 50 and 54 and then every 2 years. Women could choose to have 2 colonoscopies 10 years apart from the age of 55, or opt for the iFOBT, which was offered annually between the ages of 50 and 54 and then every 2 years. As of 1 April 2025, the screening programme was unified [7,8]: From this date onwards, men and women aged 50 and older have the choice between a screening test using iFOBT and a screening test using colonoscopy. Screening tests using an iFOBT can be taken every 2 years. If the result of the iFOBT is positive, the individual is entitled to a colonoscopy for clarification. The entitlement to colonoscopies as a screening examination is limited to a total of 2, with the second being carried out at the earliest 10 years after the first. Following a colonoscopy, a screening test using iFOBT is only available on statutory health insurance after 10 years. If the first colonoscopy is conducted from the age of 65, there is no entitlement to a further screening colonoscopy.

There are alternatives to both the iFOBT and colonoscopy, although these are no longer used in the German screening programme in accordance with the oKFE-RL:

In 2016, the iFOBT replaced the guaiac-based faecal occult blood test (gFOBT) that had previously been used for screening for CRC in accordance with the oKFE-RL [9]. The change was justified on the grounds that the iFOBT offers better test accuracy than the gFOBT [10]. It was assumed that the benefits of screening using gFOBT, which were considered to be proven, were transferable to screening using iFOBT in terms of reducing the incidence and mortality of CRC [10].

In addition to colonoscopy, sigmoidoscopy is another endoscopic screening procedure. The effectiveness of sigmoidoscopy in CRC screening is considered well established [3,11]. However, unlike a colonoscopy, this examination does not cover all sections of the large intestine, meaning that tumours and adenomas located in the proximal section cannot be detected [11]. For this reason, colonoscopy is considered the superior method [11].

If adenomas, SSLs or early carcinomas are identified during an endoscopic (screening) examination, the lesion is completely removed (polypectomy), if possible, during the same or a subsequent colonoscopy session with subsequent follow-up colonoscopies [11]. If CRC is identified in the course of these examinations, treatment consists of endoscopic or surgical tumour resection, which may be followed by adjuvant chemotherapy [11].

Both national and international organizations strongly recommend screening for CRC, although there are differences in the preferred screening strategies. Recently, both the American Cancer Society and the American College of Gastroenterology (ACG), as well as the U.S. Preventive Services Task Force (USPSTF) reviewed their age recommendations for the start of screening in people with an average risk of CRC, proposing an age of 45 years [12-15].

This benefit assessment therefore aims to investigate whether, and to what extent, people under the age of 50 can benefit from CRC screening. It also aims to investigate the extent to which individuals benefit from participating in a colonoscopy screening programme that has been modified in terms of the number of screening tests and the intervals between them.

2 Research question

The aim of this investigation was to

- assess the benefit of CRC screening using colonoscopy or iFOBT compared with no CRC screening in people under the age of 50 years (research question 1: review of the lower age limit),
- assess the benefit of CRC screening using
  - 3 colonoscopies, each carried out at intervals of 10 years, or
  - 3 colonoscopies, each carried out at intervals of more than 10 years, or
  - 2 colonoscopies, carried out at an interval of more than 10 years,

  compared with the current CRC screening programme of colonoscopy with a maximum of 2 examinations with an interval of 10 years, for people aged 45 years and older (research question 2: review of the intervals between and number of colonoscopies).

Both research questions relate to individuals with no suspected CRC and no specific increased risk of CRC, and examine the benefits in terms of patient-relevant outcomes.

3 Methods

3.1 Benefit assessment

The benefit assessment comprised 2 research questions:

Research question 1 concerned the review of the lower age limit in CRC screening with regard to patient-relevant outcomes. The target population for research question 1 consisted of people under the age of 50 with no suspected CRC and no specific increased risk of CRC. The experimental intervention involved CRC screening using colonoscopy or iFOBT, or potentially sigmoidoscopy or gFOBT. The comparator intervention was the current strategy for CRC screening using colonoscopy or iFOBT (no CRC screening for people under the age of 50; CRC screening from the age of 50).

Research question 2 concerned the review of the intervals between and number of colonoscopies in CRC screening with regard to patient-relevant outcomes. The target population for research question 2 consisted of people aged 45 years and older with no suspected CRC and no specific increased risk of CRC. The experimental intervention in each case were strategies for CRC screening using colonoscopy modified in terms of the interval between examinations and the number of examinations (CRC screening using 3 colonoscopies at intervals of 10 years, or using 3 colonoscopies at intervals of more than 10 years each, or using 2 colonoscopies at intervals of more than 10 years). The comparator intervention was the current strategy for CRC screening using colonoscopy, with a maximum of 2 colonoscopies at least 10 years apart.

In both research questions, the following patient-relevant outcomes were taken into account in the assessment:

- Mortality (all-cause mortality and CRC-specific mortality)
- Morbidity (e.g. occurrence of CRC, occurrence of advanced adenomas, occurrence of advanced SSLs, colorectal resection, faecal incontinence, having a stoma, consequences of false screening results)
- Health-related quality of life
- Adverse events

For both research questions, only randomized controlled trials (RCTs), quasi-randomized controlled trials and prospective comparative cohort studies with active group allocation were considered for inclusion in the benefit assessment. If studies on sigmoidoscopy or gFOBT were to be included in research question 1, they would have been limited to RCTs. A further criterion for study inclusion was that the findings were expected to be transferable to the

German health care system, and that each study arm included at least 1000 participants. There were no restrictions regarding the study duration.

In parallel with the development of the report plan, a search for systematic reviews was conducted in the MEDLINE database (which also includes the Cochrane Database of Systematic Reviews) and the HTA Database, as well as on the websites of the National Institute for Health and Care Excellence (NICE) and the Agency for Healthcare Research and Quality (AHRQ).

It was ascertained whether at least one high-quality, current systematic review existed whose information retrieval could be used as a suitable basis (hereinafter: basic SR).

If that was the case, a second step followed, in which a supplementary search was conducted for studies for the time period not covered by the basic SR(s). Otherwise, the search for studies was conducted without any time restrictions.

The systematic literature search for studies was conducted in the following databases: MEDLINE, Embase and the Cochrane Central Register of Controlled Trials.

In addition, the following sources of information and search techniques were considered: trial registries, the G-BA and IQWiG websites, a review of the reference lists from identified systematic reviews, documents provided during hearing procedures, and author queries.

The selection of relevant studies was performed by 2 people independently of each other, who resolved any discrepancies by discussion.

Data were to be extracted into standardized tables. To assess the qualitative certainty of results, risk of bias criteria across outcomes and outcome-specific risk of bias criteria were to be assessed, and the risk of bias was to be rated as low or high in each case. The results of the individual studies were to be described, organized by outcomes.

In addition to comparing the results of the individual studies, meta-analyses and sensitivity analyses were to be conducted and effect modifiers were to be investigated, provided that the methodological prerequisites had been met.

For each outcome, a conclusion was to be drawn regarding the evidence base for (greater) benefit or (greater) harm, with 4 levels of certainty of conclusions: There was either proof (highest certainty of conclusions), indication (moderate certainty of conclusions), hint (lowest certainty of conclusions), or none of those 3 situations. The latter was the case if either no data were available or the available data did not allow any of the other 3 conclusions to be drawn. In this case, the conclusion ‘There is no hint of (greater) benefit or (greater) harm’ was drawn.

Finally, an assessment across all outcomes of the benefits and harms was to be carried out.

3.2 Modelling

The rationale and objectives of decision-analytical modelling

In this context, a decision-analytical model was used to enable the systematic, explicit and quantitative evaluation of possible screening strategies. By synthesizing evidence from various data sources and taking multiple target parameters (outcomes) into account, a decision-analytic model based on the available evidence can identify the 'optimal' screening strategy from different perspectives (e.g. payers) for different time horizons.

Research question 2 focused on very specific variations in the intervals between and the number of colonoscopies, in combination with a specific lower age limit for CRC screening, which were to be compared with the current, equally specific strategy for CRC screening in Germany. Given the high degree of specificity and the number of screening strategies under consideration, it was anticipated that evidence would not be available for all variations in the benefit assessment. Since decision-analytic modelling allows for the simultaneous simulation of multiple strategies, it was decided from the outset to carry out modelling in addition to the benefit assessment. In modelling, a comparatively low certainty of results is assumed due to the indirect evidence involved; consequently, hints can only be derived in certain data situations (e.g. a valid and sufficiently robust model combined with informative results from relevant RCTs on CRC screening). In the absence of such data conditions, the results of the modelling are not reliable enough to provide conclusive support for the derivation of the evidence base. Even in this case, however, the results of the decision-analytic modelling retain their significance as a potential additional source of information for the decisions to be taken on the basis of this report.

State-transition model (Markov model)

To answer the research questions, a Markov state-transition model was developed, programmed and calibrated to simulate the progression of CRC from precancerous lesions. The model was based on an existing, high-quality Markov model that has already been calibrated for Austria [16]. The data contained in the publication for the model input parameters were reviewed and, where necessary, replaced with more up-to-date data that are more relevant to Germany (i.e. with higher external validity) or data with a lower risk of systematic bias. As not all transition probabilities were known in the model, these transition probabilities were estimated through calibration, using the age-specific incidence in Germany and the Union for International Cancer Control (UICC) stage distribution. Epidemiological data were retrieved from the Centre for Cancer Registry Data (ZfKD), and clinical data from international studies on the test accuracy (sensitivity and specificity) of colonoscopy and iFOBT, as well as on adverse events associated with colonoscopy, were searched and utilized.

