



**Health
Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

DRAFT health technology assessment of extending BowelScreen to those aged 50 to 54 years

Draft report for public consultation

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About the Health Information and Quality Authority (HIQA)

The Health Information and Quality Authority (HIQA) is an independent statutory body established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

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Contents

About the Health Information and Quality Authority (HIQA)	2
Foreword	6
Acknowledgements	7
List of abbreviations used in this report	9
Plain language summary	11
Executive summary	16
1 Introduction	30
1.1 Background to the request	30
1.2 Terms of reference	31
1.3 Overall approach	32
2 Description of technology	35
2.1 Key points	35
2.2 Introduction	37
2.3 Screening for colorectal cancer	37
2.4 Colorectal cancer screening in Ireland: the BowelScreen programme	46
2.5 Colorectal cancer screening guidelines	55
2.6 Colorectal cancer screening: international practice	60
2.7 Discussion	65
3 Epidemiology	69
3.1 Key points	69
3.2 Introduction	71
3.3 Natural history of colorectal cancer	71
3.4 Symptoms of colorectal cancer	72
3.5 Diagnosis of colorectal cancer	72
3.6 Treatment of colorectal cancer	74
3.7 Quality of life of colorectal cancer survivors	79
3.8 Risk factors for colorectal cancer	79
3.9 Epidemiology of colorectal cancer	81
3.10 Burden of colorectal cancer in an international context	93
3.11 Discussion	98
4 Test accuracy of FIT for the detection of colorectal cancer: consideration of differences by age	103
4.1 Key points	103

4.2	Introduction.....	104
4.3	FIT test accuracy for the detection of colorectal cancer	105
4.4	Methods	107
4.5	Results	111
4.6	Discussion	123
5	Review of the clinical effectiveness of colorectal cancer screening in those aged 50 to 54 years	132
5.1	Key points	132
5.2	Introduction.....	134
5.3	Methods	134
5.4	Results	138
5.5	Discussion	162
6	Review of the cost-effectiveness of extending BowelScreen to those aged 50 to 54 years	176
6.1	Key points	176
6.2	Introduction.....	177
6.3	Methods	178
6.4	Results	180
6.5	Discussion	206
6.6	Conclusion.....	211
7	Resource and budget impact of extending BowelScreen to those aged 50 to 54 years	212
7.1	Key points	212
7.2	Introduction.....	215
7.3	A summary of the analysis	216
7.4	Health outcomes	218
7.5	Estimated colorectal cancer epidemiology and resource requirements.....	224
7.6	Discussion	242
8	Organisational considerations.....	251
8.1	Key points	251
8.2	Introduction.....	253
8.3	The BowelScreen programme.....	254
8.4	Healthcare system context.....	260
8.5	Quality assurance.....	272
8.6	Staffing requirements	278

8.7	Infrastructure and resources	287
8.8	Implementation	293
8.9	Education, information and awareness	294
8.10	Discussion	297
9	Ethical, patient, and social considerations	309
9.1	Key points	309
9.2	Introduction.....	310
9.3	Benefit-harm balance of screening.....	311
9.4	Autonomy and respect for persons	318
9.5	Justice and equity	320
9.6	Ethical consequences of the HTA.....	327
9.7	Discussion	329
10	Discussion	332
10.1	Introduction.....	332
10.2	The condition and intervention	332
10.3	The screening method	333
10.4	The screening programme	341
10.5	Implementation	345
10.6	Strengths and limitations	350
10.7	Conclusion.....	351
	References	353
	Appendices.....	404

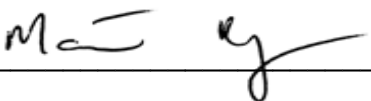
Foreword

The National Screening Advisory Committee (NSAC), established in 2019 by the Minister for Health, serves as an independent advisory body and plays a strategic role in the development and consideration of population-based screening programmes in Ireland. The role of the NSAC is to provide advice to the Minister for Health and the Department of Health on new screening proposals and proposed changes to existing screening programmes. At the request of the Department of Health, the Health Technology Assessment (HTA) directorate within the Health Information and Quality Authority (HIQA) undertakes evidence synthesis and provides evidence-based advice to NSAC on behalf of the Minister for Health.

Colorectal cancer, also called bowel cancer, refers to cancer that occurs in the lower part of the bowel, that is, the colon and rectum. Colorectal cancer usually develops from benign polyps (growths of tissue that commonly occur on the mucous membrane) in the lining of the colon or rectum. These polyps, or adenomas, may become cancerous over time. The progression of adenomas from benign to cancerous is referred to as the adenoma-carcinoma sequence. The removal of adenomas interrupts this sequence, and has the potential to impact the subsequent development of colorectal cancer.