Strategies evaluated

Table 1: Overview of the strategies investigated

Symbol/ colour	Strategy	Status / purpose of the strategy
✖	No organized screening (no screening)	
	iFOBT-based strategies	Investigational strategies for research question 1
■	iFOBT every 2 years, from the age of 35 (iFOBT [2Y, from 35])	
●	iFOBT every 2 years, from the age of 40 (iFOBT [2Y, from 40])	
◇	iFOBT every 2 years, from the age of 45 (iFOBT [2Y, from 45])	
□	iFOBT every 3 years, from the age of 35 (iFOBT [3Y, from 35])	
	Colonoscopy-based strategies	
▲	Colonoscopy every 10 years from the age of 40, up to a maximum of 3 colonoscopies (colonoscopy [10Y, 40, 50 and 60])	
◆	Colonoscopy every 10 years from the age of 45, up to a maximum of 2 colonoscopies (colonoscopy [10Y, 45 and 55])	
■	Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75])	
▲	Colonoscopy every 15 years from the age of 35, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 35, 50 and 65])	
◆	Colonoscopy every 15 years from the age of 40, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 40, 55 and 70])	
◆	Colonoscopy every 10 years from the age of 45, up to a maximum of 3 colonoscopies (colonoscopy [10Y, 45, 55 and 65])	Investigational strategies for research question 2
○	Colonoscopy every 15 years from the age of 45, up to a maximum of 2 colonoscopies (colonoscopy [15Y, 45 and 60])	
●	Colonoscopy every 15 years from the age of 45, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 45, 60 and 75])	
□	Colonoscopy every 20 years from the age of 45, up to a maximum of 2 colonoscopies (colonoscopy [20Y, 45 and 65])	
	iFOBT-based strategies	
■	iFOBT every year, from the age of 50 (iFOBT [1Y, from 50])	Supplementary investigational strategies
	Colonoscopy-based strategies	
●	Colonoscopy every 10 years from the age of 50, up to a maximum of 3 colonoscopies (colonoscopy [10Y, 50, 60 and 70])	
□	Colonoscopy every 15 years from the age of 50, up to a maximum of 2 colonoscopies (colonoscopy [15Y, 50 and 65])	
■	Colonoscopy every 15 years from the age of 50, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 50, 65 and 80])	

iFOBT: immunological faecal occult blood test; Y: years

Analyses and outcomes

Deterministic cohort simulations were conducted with the following outcomes: remaining life expectancy at age 35, prevented cases of CRC and deaths from CRC, number of colonoscopies (consisting of screening, clarification, surveillance and indicated colonoscopies), the number of positive (for both the iFOBT and colonoscopy) and false-positive (for the iFOBT) test results, as well as the number of adverse events associated with colonoscopy. Adverse events were defined as events that require medical treatment (e.g. severe bleeding and perforations). The reference case analysis showed, from the participants' perspective, the expected impact on the above-mentioned outcomes for a cohort of men/women who participate regularly and fully in the screening programme (100% participation) and who fully adhere to any clarification tests for positive findings and surveillance. Base-case and sensitivity analyses, as well as external validations, were additionally carried out.

Harm-benefit diagrams

In the following (see Section 4.2), the terms 'benefit' and 'harm' are used in the harm-benefit diagrams differently from their use in benefit assessment, but in line with their usage in the field of decision-analytic modelling. This is intended merely as a description in terms of undesirable ('harm') and desirable outcomes ('benefit') and should not be interpreted as a conclusion regarding the benefit.

Average values for desired and undesired outcomes were calculated for each of the screening strategies, with the disadvantage being measured using the outcome 'number of colonoscopies' (consisting of screening, clarification, surveillance and indicated colonoscopies) for resources invested, whilst the advantages were expressed in terms of the outcomes 1) number of CRC cases prevented and 2) number of life years gained. The ratio of additional colonoscopies required to prevent one additional case of CRC or to gain one additional year of life was a key finding of the modelling. To calculate this, the difference in the number of total colonoscopies (incremental colonoscopies) is divided by, for example, the difference in the number of CRC cases prevented (incremental CRC cases prevented) between 2 screening alternatives, with the comparison being carried out step by step against the next-best[2] alternative.

When determining the efficiency frontier, both dominated strategies and strategies with extended dominance are excluded. Dominant strategies are those which have a better ratio of additional colonoscopies per one additional case of CRC prevented or per one life year gained than the next-best strategy (e.g. a higher number of colonoscopies and lower positive effectiveness in terms of life years gained or cases of CRC prevented). Extended dominance is present when the linear combination of 2 strategies investigated that lie on the efficiency

[2]The next, less effective strategy on the efficiency frontier

frontier (i.e. part of the population receives strategy A, the rest strategy B) outperforms a single other strategy that lies below the efficiency frontier. In concrete terms, this means that the ratio of additional colonoscopies required to prevent one additional case of CRC or to gain one additional year of life under the single strategy is higher than the ratio of additional colonoscopies required to prevent one additional case of CRC or to gain one additional year of life under the weighted combination of the other 2 strategies (see Section A3.2).

4 Results

4.1 Benefit assessment

4.1.1 Results of the information retrieval

For research question 1, one systematic review was taken into account as a basic SR for the identification of primary studies. For research question 2, no systematic review was taken into account as a basic SR for the identification of primary studies.

The information retrieval did not identify any studies relevant to the research questions. No planned or ongoing studies were identified. In addition, one study with an unclear status was identified.

The search strategies for bibliographic databases and trial registries can be found in the appendix. The last search was conducted on 29 December 2025.

4.1.2 Summarized assessment of the results

No relevant studies were identified for either of the 2 research questions.

With regard to research question 1, there is no hint of a benefit or harm of CRC screening in people under the age of 50 with no suspected CRC and no specific increased risk of CRC.

With regard to the study mentioned in Section 4.1.1 (and described in Section A4.1.4) on reviewing the lower age limit with unclear status, it remains unclear whether the study was continued and whether the results are likely to be published in the foreseeable future.

With regard to research question 2, there is no hint of a benefit or harm for any of the strategies to be evaluated in people aged 45 years and older with no suspected CRC and no specific increased risk of CRC.

Overall, no studies were identified that are expected to yield relevant findings on either of the 2 research questions in the future.

4.2 Modelling

In addition to the benefit assessment, decision-analytic modelling was carried out in the context of both research questions (see Section 3.2).

Remaining life expectancy at age 35 and events prevented

Compared with no screening, CRC screening was associated with an increase in average remaining life expectancy in men at age 35 by 2.16 to 3.36 months (0.18 to 0.28 years) for iFOBT-based strategies, and by 4.44 to 5.76 months (0.37 to 0.48 years) for colonoscopy-based strategies. In women, compared with no screening, the remaining life expectancy at age 35

was increased by 1.68 to 2.64 months (0.14 to 0.21 years) with iFOBT-based screening strategies, and by 2.88 to 3.72 months (0.24 to 0.31 years) with colonoscopy-based strategies.

Among iFOBT-based strategies, an annual iFOBT from the age of 50 (iFOBT [1Y from 50]) showed the highest figures for remaining life expectancy at age 35 and for the number of CRC deaths prevented for both men and women, as a supplementary investigational strategy versus no screening.

Among the colonoscopy-based strategies, the following screening strategies had very similar results in research question 1 for men. The highest values for the outcome 'average remaining life expectancy at age 35' were found for the following strategies:

- Colonoscopy every 15 years from the age of 35, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 35, 50 and 65]),
- Colonoscopy every 15 years from the age of 40, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 40, 55 and 70]) and
- Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75])

The latter colonoscopy-based strategy also showed the highest number of prevented CRC cases and CRC deaths.

In all these outcomes, the following screening strategy was superior to all other screening strategies in women:

- Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75])

Adverse events and positive test results

The modelling results showed that as the intensity of screening increases, not only do positive test results increase, but so do adverse events. In iFOBT-based screening, this was the case for tests with shorter intervals between them or where the lower age limit for the start of screening was reduced; in colonoscopy, this was the case in particular for an increase in the maximum possible number of colonoscopies.

An annual iFOBT from the age of 50 (iFOBT [1Y from 50]) showed the highest figures for men and women respectively in terms of positive (2356 and 2307) and false-positive (667 and 865) test results per 1000 people, as well as the highest number of adverse events of colonoscopy requiring intervention (severe bleeding + perforations: 4.67 and 4.61 respectively) compared with the other strategies.

In research question 1, the following colonoscopy-based screening strategies showed the highest numbers of adverse events requiring intervention per 1000 people for both men and women, compared with the other strategies:

- Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75]), at 7.59 and 8.06, respectively,
- Colonoscopy every 15 years from the age of 35, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 35, 50 and 65]), at 6.96 and 7.02, respectively, and
- Colonoscopy every 15 years from the age of 40, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 40, 55 and 70]), at 6.72 and 6.90, respectively.

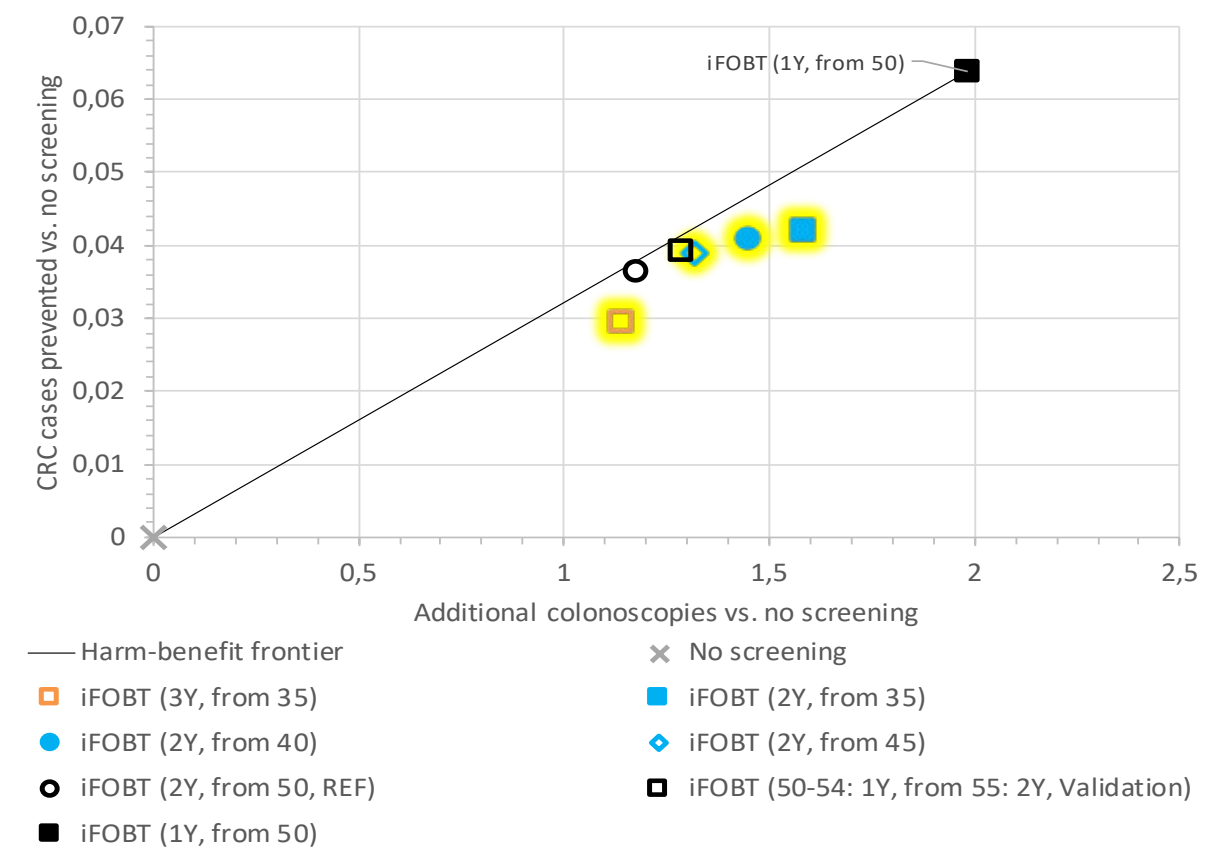
The highest number of positive test results per 1000 people resulted from

- Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75]) (investigational strategy in research question 1), at 689 and 573, respectively,
- Colonoscopy every 15 years from the age of 45, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 45, 60 and 75]) (investigational strategy in research question 2), at 630 and 534, respectively, and
- Colonoscopy every 15 years from the age of 50, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 50, 65 and 80]) (supplementary investigational strategy), at 634 and 550, respectively

Harm-benefit diagrams

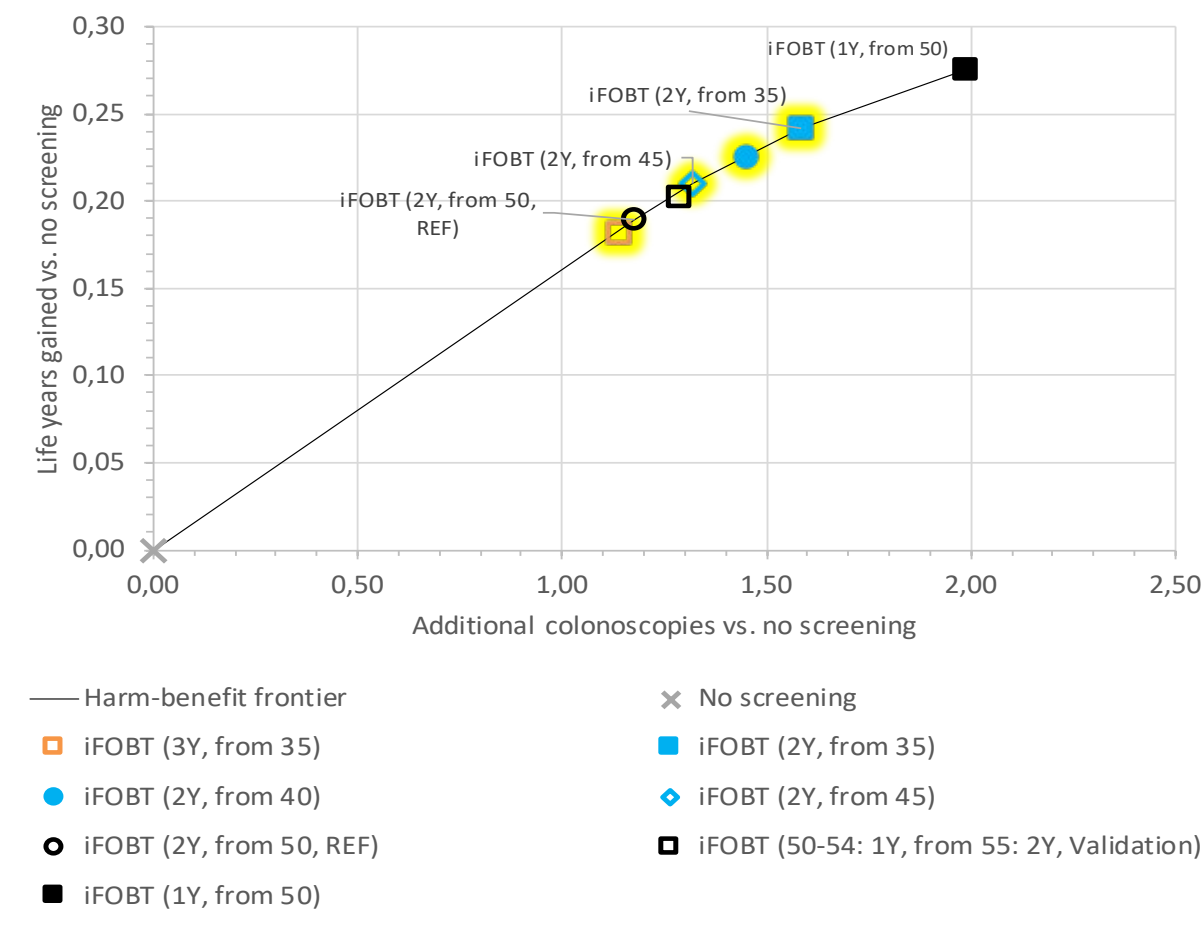
iFOBT-based strategies

Below are the harm-benefit diagrams for the iFOBT-based strategies.



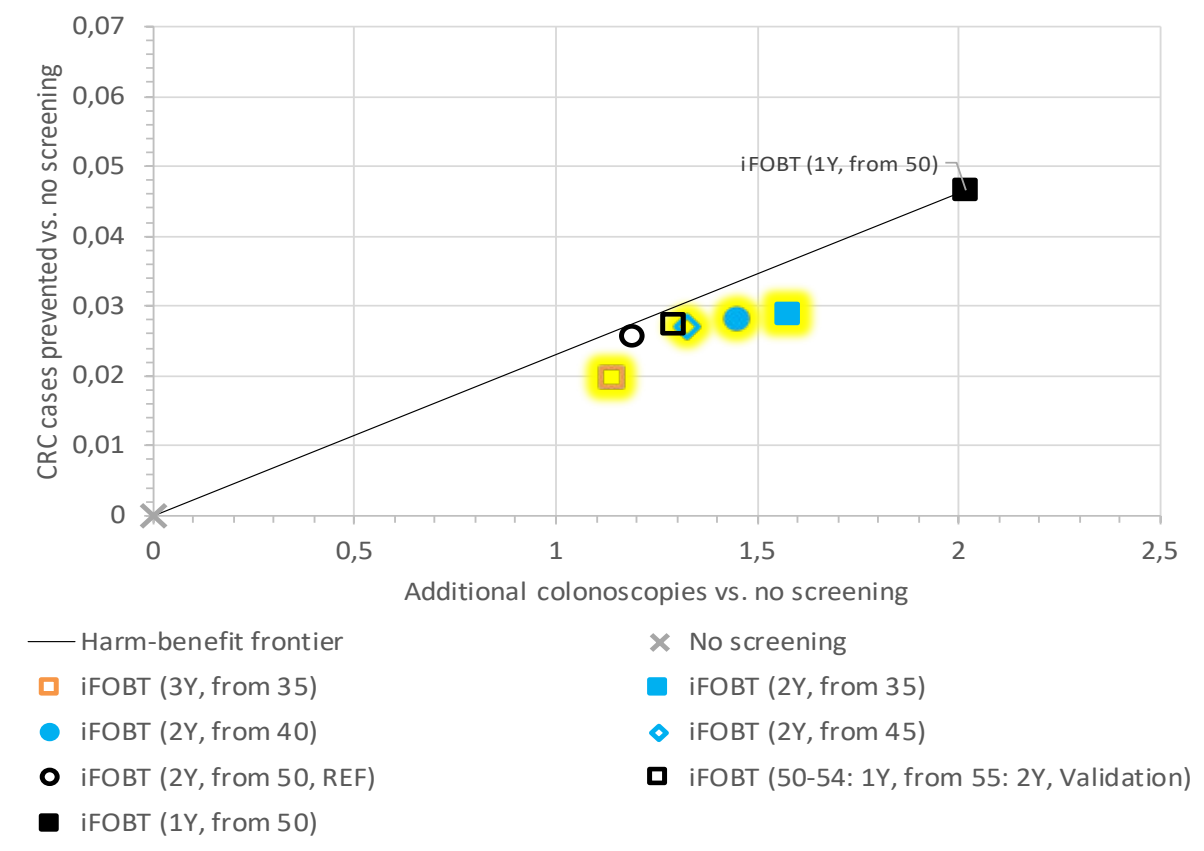
iFOBT: immunological faecal occult blood test; REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1.