BowelScreen, the National Bowel Screening Programme, commenced in October 2012 with the aim of offering free colorectal cancer screening to people aged 55 to 74 years on a two-yearly cycle. As of April 2025, BowelScreen invites people aged 59 to 70 years for screening, and further expansion has been committed to as per the original aim of BowelScreen. The scope of this HTA, which was requested by the National Screening Advisory Committee, is to consider a proposal for additional extension of the BowelScreen programme to people aged 50 to 54 years.

Work on the HTA was undertaken by an Evaluation Team from the HTA Directorate in HIQA. A multidisciplinary Expert Advisory Group was convened to advise the Evaluation Team during the course of the HTA. HIQA would like to thank the Evaluation Team, the members of the Expert Advisory Group and all who contributed to the preparation of this report.



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Conflicts of Interest

Conflict of Interest declarations were reviewed by the Director of HTA and no relevant conflicts of interest were identified.

List of abbreviations used in this report

AA	advanced adenoma
AAPC	average annual percentage change
AN	advanced neoplasia
CEA	cost-effectiveness analysis
CI	confidence interval
CPI	consumer price index
CRC	colorectal cancer
CSO	Central Statistics Office
CT	computed tomography
CTC	computed tomography colonography
CUA	cost utility analysis
EAG	expert advisory group
EU	European Union
f-Hb	faecal haemoglobin concentration
FIT	faecal immunochemical test
FOBT	faecal occult blood test
FSIG	flexible sigmoidoscopy
GDP	gross domestic product
gFOBT	guaiac-based faecal occult blood test
Hb	haemoglobin
HIPE	Hospital InPatient Enquiry
HIQA	Health Information and Quality Authority
HSE	Health Service Executive (Ireland)
HTA	health technology assessment
ICD	International Classification of Diseases
ICER	incremental cost effectiveness ratio
iFOBT	immunochemical faecal occult blood test
INAB	Irish National Accreditation Board
INMB	incremental net monetary benefit
LYG	life years gained
MISCAN-Colon	MIcrosimulation Screening Analysis (MISCAN) Colorectal Cancer Model
NCRI	National Cancer Registry Ireland
NDTP	National Doctors Training & Planning
NEQI	National Gastrointestinal Endoscopy Quality Improvement programme
NHB	net health benefit

NHQI	National Histopathology Quality Improvement programme
NMB	net monetary benefit
NRQI	National Radiology Quality Improvement programme
NSAC	National Screening Advisory Committee
NTPF	National Treatment Purchase Fund
PICOS	Population, Intervention, Comparison, Outcome, Study design (Framework for identifying the scope of a review question)
PIT	Population, Index test, Target condition (Framework for identifying the scope of a test accuracy review question)
PPP	purchasing power parity
PSA	probabilistic sensitivity analysis
QA	quality assurance
QALY	quality-adjusted life year
QoL	quality of life
RCT	randomised controlled trial
SchARR	School of Health and Related Research (University of Sheffield)
TAT	turnaround time
USPSTF	United States Preventive Services Task Force
WTP	willingness-to-pay

Plain language summary

What is the BowelScreen programme?

Cancer screening involves looking for cancer in people who do not have any symptoms. This can help find cancer at an early stage, when it is easier to treat or cure. Bowel cancer, which is also known as colon cancer, rectal cancer, or colorectal cancer, develops in the colon or rectum. These parts of the body are also known as the large bowel or large intestine. The BowelScreen Programme in Ireland started in 2012 and people are invited for bowel cancer screening every two years. As of 2025, BowelScreen is available to people aged 59 to 70. The programme is already aiming to expand screening to people aged 55 to 74 in the coming years.

What is this report about?

The National Screening Advisory Committee asked the Health Information and Quality Authority (HIQA) to look at whether people aged 50 to 54 should also be included in the BowelScreen programme in the future. HIQA conducted a health technology assessment (HTA) to examine this question. This kind of assessment looks at the health benefits and risks of using a health technology. In this case, the health technology is the BowelScreen programme and if it should be extended to include those aged 50 to 54. The assessment also looks at costs and any wider impacts that screening might have on the population being assessed or on society, and what needs to be in place to make it possible.

HIQA produced this report for the National Screening Advisory Committee. The committee will consider the findings of the report, which are summarised below, and make a recommendation to the Minister for Health on whether people aged 50 to 54 should be offered bowel cancer screening.

How common is bowel cancer in Ireland?

In Ireland, bowel cancer is the second most common cancer in men and the third most common in women. Around 2,750 people are diagnosed with bowel cancer in Ireland each year. Bowel cancer is the third leading cause of cancer death in Ireland. Around 1,000 people in Ireland die from bowel cancer each year. Bowel cancer is generally more common in people aged 50 years and above. While it is becoming more common in people aged under 50, the number of cancers in this age group is small. While the number of new cases of bowel cancer diagnosed each year in older adults has decreased over time, it has stayed the same in those aged 50 to 54 for the last number of years.