Figure 1: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of CRC cases prevented per person for various iFOBT-based screening strategies in men



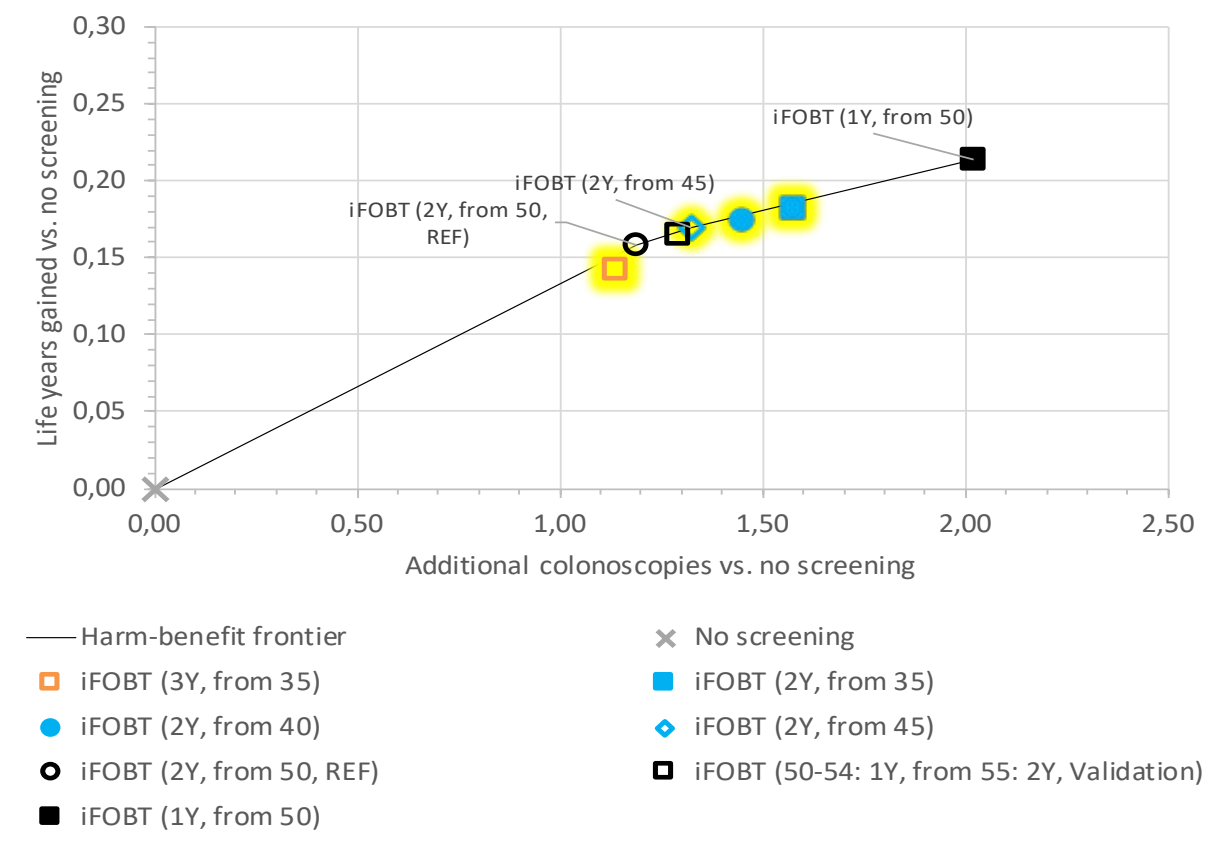
iFOBT: immunological faecal occult blood test; REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1.

Figure 2: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of additional life years per person for various iFOBT-based screening strategies in men



iFOBT: immunological faecal occult blood test; REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1.

Figure 3: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of CRC cases prevented per person for various iFOBT-based screening strategies in women



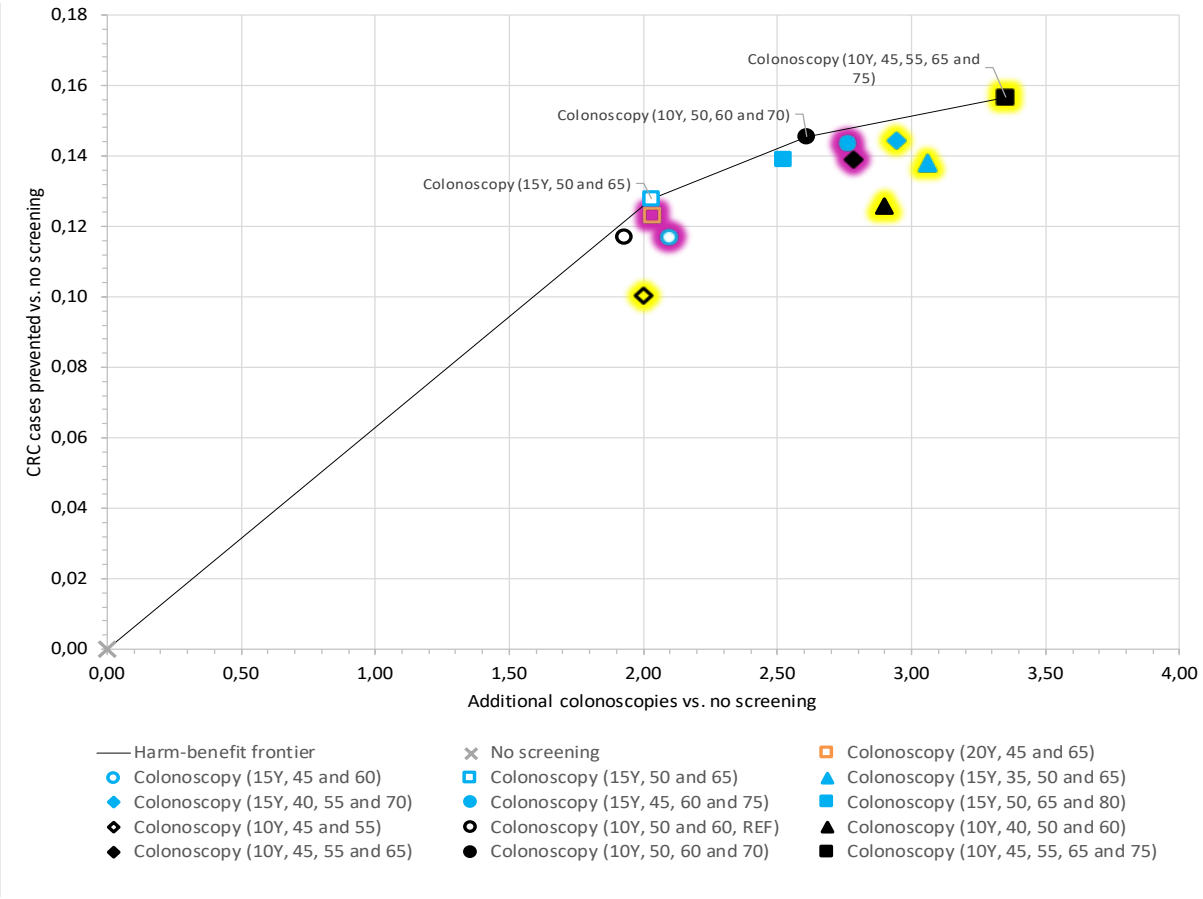
iFOBT: immunological faecal occult blood test; REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1.

Figure 4: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of additional life years per person for various iFOBT-based screening strategies in women

Among the iFOBT-based strategies, with regard to the 2 outcomes – life years gained and CRC cases prevented – an annual iFOBT from the age of 50 (iFOBT [1Y from 50]) for men and women, compared with no screening, was on the efficiency frontier (see Figure 1, Figure 2, Figure 3 and Figure 4). For men, this meant 31 additional colonoscopies for every additional CRC case prevented; for women, 43 additional colonoscopies for every additional CRC case prevented. In terms of life years gained, for the iFOBT, carried out annually from the age of 50 (iFOBT [1Y from 50]), there were 12 additional colonoscopies per life year gained for men and 16 additional colonoscopies per life year gained for women, compared with the next-best alternative. Furthermore, the current iFOBT-based screening (iFOBT [2Y, from 50, REF]), compared with no screening, was undominated in terms of life years gained in men and women (see Figure 2 and Figure 4). There were 6 additional colonoscopies per life year gained for men and 7 for women.