Bowel cancer screening in Ireland

One sign of bowel cancer is blood in a person's poo, even if the amount of blood is not visible and is so low that it can only be identified in a lab. In Ireland, screening for bowel cancer involves a person using a home test kit (called a 'FIT') and sending a small sample of poo (stool sample) to a lab for testing. The sample is examined in the lab and if the amount of blood is over a certain level, the person will be asked to go to a hospital to have a colonoscopy.

A colonoscopy is an examination of the bowel that checks for signs of bowel cancer and small lumps, called polyps. Polyps could turn into cancer if left to grow. If a polyp is found, the doctor will remove it and send it to a lab to test for cancer. If a person is found to have cancer, they will be referred for treatment.

Do other countries screen people aged 50 to 54 for bowel cancer?

We looked at the screening programmes of European countries, as well as the United States, Canada, Australia, and New Zealand. Screening in these countries generally included people between the ages of 50 to 75 years. However, some countries start screening at older ages and stop screening earlier.

We also reviewed guidelines for bowel cancer screening. Most of the guidelines we looked at suggested that screening should start from age 50.

How well does bowel cancer screening work in people aged 50 to 54?

It is important to make sure that the tests being used by a screening programme can correctly identify people with the condition being screened for. This is referred to as 'test accuracy'.

To see how well the FIT test works in younger people compared to older people, we looked at scientific studies of bowel cancer screening using FIT. Based on the results of the studies we identified, there does not appear to be a difference in how well the test performs in younger people when compared to older people.

We also examined study findings on whether bowel cancer screening in those aged 50 to 54 helps to reduce deaths from bowel cancer. Most of the studies we found did not focus on the effects of screening in people aged 50 to 54 only but also included younger or older participants. Nine of the ten studies we found showed that bowel cancer screening from the age of 50 upwards can reduce the number of people dying from bowel cancer. Five studies also showed that it might be possible for screening to reduce the number of people who get bowel cancer. This is because screening helps to find and remove polyps, which can turn into cancer over time if they are not removed.

Even though the colonoscopy is very safe, a very small number of people can be hurt during the procedure. For example, very rarely, the bowel can be damaged or torn during colonoscopy. This can cause bleeding and serious complications. These harms are very uncommon, and may be even less common in those aged 50 to 54 compared to older people.

Is bowel cancer screening in people aged 50 to 54 cost effective?

Another important factor is to make sure that extending screening to those aged 50 to 54 would be a good use of resources. This is because investment would be needed, and this money could be used elsewhere in healthcare services. To see if screening from age 50 is a good use of resources compared to starting screening from age 55, we looked at studies from around Europe that examined this question.

These are known as cost effectiveness studies. We found six relevant studies. The studies found that there was a good balance between the benefits and the costs associated with starting screening from age 50. This means that there is a good chance that screening from age 50 would be a good use of resources for the healthcare service in Ireland.

How much will it cost to screen people aged 50 to 54 for bowel cancer?

Screening from age 50 would need extra resources and investment in the screening programme and health service. We looked at the budget impact of extending the programme to those aged 50 to 54. We calculated the resources that would be needed and how much they would cost in the first ten years of the programme. As part of this, we calculated how many extra colonoscopies, tests, and other services would be needed. If screening is extended to those aged 50 to 54, up to 219,000 more people could be invited to participate each year. In the first ten years of the programme, over 2,000 extra colonoscopies may be needed each year.

The programme could be rolled out at different paces. The following are examples of different ways the programme could be rolled out:

1. It could include everyone aged 50 to 54 immediately.
2. It could start by adding those aged 54 and then add those aged 53 the following year, and so on.
3. It could add a new group of people (by age) every second year.

Depending on how the programme is rolled out, screening those aged 50 to 54 could cost an extra €45 million to €66 million over ten years (versus just screening people aged 55 to 74).

What needs to happen in the health service to include people aged 50 to 54 in bowel cancer screening?

We looked at what might need to be changed in how we organise health services so that people aged 50 to 54 can be included in bowel cancer screening. This included considering staffing needs and how to make sure that delays do not happen for people undergoing tests and procedures. There are already challenges facing the BowelScreen programme and in colorectal cancer diagnosis and treatment services. For example, there are long waiting lists for colonoscopies for people outside the BowelScreen programme. These waiting lists include people who have symptoms that might mean they have bowel cancer, so their doctor has referred them for a colonoscopy.

It is important to remember that there is already a plan to extend the BowelScreen programme to those aged 55 to 74. As of 2025, the programme includes people aged between 59 and 70 and it will take several years before the programme can include those aged 55 to 74. This is because of the extra colonoscopies and other tests that will be needed by the people in the new age groups.

Including people aged 50 to 54 in BowelScreen will further increase the number of people having colonoscopies, which could lead to longer waiting times for appointments. The workload for labs will also increase, which could increase waiting times for test results. There are currently staff shortages in some areas, and training new staff can take a long time. As a result, lowering the screening age might need to happen slowly and would need to be carefully planned.