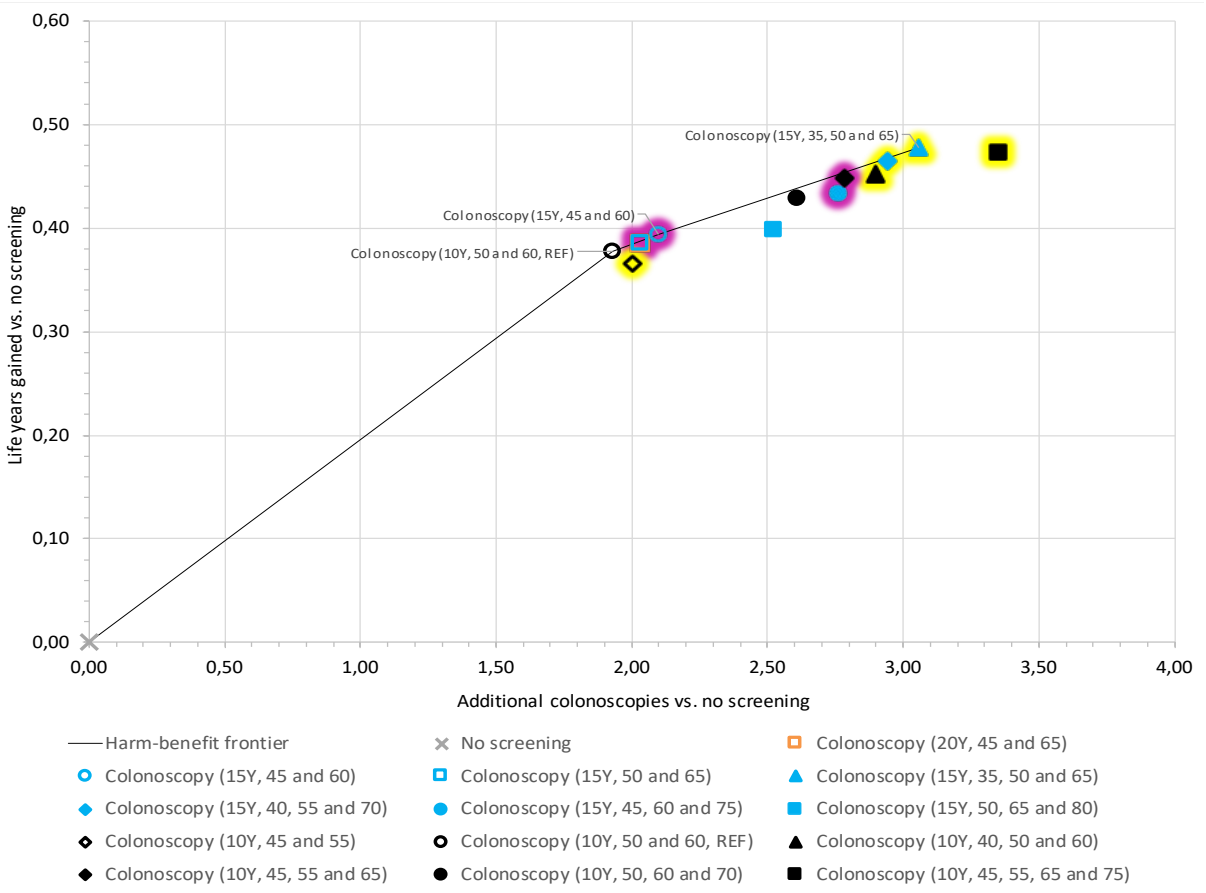
Colonoscopy-based strategies

Below are the harm-benefit diagrams for the colonoscopy-based strategies.



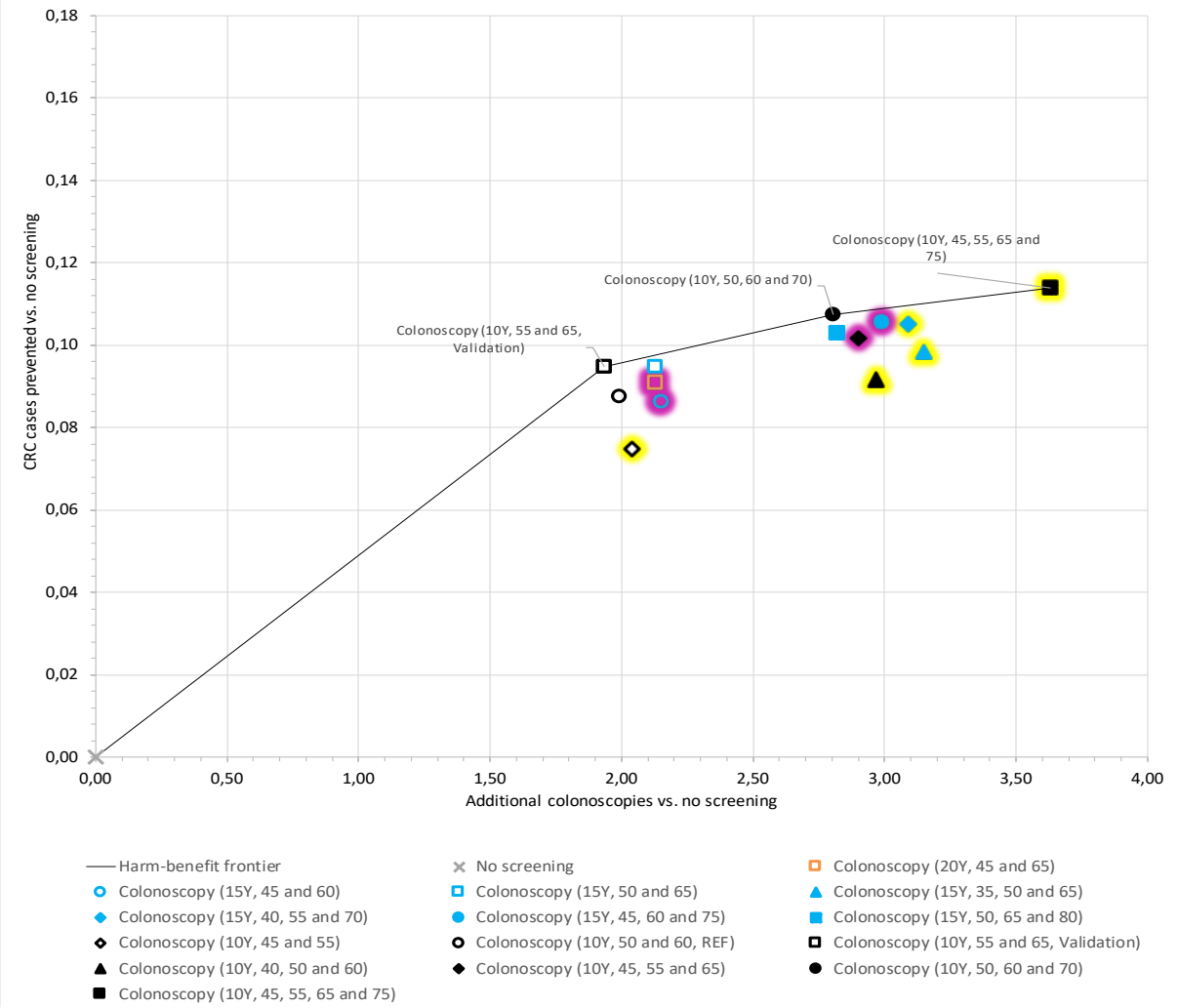
REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1, and magenta investigational strategies of research question 2.

Figure 5: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of CRC cases prevented per person for various colonoscopy-based screening strategies in men



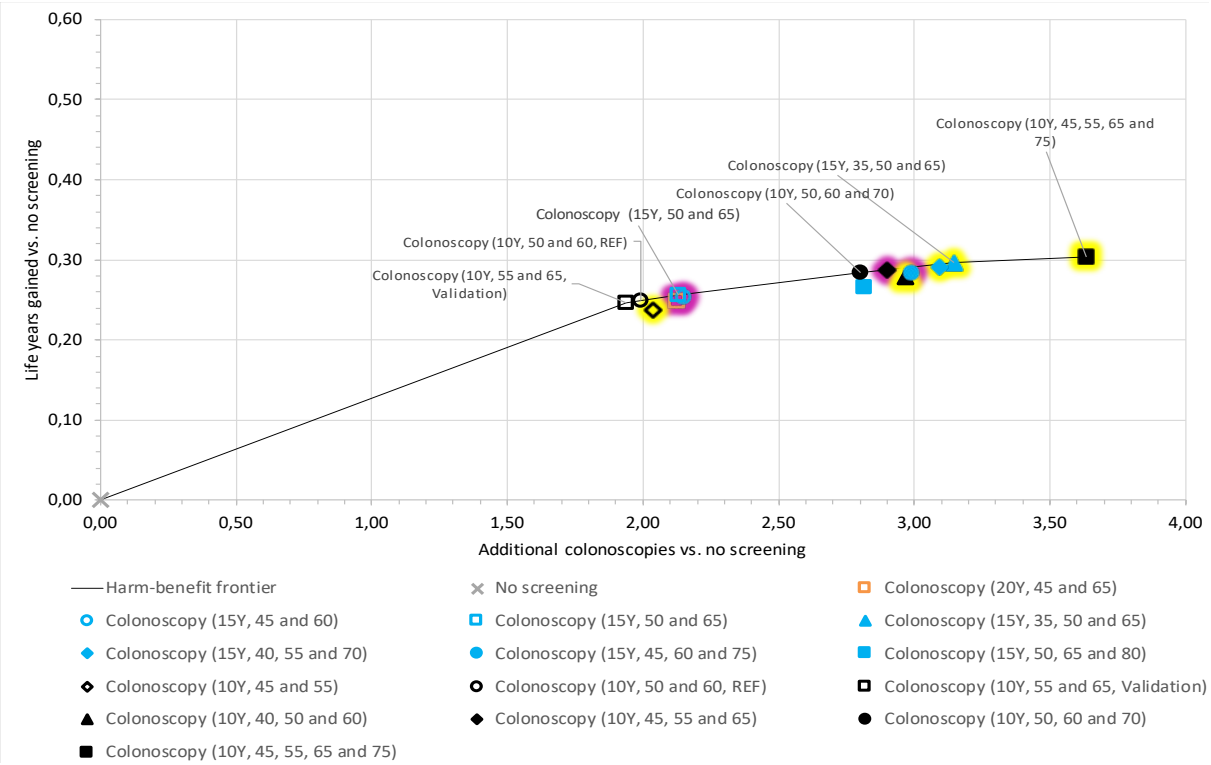
REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1, and magenta investigational strategies of research question 2.