Weighing up the pros and cons of screening

It is important for people to know that the FIT screening test only looks for a level of blood in the stool sample. Even if the amount of blood is below the level tested for by BowelScreen, a person could still have bowel cancer. This is because not all cancers or polyps bleed all the time. Some people who are screened and who have bowel cancer may not be picked up by screening. Also, because younger people are less likely to have cancer in general, fewer young people will be found with cancer than older people. This means that younger people overall may get less benefit from being screened than older people. Generally, it is important that people know the risks, benefits and limitations of bowel cancer screening before they decide to take part.

In summary, bowel cancer is a very serious condition. Screening for bowel cancer appears to be as accurate in those aged 50 to 54 as it is in older people. Screening in those aged 50 to 54 is likely to reduce deaths from bowel cancer and is expected to be a good use of resources. However, lowering the screening age to 50 will increase costs. The workload of the healthcare services and staff involved in

screening will also increase. It would be important to carefully plan for an extension of BowelScreen to include people aged 50 to 54, to avoid increases in waiting times for appointments and test results. These points should be considered before a decision is made on whether the screening age for BowelScreen is lowered.

DRAFT

Executive summary

A health technology assessment (HTA) is a multidisciplinary process that summarises information about the clinical, economic, and ethical issues related to the use of a health technology and does so in a systematic, transparent, unbiased, and robust manner. A HTA is intended to support evidence-based decision-making regarding the optimal use of resources in healthcare services. The aim of this HTA was to establish the clinical, economic, resource and ethical considerations associated with the extension of the BowelScreen colorectal cancer screening programme to include those aged 50 to 54.

Background

Following submissions received by the National Screening Advisory Committee (NSAC) in relation to modification of the BowelScreen programme, the NSAC requested that HIQA undertake a HTA of extending the BowelScreen programme to those aged 50 to 54.

Methods

This research was carried out in accordance with HIQA's guidelines for the conduct of HTAs. In summary, the following took place:

- The Terms of Reference and deliverables for the HTA were agreed between HIQA and the Chair of the NSAC, on behalf of the NSAC.
- An Expert Advisory Group (EAG) was convened by HIQA comprising representation from relevant stakeholders. These included representation from the National Screening Service, BowelScreen, the Irish Cancer Society, Patients for Patient Safety, the National Cancer Control Programme, the National Clinical Programme for Gastroenterology and Hepatology, the National Cancer Registry Ireland, the HSE Endoscopy Programme, the HSE Laboratory Services Reform Programme, the Faculty of Radiologists and Radiation Oncologists, the Department of Health, the National Centre for Pharmacoeconomics, and HIQA.
- The existing BowelScreen programme pathway, and international practice regarding colorectal cancer screening, were described.
- The epidemiology and burden of disease of colorectal cancer in Ireland and internationally in those aged 50 to 54 was described.
- A review of the test accuracy of faecal immunochemical testing (FIT) for the detection of colorectal cancer in those aged 50 to 54 was conducted.

- A review of the clinical effectiveness and harms of screening in those aged 50 to 54 was conducted.
- A review of the cost effectiveness of screening for colorectal cancer in those aged 50 to 54 was conducted.
- The budgetary implications of extending the BowelScreen programme to those aged 50 to 54 were estimated.
- The organisational implications of extending the BowelScreen programme to those aged 50 to 54 were described.
- The ethical, patient, and social considerations of extending the programme were described.
- A draft report summarising the findings of this HTA was produced and discussed at meetings of the EAG and subsequently amended, where appropriate.
- The final draft report was circulated to the EAG for review, and was subsequently published for public consultation.

The following are due to take place:

- Following review by the EAG post public consultation, the final draft of the HTA will be submitted to the Board of HIQA for approval.
- Following its approval, the finalised HTA will be submitted to NSAC for consideration and published on the HIQA website.

Description of technology

In Ireland, colorectal cancer (CRC) is the second most common cancer in men and the third most common cancer in women. CRC is also the third leading cause of cancer death in Ireland. CRC occurs in the lower part of the bowel; that is, the colon and the rectum. CRC typically develops from benign polyps or adenomas, which may become cancerous over time.

Colorectal cancer screening aims to reduce mortality through the earlier detection of cancer and the removal of pre-cancerous lesions. The most commonly-used screening tests for CRC are either stool-based, that is, testing of a person's stool sample, or visualisation tests, in which the examiner obtains a visual image or representation of the colon to identify potential abnormalities. Stool-based tests include faecal occult blood tests (FOBT), which detect hidden (occult) blood in stool,

a potential indication of adenomas or CRC. A positive stool-based test result is typically followed up with a confirmatory visualisation test such as colonoscopy.

Quantitative FIT are a type of FOBT that quantify the concentration of haemoglobin (Hb) in stool, measured in micrograms (μg) of haemoglobin per gram of faeces, or nanograms (ng) of haemoglobin per ml of buffer solution. The concentration of Hb at or above which an individual is considered to have a positive screening test result is commonly referred to as the 'FIT threshold'. FIT thresholds are linked to the effectiveness of screening and to resource requirements and constraints of individual programmes. Colonoscopy is highly effective in detecting both cancer and pre-cancerous polyps. In the context of screening, it is primarily carried out following a positive indication on a non-invasive test, such as FIT.

BowelScreen

BowelScreen, Ireland's national CRC screening programme, commenced in 2012. As of April 2025, people aged 59 to 70 are invited for screening every two years. The current planned expansion of the programme to those aged 55 to 74 years would see participating individuals eligible for up to 10 rounds of screening. Under the proposed extension involving lowering the starting age to 50, participating individuals would be eligible for up to 13 rounds of screening. Screening uptake rates within the BowelScreen programme have ranged from 38% in those aged 60–64 to just below 50% in those aged 65–69.

The primary screening test for BowelScreen is FIT, with a positivity threshold of $45\mu\text{g}$ Hb/g faeces. Individuals who receive a positive FIT result are referred for colonoscopy. Depending on the results of the colonoscopy, individuals are either returned to routine screening, enter a surveillance pathway, or, if cancer is detected, are referred for treatment.

BowelScreen FIT positivity rates have ranged from 3.0% to 4.0% in those aged 60–64 years, and from 3.2% to 5.4% in those aged 65–69. The percentage of participants who undergo colonoscopy following a positive FIT result has ranged from 79.2% to 82.4% in the younger age group, and from 77.0% to 82.2% in the older age group.

The cancer detection rate in those aged 60–64 years ranged from 2.36 per 1,000 screened in the first screening round (2012–2015) to 1.54 per 1,000 screened in those aged 59–64 in 2022–2023. In those aged 65–69, the cancer detection rate ranged from 2.71 per 1,000 in 2012–2015 to 1.57 in 2022–2023. Adenoma detection rates have consistently exceeded 55% in each round of the programme, with similar adenoma detection rates in both age groups.

International practice and guidelines

A review of international practice was conducted up to April 2025. Of the 22 countries included in the review, 20 were found to have some form of organised colorectal cancer screening programme in place. Most of the countries reviewed use FIT as the primary screening test, though there is variation in FIT positivity thresholds between countries. Across European countries examined, the age of eligibility for screening ranged from 50 to 75, though some countries had a later starting age and or an earlier stopping age. Considering non-European countries, Australia was noted to have lowered the starting age of screening from 50 to 45 as of 2024. In addition to the review of international practice, a review of international guidelines was conducted. Of eight colorectal cancer screening guidelines, seven recommended colorectal cancer screening from the age of 50. The European Council has recommended colorectal cancer screening in those aged 50 to 74 since 2003, subject to national considerations regarding epidemiology and resource implications.

Epidemiology

Symptoms of CRC may include:

- rectal bleeding
- abdominal pain, abdominal mass
- unexplained weight loss
- a change in bowel habits, such as increased bowel movement frequency, persistent diarrhoea or constipation.

However, symptoms are often subtle, absent, or lack specificity at the earlier stages of cancer development. High-income countries, including Ireland, are at elevated risk. Demographic risk factors such as increasing age, male sex, and taller height have been linked to higher risk of CRC. Modifiable risk factors including smoking, the consumption of processed meat, alcohol intake, adiposity, and physical inactivity have also been identified as having an established or convincing risk of CRC. The population burden of CRC, both in terms of incidence and mortality rate, is generally higher in older people as well as in men compared to women.

In Ireland, an average of 2,750 new CRC cases were diagnosed annually based on data from 2021–2022. Between 2012 and 2020, approximately 1,000 deaths were attributed to CRC annually. While colorectal cancer mortality in age groups older than 60 in Ireland has declined over time, it has remained stable in younger age groups.

In those aged 50–54, the CRC incidence rate remained relatively stable between 2013 and 2021, with an average annual incidence rate of 47.3 per 100,000. This is comparable to the European-wide incidence rate of 48.4 per 100,000. The incidence

rate of CRC is rising in people aged 50 or younger around the world, including in Ireland, despite decreasing incidence rates in older populations. This increasing burden in the younger cohort raises the possibility of an increase in CRC incidence in older cohorts, most imminently for those aged 50–54, as the cohort matures.

Based on a 2019 National Cancer Registry Ireland (NCRI) report on cancer incidence projections, the number of CRC cases in Ireland is projected to roughly double by 2045 (compared to 2015), as a result of an increasing and ageing population. Nonetheless, NCRI projections suggest that the incidence rate is expected to remain constant over the same timeframe.

Diagnosis of CRC involves a biopsy, taken during a colonoscopy, supplemented by imaging studies to allow for cancer staging. Cancer stage is a key determinant of treatment plans and patient survival. Treatment plans may include a combination of surgery, chemotherapy, and or radiotherapy.