Figure 6: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of life years gained per person for various colonoscopy-based screening strategies in men



REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1, and magenta investigational strategies of research question 2.

Figure 7: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of CRC cases prevented per person for various colonoscopy-based screening strategies in women



REF: reference; Y: years
Yellow shading indicates investigational strategies of research question 1, and magenta investigational strategies of research question 2.

Figure 8: Harm-benefit diagram of the additional number of colonoscopies per person compared with the additional number of life years gained per person for various colonoscopy-based screening strategies in women

When considering colonoscopy-based strategies, the following screening strategies were on the efficiency frontier in terms of the number of CRC cases prevented in men:

- Colonoscopy every 15 years from the age of 50, up to a maximum of 2 colonoscopies (colonoscopy [15Y, 50 and 65]),
- Colonoscopy every 10 years from the age of 50, up to a maximum of 3 colonoscopies (colonoscopy [10Y, 50, 60 and 70]) and
- Colonoscopy every 10 years from the age of 45, up to a maximum of 4 colonoscopies (colonoscopy [10Y, 45, 55, 65 and 75])

(See Figure 5.) Accordingly, in an incremental comparison starting from no screening, there were 16, 32 and 67 additional colonoscopies per additional CRC case prevented for the above-mentioned strategies on the efficiency frontier to the next best alternative.

When considering life years gained, the following screening strategies were on the efficiency frontier for men:

- The current reference strategy (colonoscopy at ages 50 and 60, with a 10-year interval) (colonoscopy [10Y, 50 and 60, REF and validation])
- Colonoscopy at the ages of 45 and 60, with a 15-year interval (colonoscopy [15Y, 45 and 60]) and
- Colonoscopy at the ages of 35, 50 and 65, with a 15-year interval (colonoscopy [15Y, 35, 50 and 65])

(See Figure 6)

For men, in an incremental comparison starting from no screening, there were 5, 10 and 11 additional colonoscopies per life year gained for the above-mentioned strategies on the efficiency frontier to the next best alternative.

In women, the following screening strategies were on the efficiency frontier in terms of the number of CRC cases prevented:

- Colonoscopy at the ages of 55 and 65, with a 10-year interval (colonoscopy [10Y, 55 and 65, validation]), as well as
- Colonoscopy at the ages of 50, 60 and 70, with a 10-year interval (colonoscopy [10Y, 50, 60 and 70]), and equally
- Colonoscopy at the ages of 45, 55, 65 and 75, with a 10-year interval (colonoscopy [10Y, 45, 55, 65 and 75])

(See Figure 7)

Accordingly, in women, in an incremental comparison starting from no screening, there were 20, 67 and 128 additional colonoscopies per additional CRC case prevented for the above-mentioned strategies on the efficiency frontier to the next best alternative.

Exactly the same strategies were on the efficiency frontier when considering the life years gained in women (see Figure 8). The corresponding incremental ratios here were 8, 23 and 63 additional colonoscopies per life year gained. The following strategies were additionally on the efficiency frontier:

- The current reference strategy (colonoscopy every 10 years from the age of 50, up to a maximum of 2 colonoscopies; colonoscopy [10Y, 50 and 60, REF]) and
- Colonoscopy every 15 years from the age of 35, up to a maximum of 3 colonoscopies (colonoscopy [15Y, 35, 50 and 65]),

with corresponding incremental ratios of 19 and 29 additional colonoscopies per life year gained versus the next-best strategy.

The impact of participation probabilities on strategies lying on the efficiency frontier, compared with the reference case

iFOBT-based strategies

The following conclusion was reached in the preliminary report: 'For screening using iFOBT, a strategy involving biennial testing from the age of 45, rather than the current age of 50, would, for example, be potentially advantageous'. It became apparent that biennial testing from the age of 45 was only partially on the efficiency frontier. Reducing the interval to an annual iFOBT was shown to be a robust option.

Colonoscopy-based strategies

The following conclusion was reached in the preliminary report: 'In the case of colonoscopy-based screening, it would seem more advantageous to conduct CRC screening over a longer period than to start it earlier. This could be achieved by adopting a strategy involving 3 colonoscopies instead of the current 2, whilst maintaining the current lower age limit of 50 years.' This finding was robust for both men and women with regard to the outcome of CRC cases prevented. However, if the lower age limit for starting screening were to be reduced, the picture that emerges varies depending on the variation in the reduction of the probability of participation. For men, for example, in these scenarios, 3 colonoscopies from the age of 40, at 10-year intervals, would be the most beneficial option in terms of life expectancy. For women, 3 colonoscopies from the age of 45, carried out at 10-year intervals, would tend to offer a greater advantage in terms of life years compared with the reference case.

The following conclusion was reached in the preliminary report: 'If the maximum possible number of 2 colonoscopies in the current CRC screening programme is not to be exceeded, extending the screening interval to 15 years, for example, would potentially be superior'. It became apparent that, given the lower probability of participation, maintaining the current screening strategy for men and returning to the earlier screening strategy for women seems to show a greater advantage in terms of the number of CRC cases prevented.

Impact of test accuracy

Compared with the reference case, variations in the lower and upper limits of the test accuracy had only a marginal effect on selected outcomes. The variation had an effect on some of the strategies lying on the efficiency frontier, whilst others remained unchanged compared with the reference case.

5 Conclusion

Benefit assessment

In the benefit assessment, no relevant studies were identified for either of the 2 research questions. It is therefore not proven whether people under the age of 50 with no suspected CRC and no specific increased risk of CRC can benefit from CRC screening. It also remains unproven whether people aged 45 and over, with no suspected CRC and no specific increased risk of CRC, would benefit from a colonoscopy screening programme with modifications in terms of the number of screenings and the intervals between them. Overall, therefore, in the absence of direct evidence, no benefit can be derived.

Modelling

In addition to the benefit assessment, decision-analytic modelling was therefore conducted to obtain information on different options for CRC screening. It should be noted that the results were determined from the perspective of participants who attend the screening regularly and fully (100%) and who fully adhere to any clarification tests for positive findings and surveillance procedures.

The key findings of the modelling show the ratio of additional colonoscopies (disadvantage) for one additional case of CRC prevented and, furthermore, for one life year gained (both advantages). These are calculated as the difference in the total number of colonoscopies (incremental colonoscopies) divided by the difference in the respective outcome (incremental cases of CRC prevented or life years gained) when comparing 2 undominated screening strategies. Strategies that involve, for example, fewer colonoscopies whilst at the same time being associated with more cases of CRC or more years of life gained, compared with other strategies, lie on what is known as the efficiency frontier. All undominated strategies lie on the efficiency frontier and represent screening alternatives from which the optimal strategy can be selected, depending on a threshold value. It should be noted, however, that recommending specific screening strategies based on the modelling results requires the establishment of a threshold value for an acceptable ratio (e.g. measured in terms of the number of additional colonoscopies per life year gained). Setting such a threshold value would involve a value judgement and is therefore not undertaken in this report.

For screening using iFOBT, for example, a strategy involving tests every 2 years from the age of 45, rather than from the current age of 50, could potentially offer an advantage. However, when varying the probability of participation, this finding was only partially confirmed in men, and was not confirmed in women. Modelling showed that shortening the interval to an annual iFOBT resulted in a further increase in effectiveness, i.e. a slightly higher number of CRC cases prevented and life years gained; however, this was associated with a substantially greater number of colonoscopies.

In the case of colonoscopy-based screening, it would seem more advantageous to conduct CRC screening over a longer period than to start it earlier. One way to achieve this would be to adopt a strategy involving 3 colonoscopies instead of the current 2, whilst maintaining the current lower age limit of 50 years for starting screening. This finding was confirmed when varying the reduction in the probability of participation. If the maximum possible number of 2 colonoscopies in the current CRC screening programme is not to be exceeded, extending the screening interval to 15 years, for example, would potentially be superior to the current screening programme. However, when varying the reduction in the probability of participation, this finding was not confirmed. For women, CRC screening is potentially advantageous even in later life, whereas for men, starting screening at an earlier age is likely to offer a greater advantage compared with the current screening programme. If the lower age limit is to be reduced, then CRC screening starting at the age of 45 would also be a potentially advantageous option (compared with younger lower age limits, it would be at least as effective whilst requiring substantially fewer colonoscopies). However, if the lower age limit for starting screening were to be reduced, the screening interval would need to be extended to 20 years, or the maximum possible number of colonoscopies would need to be increased, as otherwise the overall screening period would be too short.

6 References for English extract

Please see full final report for full reference list.

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The full report (German version) is published at

https://www.iqwig.de/en/projects/s24-02.html

A1 Search strategies for the benefit assessment

A1.1 Searches in bibliographic databases

Search for systematic reviews

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to November 08, 2024

The following filter was adopted:

- Systematic review: Wong [17] – High specificity strategy (adapted)

#	Searches
1	exp Colorectal Neoplasms/
2	Colonic Polyps/
3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
4	or/1-3
5	(screening* or screened*).mp.
6	Mass Screening/
7	Early Detection of Cancer/
8	or/5-7
9	exp Colonoscopy/
10	Colonography, Computed Tomographic/
11	(colonoscop* or sigmoidoscop* or colonograph*).ti,ab.
12	Occult Blood/
13	Guaiac/
14	(f?ecal* or immunochemical or guaiac* or (occult adj1 blood) or h?emoccult*).ti,ab.
15	or/9-14
16	and/4,8,15
17	cochrane database of systematic reviews.jn.
18	(search or MEDLINE or systematic review).tw.
19	(meta analysis or systematic review).pt.
20	or/17-19
21	20 not (exp animals/ not humans.sh.)
22	and/16,21
23	22 and (english or german or multilingual or undetermined).lg.
24	23 and 202110:3000.(dt).

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to June 07, 2021

The following filter was adopted:

- Systematic review: Wong [17] – High specificity strategy

#	Searches
1	exp Colorectal Neoplasms/
2	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
3	or/1-2
4	screening*.mp.
5	Colonoscopy/
6	(colonoscop* or endoscop*).ab,ti.
7	Occult Blood/
8	Reagent Kits, Diagnostic/
9	(stool or fece* or faece* or fecal* or faecal* or blood or occult or bleed* or fob*).ab,ti.
10	immunochemical*.ab,ti.
11	(haemoccult* or hemoccult*).ab,ti.
12	or/5-11
13	cochrane database of systematic reviews.jn.
14	(search or MEDLINE or systematic review).tw.
15	meta analysis.pt.
16	or/13-15
17	3 and 4 and 12 and 16
18	limit 20 to yr="2016 -Current"

2. International HTA Database

Search interface: INAHTA

#	Searches
1	Colorectal Neoplasms[mhe]
2	Colonic Polyps[mh]
3	(colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) and (cancer* or metastas* or carcinom* or neoplas* or malignan* or tumor* or tumour* or adenomatous* or adenocarcinoma* or adenoma* or polyp*)
4	#3 OR #2 OR #1
5	Mass Screening[mh]
6	Early Detection of Cancer[mh]

#	Searches
7	screening* or screened*
8	#7 OR #6 OR #5
9	#8 AND #4
10	(*) FROM 2021 TO 2024
11	#10 AND #9

Search interface: INAHTA

#	Searches
1	("Colorectal Neoplasms"[mhe]) OR ((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) AND (cancer* or metastas* or carcinom* or neoplas* or malignan* or tumor* or tumour* or adenomatous* or adenocarcinoma* or adenoma* or polyp*))[Title] OR ((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) AND (cancer* or metastas* or carcinom* or neoplas* or malignan* or tumor* or tumour* or adenomatous* or adenocarcinoma* or adenoma* or polyp*))[abs] FROM 2016 TO 2021

Search for primary studies research question 1

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to December 18, 2025

The following filter was adopted:

- RCT: Lefebvre [18] – Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2023 revision)
- Non-RCT: Search filter with best sensitivity for controlled NRS (Ovid MEDLINE, adapted from PubMed) [19]

	Searches
1	exp Colorectal Neoplasms/
2	Colonic Polyps/
3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
4	or/1-3
5	(screening* or screened*).mp.
6	*Mass Screening/
7	*"Early Detection of Cancer"/mt [Methods]
8	or/5-7
9	exp Colonoscopy/

	Searches
10	Colonography, Computed Tomographic/
11	(colonoscop* or sigmoidoscop* or colonograph*).ti,ab.
12	Occult Blood/
13	Guaiac/
14	(f?ecal* or immunochemical or guaiac* or occult blood or h?emoccult*).ti,ab.
15	or/9-14
16	and/4,8,15
17	exp Randomized controlled Trial/
18	controlled clinical trial.pt.
19	(randomized or placebo or randomly or trial or groups).ab.
20	drug therapy.fs.
21	or/17-20
22	21 not (exp animals/ not humans.sh.)
23	and/16,22
24	exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/
25	((control and (group* or study)) or (time and factors) or program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp.
26	or/24-25
27	(animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
28	hi.fs. or case report.mp.
29	or/27-28
30	26 not 29
31	and/16,30
32	or/23,31
33	32 and (english or german or multilingual or undetermined).lg.
34	33 and 20191201:3000.(dt).

2. Embase

Search interface: Ovid

- Embase 1974 to 2025 December 17

The following filter was adopted:

- RCT: Wong [17] – Strategy minimizing difference between sensitivity and specificity

#	Searches
1	exp colon cancer/
2	exp colorectal tumor/
3	colon polyp/
4	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumo?r? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ti,ab.
5	or/1-4
6	exp screening/
7	(screening* or screened*).mp.
8	or/6-7
9	colonoscopy/
10	sigmoidoscopy/
11	computed tomographic colonography/
12	(colonoscop* or sigmoidoscop* or colonograph*).ti,ab.
13	occult blood/
14	occult blood test/
15	guaiac/
16	(f?ecal* or immunochemical or guaiac* or occult blood or h?emoccult*).ti,ab.
17	or/9-16
18	and/5,8,17
19	(random* or double-blind*).tw.
20	placebo*.mp.
21	or/19-20
22	and/18,21
23	22 not medline.cr.
24	23 not (exp animal/ not exp human/)
25	24 not ((Conference Abstract or Conference Review or Editorial).pt. or NCT*.ui.)
26	25 not ((afrikaans or albanian or arabic or armenian or azerbaijani or basque or belorussian or bosnian or bulgarian or catalan or chinese or croatian or czech or danish or dutch or english or esperanto or estonian or finnish or french or gallegan or georgian or german or greek or hebrew or hindi or hungarian or icelandic or indonesian or irish gaelic or italian or japanese or korean or latvian or lithuanian or macedonian or malay or norwegian or persian or polish or polyglot or portuguese or pushto or romanian or russian or scottish gaelic or serbian or slovak or slovene or spanish or swedish or thai or turkish or ukrainian or urdu or uzbek or vietnamese) not (english or german)).lg.
27	26 and 20191201:3000.(dc).

3. The Cochrane Library

Search interface: Wiley

- Cochrane Central Register of Controlled Trials: Issue 11 of 12, November 2025

#	Searches
#1	[mh "Colorectal Neoplasms"]
#2	[mh ^"Colonic Polyps"]
#3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) NEAR/5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumo?r? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)):ti,ab
#4	#1 OR #2 OR #3
#5	[mh ^"Mass Screening"]
#6	MeSH descriptor: [Early Detection of Cancer] this term only and with qualifier(s): [methods - MT]
#7	(screening* or screened*):ti,ab,kw
#8	#5 OR #6 OR #7
#9	[mh "Colonoscopy"]
#10	[mh ^"Colonography, Computed Tomographic"]
#11	(colonoscop* or sigmoidoscop* or colonograph*):ti,ab
#12	[mh ^"Occult Blood"]
#13	[mh ^"Guaiac"]
#14	(f?ecal* or immunochemical or guaiac* or occult blood or h?emoccult*):ti,ab
#15	#9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	#4 AND #8 AND #15
#17	#16 not (*clinicaltrial*gov* or *trialsearch*who* or *clinicaltrialsregister*eu* or *anzctr*org*au* or *trialregister*nl* or *irct*ir* or *isrctn* or *controlled*trials*com* or *drks*de*):so
#18	#17 not ((language next (afr or ara or aze or bos or bul or car or cat or chi or cze or dan or dut or es or est or fin or fre or gre or heb or hrv or hun or ice or ira or ita or jpn or ko or kor or lit or nor or peo or per or pol or por or pt or rom or rum or rus or slo or slv or spa or srp or swe or tha or tur or ukr or urd or uzb)) not (language near/2 (en or eng or english or ger or german or mul or unknown))) with Publication Year from 2019 to 2025, in Trials

Search for primary studies research question 2

MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to December 18, 2025

The following filter was adopted:

- RCT: Lefebvre [18] – Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2023 revision)
- Non-RCT: Search filter with best sensitivity for controlled NRS (Ovid MEDLINE, adapted from PubMed) [19]

	Searches
1	exp Colorectal Neoplasms/
2	Colonic Polyps/
3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
4	or/1-3
5	Mass Screening/
6	*"Early Detection of Cancer"/
7	or/5-6
8	interval*.mp.
9	and/7-8
10	(interval* adj7 screen*).mp.
11	or/9-10
12	exp Colonoscopy/
13	Colonography, Computed Tomographic/
14	(colonoscop* or colonograph*).ti,ab.
15	or/12-14
16	and/4,11,15
17	exp Randomized controlled Trial/
18	controlled clinical trial.pt.
19	(randomized or placebo or randomly or trial or groups).ab.
20	drug therapy.fs.
21	or/17-20
22	21 not (exp animals/ not humans.sh.)
23	and/16,22
24	exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/

	Searches
25	((control and (group* or study)) or (time and factors) or program or survey* or ci or cohort or comparative stud* or evaluation studies or follow-up*).mp.
26	or/24-25
27	(animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
28	hi.fs. or case report.mp.
29	or/27-28
30	26 not 29
31	and/16,30
32	or/23,31
33	32 and (english or german or multilingual or undetermined).lg.