Between 2016 and 2020, screen-detected CRC accounted for approximately one fifth to one quarter of all CRC detected in Ireland in the population eligible for screening. Most screen-detected cancers are found at early stages (stages I or II, 62%). The percentage of symptomatically-detected CRC cases occurring between 2012 and 2020 that were diagnosed at advanced stages (Stages III and IV) ranged from 62% in those aged 65–69 to 67% in those aged 50–54. The five-year net survival of CRC cases, based on the period 2013–2018, was estimated at 71% in those aged 60–69 (the age group eligible for screening during that time), compared with 68% in those aged 55–59.

Colorectal cancer typically develops slowly and may present with subtle symptoms, underscoring the need for early detection and intervention. The BowelScreen programme has been effective in identifying cancers at an early stage. However, CRC incidence is rising overall in Ireland, particularly in individuals under 50. As the age cohorts mature, a similar increase is anticipated in older groups, especially those aged 50–54.

Test accuracy

A review of evidence for the clinical test accuracy of FIT for the detection of colorectal cancer was conducted. This review considered asymptomatic, average-risk populations at thresholds similar to that used by the BowelScreen programme in Ireland (that is, 45µg of haemoglobin (Hb) per gram of faeces, µg/g). A 2019 systematic review of the effect of age and positivity threshold on FIT test accuracy was used as a key source to identify relevant studies. An additional systematic search was performed to capture studies published since this review.

Eleven studies met the inclusion criteria, with FIT thresholds ranging from 40 to 50µg/g. One of the studies used thresholds of 40µg/g for women and 80µg/g for men. Six studies, with a colonoscopy reference standard, primarily focused on advanced neoplasia (AN) (a composite that includes both CRC and advanced adenoma (AA)) as the target condition. The reference standard for the remaining five studies was cancer registry or medical record follow-up to identify interval cancers, and reported CRC as the target condition. Sample sizes, based on the number of participants with a valid FIT and colonoscopy or registry follow-up, ranged from 779 to 2,302,711.

Five studies included data stratified by age for FIT thresholds ranging from 40 to 80µg/g. Based on these limited data, no clear or consistent evidence was identified to suggest that FIT test accuracy for the detection of CRC at a threshold of 45µg/g varies significantly by age. The remaining seven studies reported data at FIT thresholds ranging from 40 to 45µg/g, without age stratification. Sensitivity and specificity of FIT for the detection of CRC varied considerably across all of these studies. With a colonoscopy reference standard, sensitivity of the OC-Sensor™ FIT device at a threshold of 40µg/g ranged from 60% (95% Confidence Interval [CI]: 26%, 88%), among participants aged 40–79 in a cohort study in Japan, to 80% (95% CI 35%, 100%) in participants aged 50–69 in a colonoscopy screening trial in Spain. The specificity values for these studies were 97% and 95%, respectively.

Sensitivity for the detection of AN was similarly uncertain, with estimates ranging from 10% with the OC-Sensor™ FIT device in people aged 60 participating in a screening trial in Sweden, to 29% with FOB Gold® in colonoscopy screening participants aged 50–79 in Germany, both at a threshold of 40µg/g.

One study with a registry reference standard, based on data from over 500,000 participants in the Danish CRC screening programme, reported data for the same FIT device, threshold, and target age range of the BowelScreen programme. Sensitivity of the OC-Sensor™ FIT device for the detection of CRC at a threshold of 45µg/g in participants aged 50–74 was 76% (95% CI: 74%, 77%), with a specificity of 96% (95% CI: 96%, 96%).

FIT test accuracy for the detection of CRC may be impacted by a range of factors, including the FIT device and buffer solution used, as well as the presence of other health conditions and use of certain medications. Some of these may interact with age, limiting the comparisons that can be made across different settings and populations. Few studies have reported age-stratified results for FIT thresholds between 40 and 50µg/g. Based on the limited available data, no clear or consistent evidence was identified to suggest that FIT test accuracy for the detection of CRC at a threshold of 45µg/g varies significantly by age.

Clinical effectiveness

A review of the evidence on the clinical effectiveness and safety of colorectal cancer screening with a starting age of 50, compared to a starting age of 55, was undertaken. Given a relative lack of evidence specific to screening with faecal immunochemical tests, evidence for a broad range of screening modalities was considered.

A 2021 systematic review from the United States Preventive Services Task Force (USPSTF), and a 2023 review from the European Commission Initiative on Colorectal Cancer (ECICC) Working Group, were used as key sources to identify relevant studies of clinical effectiveness and safety. An additional de novo search was performed to identify relevant studies published since these systematic reviews.