2. Embase

Search interface: Ovid

- Embase 1974 to 2025 December 17

The following filter was adopted:

- RCT: Wong [17] – Strategy minimizing difference between sensitivity and specificity

#	**Searches**
1	exp colon cancer/
2	exp colorectal tumor/
3	colon polyp/
4	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumo?r? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ti,ab.
5	or/1-4
6	exp screening/
7	interval*.mp.
8	and/6-7
9	(interval* adj7 screen*).mp.
10	or/8-9
11	colonoscopy/
12	computed tomographic colonography/
13	(colonoscop* or colonograph*).ti,ab.
14	or/11-13
15	and/5,10,14

#	Searches
16	(random* or double-blind*).tw.
17	placebo*.mp.
18	or/16-17
19	and/15,18
20	19 not medline.cr.
21	20 not (exp animal/ not exp human/)
22	21 not ((Conference Abstract or Conference Review or Editorial).pt. or NCT*.ui.)
23	22 not ((afrikaans or albanian or arabic or armenian or azerbaijani or basque or belorussian or bosnian or bulgarian or catalan or chinese or croatian or czech or danish or dutch or english or esperanto or estonian or finnish or french or gallegan or georgian or german or greek or hebrew or hindi or hungarian or icelandic or indonesian or irish gaelic or italian or japanese or korean or latvian or lithuanian or macedonian or malay or norwegian or persian or polish or polyglot or portuguese or pushto or romanian or russian or scottish gaelic or serbian or slovak or slovene or spanish or swedish or thai or turkish or ukrainian or urdu or uzbek or vietnamese) not (english or german)).lg.

3. The Cochrane Library

Search interface: Wiley

- Cochrane Central Register of Controlled Trials: Issue 11 of 12, November 2025

#	Searches
#1	[mh "Colorectal Neoplasms"]
#2	[mh ^"Colonic Polyps"]
#3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) NEAR/5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)):ti,ab
#4	#1 OR #2 OR #3
#5	[mh ^"Mass Screening"]
#6	[mh ^"Early Detection of Cancer"]
#7	#5 OR #6
#8	interval*
#9	#7 AND #8
#10	interval* NEAR/7 screen*
#11	#9 or #10
#12	[mh Colonoscopy]
#13	[mh ^"Colonography, Computed Tomographic"]
#14	(colonoscop* or colonograph*):ti,ab
#15	#12 or #13 or #14
#16	#4 and #11 and #15
#17	#16 not (*clinicaltrial*gov* or *trialsearch*who* or *clinicaltrialsregister*eu* or *anzctr*org*au* or *trialregister*nl* or *irct*ir* or *isrctn* or *controlled*trials*com* or *drks*de*):so

#	Searches
#18	#17 not ((language next (afr or ara or aze or bos or bul or car or cat or chi or cze or dan or dut or es or est or fin or fre or gre or heb or hrv or hun or ice or ira or ita or jpn or ko or kor or lit or nor or peo or per or pol or por or pt or rom or rum or rus or slo or slv or spa or srp or swe or tha or tur or ukr or urd or uzb)) not (language near/2 (en or eng or english or ger or german or mul or unknown)))
#19	#18 in Trials

A1.2 Searches in study registries

1. ClinicalTrials.gov

Provider: U.S. National Institutes of Health

- URL: https://clinicaltrials.gov/expert-search
- Type of search: Expert Search

Search strategy
AREA[ConditionSearch] (colorectal cancer OR colon cancer OR colorectal polyp OR colon polyp OR colorectal neoplasms OR colon neoplasms OR colorectal adenoma OR colon adenoma OR rectal cancer) AND AREA[InterventionSearch] (colonoscopy OR sigmoidoscopy OR colonography OR occult blood OR guaiac OR immunochemical OR haemoccult OR hemoccult or fecal OR faecal OR FIT OR iFOBT OR gFOBT OR FOBT) AND (screening OR screened)

2. International Clinical Trials Registry Platform Search Portal

Provider: World Health Organization

- URL: https://trialsearch.who.int
- Type of search: Basic Search

Search strategy
(colorectal cancer OR colon cancer OR colorectal polyp OR colon polyp OR colorectal neoplasms OR colon neoplasms OR colorectal adenoma OR colon adenoma OR rectal cancer) AND (colonoscopy OR sigmoidoscopy OR colonography OR occult blood OR guaiac OR immunochemical OR haemoccult OR hemoccult or fecal OR faecal OR FIT OR iFOBT OR gFOBT OR FOBT)

A1.3 Further information sources and search techniques

G-BA website und IQWiG website

G-BA

- URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/

Suchbegriffe
Diagnostik

IQWiG

- URL: https://www.iqwig.de/projekte/projekte-und-ergebnisse/

Suchbegriffe
Darmkrebs Früherkennung

A2 Search strategies modelling

A2.1 Searches in bibliographic databases

Search for existing models

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to November 19, 2024

#	Searches
1	exp Colorectal Neoplasms/
2	Colonic Polyps/
3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
4	or/1-3
5	(screening* or screened*).mp.
6	Mass Screening/
7	Early Detection of Cancer/
8	or/5-7
9	exp Colonoscopy/
10	Colonography, Computed Tomographic/
11	(colonoscop* or sigmoidoscop* or colonograph*).ti,ab.
12	Occult Blood/
13	Guaiac/
14	(f?ecal* or immunochemical or guaiac* or (occult adj1 blood) or h?emoccult*).ti,ab.
15	or/9-14
16	(model* adj5 (stud* or simulation* or markov* or microsimulation*)).mp.
17	and/4,8,15-16
18	17 not (exp animals/ not humans.sh.)
19	18 and (english or german or multilingual or undetermined).lg.
20	19 and 2014:3000.(dp).

2. International HTA Database

Search interface: INAHTA

#	Searches
1	Colorectal Neoplasms[mhe]
2	Colonic Polyps[mh]
3	(colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) and (cancer* or metastas* or carcinom* or neoplas* or malignan* or tumor* or tumour* or adenomatous* or adenocarcinoma* or adenoma* or polyp*)
4	#3 OR #2 OR #1
5	Mass Screening[mh]
6	Early Detection of Cancer[mh]
7	screening* or screened*
8	#7 OR #6 OR #5
9	model*
10	#9 AND #8 AND #4
11	(*) FROM 2014 TO 2024
12	#11 AND #10

Search for data on test accuracy of iFOBT and colonoscopy, and for data on side effects of colonoscopy

1. MEDLINE

Search interface: *Ovid*

- Ovid MEDLINE(R) ALL 1946 to November 08, 2024

The following filter was adopted:

- Systematic review: Wong [17] – High specificity strategy (adapted)
- Diagnostic studies: Haynes [20] – Top three search strategies for optimising sensitivity and specificity.
- Adverse events: Golder [21] – Adverse effects of surgical interventions

#	Searches
1	exp Colorectal Neoplasms/
2	Colonic Polyps/
3	((colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) adj5 (cancer? or metastas* or carcinom* or neoplas* or malignan* or tumor? or tumour? or adenomatous* or adenocarcinoma* or adenoma* or polyp*)).ab,ti.
4	or/1-3

#	Searches
5	exp Colonoscopy/
6	Colonography, Computed Tomographic/
7	Occult Blood/
8	Guaiac/
9	(colonoscop* or colonograph*).ti,ab.
10	(f?ecal* or immunochemical or guaiac* or occult blood or h?emoccult*).ti,ab.
11	or/5-10
12	or/5-6,9
13	Cochrane database of systematic reviews.jn.
14	(search or MEDLINE or systematic review).tw.
15	(meta analysis or systematic review).pt.
16	or/13-15
17	16 not (exp animals/ not humans.sh.)
18	and/4,11,17
19	and/4,12,17
20	(sensitiv: or diagnostic).mp. or predictive value:.tw.
21	and/18,20
22	complication*.ti,ab.
23	ae.fs.
24	safe*.ti,ab.
25	co.fs.
26	Postoperative Complications/
27	((hospital* adj2 admiss*) or hospitali?ation* or mortality*).mp.
28	or/22-27
29	and/19,28
30	or/21,29
31	30 and (english or german or multilingual or undetermined).lg.
32	limit 31 to yr="2020 -Current"

2. International HTA Database

Search interface: INAHTA

#	Searches
1	Colorectal Neoplasms[mhe]
2	Colonic Polyps[mh]
3	(colorectal* or rectal* or colon* or sigma* or sigmo* or rectum*) and (cancer* or metastas* or carcinom* or neoplas* or malignan* or tumor* or tumour* or adenomatous* or adenocarcinoma* or adenoma* or polyp*)
4	#3 OR #2 OR #1
5	Mass Screening[mh]
6	Early Detection of Cancer[mh]
7	screening* or screened*
8	#7 OR #6 OR #5
9	#8 AND #4
10	(*) FROM 2021 TO 2024
11	#10 AND #9