Ten studies, reported across 12 publications, were identified that met the inclusion criteria for the review. These included four randomised controlled trials (RCTs) of CRC screening with guaiac-based faecal occult blood tests (gFOBT), one RCT of screening with flexible sigmoidoscopy (FSIG) with or without FIT, and five observational studies of screening with FIT. All studies assessed the effectiveness of screening (or invitation to screening) compared to no screening. No study directly compared the clinical effectiveness of CRC screening with a starting age of 50 to a starting age of 55.

There was consistent evidence from nine of the ten included studies that screening reduces CRC mortality. Based on four RCTs, gFOBT screening was associated with a reduction in CRC mortality of between 6% and 22% compared to no screening at 30 years of follow-up, in participants ranging in age from 45–80. The included observational FIT studies generally reported larger reductions in CRC mortality, although estimates varied widely: reductions ranged from 10% with six years of follow-up to 65% with 11 years of follow-up in participants ranging in age from 50–69.

All five RCTs reported CRC incidence outcomes. Significant relative reductions in CRC incidence with screening, compared with no screening, were reported by two of the five RCTs. These ranged from a reduction of 15% at 18 years of follow-up in those screened with gFOBT, to a reduction of 22% at 15 years in those screened with FSIG with or without FIT. Effects on incidence were reported by three of the five observational studies of FIT screening; these suggested reductions in CRC incidence ranging from 31% with 11 years of follow-up to 33% with five years of follow-up.

Evidence on screening effectiveness specifically for those aged 50–54 was limited to one observational FIT study and one RCT that reported data for this age group. Based on data from the RCT, which examined screening with FSIG with or without FIT, screening was associated with a 35% reduction in CRC incidence in males aged

50–54 at 14.8 years of follow-up, with no reduction among females. However, this trial was not powered to detect an effect in this age group. The observational study found that, compared to no screening, screening with FIT in those aged 50–54 was associated with a CRC mortality reduction of 64% in females and 71% in males, and a CRC incidence reduction of 25% in females and 30% in males at 11 years of follow-up.

It is important to note that evidence of the effectiveness of FIT-based screening, specifically, is from observational studies. These studies represent a weaker form of evidence than RCTs and are subject to important limitations, which may artificially inflate the effect estimates observed and lead to an overestimation of the added value of screening.

Three studies reported on the physical harms of colonoscopy (for example, pain, bleeding, or perforation risk) following a positive FIT. In two studies, harms, which were of low risk overall, were lower in younger age groups. Three studies reported on the impact of FIT-based screening on psychosocial outcomes, one of which considered age. While age was not associated with experiencing general psychological consequences following colonoscopy after a positive FIT, worry about developing cancer appeared to increase slightly with decreasing age.

While the evidence identified is subject to limitations, there is consistent evidence that screening from age 50 reduces CRC mortality compared to no screening. While some evidence suggests that FIT screening may reduce CRC incidence, this was based mainly on observational studies, with a higher risk of bias.

Cost-effectiveness

The cost effectiveness of lowering the starting age of eligibility for population-based colorectal cancer screening was reviewed. The evidence review focused on European studies that considered the age group of interest (that is, those aged 50–54). The potential relevance, credibility, and transferability of the findings to the Irish setting were considered.

The aim of the review was to address whether, for the population in Ireland at average risk of colorectal cancer, providing two-yearly FIT-based colorectal cancer screening at a FIT threshold of 45µg Hb/g faeces (FIT45) to persons aged 50 to 74 years, is likely to be cost-effective relative to screening those aged 55 to 74. A 2023 systematic review of the cost effectiveness of CRC screening was used as a key source to identify relevant studies. An additional systematic search was performed to capture studies published since this systematic review.

Eight studies met the inclusion criteria for the review. However, none of the studies directly addressed the question of interest of the present HTA, that is, the cost

effectiveness of screening all adults aged 50–74, versus those aged 55–74, using a FIT45 threshold and two-yearly screening intervals. Most studies reported costs and quality-adjusted life years gained (QALYs) for broadly similar strategies, where either the FIT threshold, screening interval, or age range varied; these strategies were used to consider the potential cost effectiveness of extending the age of eligibility for screening from 55–74 to 50–74 years in Ireland.

Six studies were deemed sufficiently relevant to the present HTA. Among these, the validity, design, and choice of data inputs were largely robust and considered 'sufficiently credible' to support decision-making in the context of Ireland. The six studies were considered to be of high quality overall. However, a number of concerns were identified in relation to the historical nature of costs, scale of cost inputs, choice of utility weights, and lack of detailed reporting of data sources.

Study results were disaggregated to examine the model findings for the effectiveness of screening from age 50 versus screening from age 55. Based on three studies, which modelled screening strategies that had a greater or lesser intensity to that used in the BowelScreen programme, estimates of CRC incidence reduction ranged from less than one to four additional CRC cases prevented per 1,000 people screened. For CRC mortality, these studies estimated between one and two additional CRC deaths avoided per 1,000 people screened. However, these estimates are uncertain and the applicability to Ireland is unclear.

The cost per QALY could be estimated from four studies deemed sufficiently relevant to the present HTA. Incremental cost-effectiveness ratios (ICERs) ranged from €1,548 to €10,401 per QALY. The impact of the quality and transferability concerns identified is not expected to result in an ICER of above €20,000 per QALY.

In the context of Ireland, the overall evidence suggests that screening all adults from age 50 to 74 years is likely cost-effective versus screening all adults from age 55 to 74, based on a willingness-to-pay threshold of €20,000 per QALY gained.

Resource and budget impact

An analysis was carried out to evaluate the resource implications of extending colorectal cancer screening to ages 50–74, compared to the range of 55–74. The analysis estimated changes in CRC incidence, additional resources required, and incremental costs of the proposed extension. Several scenarios were considered, involving different paces of expansion and varying assumptions about programme uptake and migration projections. It should be noted that the aim of this model was not to predict the clinical effectiveness or cost-effectiveness associated with an age extension. The analysis adopted a 10-year time-horizon, with expansion assumed to commence from 2031. This model indicates the initial effects of screening in terms of early identification of CRC cases, but does not capture the long-term benefits.

Lowering the starting age of CRC screening from 55 to 50 would increase the eligible population by 27% (over 400,000 additional people), necessitating careful planning and allocation of health service resources. Incremental cases of CRC in those aged 50–54 were predicted to peak within the 10-year time horizon, stabilising at around 40 to 60 incremental cases of CRC per year by 2040. The expanded programme may result in up to 2,100 additional screening colonoscopies, and 800 additional people requiring histopathology annually, with around 600 additional colonoscopies required for surveillance of high-risk adenomas each year. Since surveillance colonoscopies follow on from initial screening, the years with the highest resource requirements for screening and surveillance colonoscopies may be different.

Expanding the screening programme to include those aged 50–54 will extend the benefits of early detection, resulting in fewer advanced-stage CRC cases. By year 10, advanced stage cancers were expected to reduce by 34, 26, and 14 cases annually for the immediate, 1-yearly, and 2-yearly expansion scenarios. FIT-based CRC screening identifies and removes pre-cancerous polyps, reducing CRC incidence. Immediate and 1-yearly expansions to those aged 50–54 were predicted to lead to an overall reduction in CRC cases by year 10. The 2-yearly expansion scenario did not predict case reductions within 10 years but is expected to show a longer-term decrease.

Expanded screening increases early detection of CRC and demand for diagnostic resources, including colonoscopy, CT colonography, and examination of samples taken during colonoscopy. However, for resources relating to cancer staging and grading (for example, diagnostic radiology and further histological examination), the increased demand from patients identified through screening will be partially offset by the reduced demand from patients presenting in the symptomatic services.

Faster implementations were predicted to incur higher cumulative incremental costs over 10 years, with immediate, 1-yearly, and 2-yearly expansions costing an additional approximately €66 million, €57 million, and €45 million, respectively. Immediate implementation was estimated to incur the highest initial cost, amounting to approximately €9.2 million in the first year versus screening only in those aged 55–74. By year 10, however, the annual incremental cost of immediate expansion was lower than slower expansion scenarios. The largest drivers of overall incremental costs were related to colonoscopy (45%), treatments (25%), FIT tests (19%), histopathology (4%), BowelScreen contributions to related services (4%), and additional programme staff (3%). Once established, the model predicted that the overall incremental cost would decline over time due to earlier cancer detection, reducing the need for costly advanced-stage treatments.

CRC screening uptake rates in Ireland have been relatively low, ranging from 38.1% among those aged 60–64 to 49.9% among those aged 65–69 years. Achieving the

target uptake rate of 60% would reduce CRC cases, but would lead to greater resource requirements and an estimated additional cost of €5 to 10 million by 2040 depending on the pace of expansion. Higher inward migration scenarios predicted a larger population, leading to more CRC cases and increased resource and budgetary requirements. High and low migration scenarios were estimated to contribute to a variability of plus or minus €3 million by 2040, compared to the moderate migration scenario.

In summary, over the 10-year period, the model estimated the incremental budget impact associated with immediate, 1-yearly, and 2-yearly expansions as €66, €57, and €45 million, respectively. These values were influenced by the assumed pace of expansion, programme uptake, and migration projections, as well as uncertainty in the underlying parameters. Therefore, the figures should be viewed as broad indications rather than accurate estimates. Expanding BowelScreen to include those aged 50–54 is expected to lead to population health benefits by reducing CRC cases and detecting cancers at less advanced stages. This expansion will place substantial demands on health service resources and budgets. Slower implementation options may be necessary to manage initial resource requirements more effectively.

Organisational considerations

A successful colorectal cancer screening programme is contingent on timely access to the various elements of the screening and diagnostic pathway, including high-quality endoscopy services for participants who receive a positive FIT result, histopathology to process samples taken during colonoscopy, and diagnostic radiology for suspected cancer cases. These services have experienced ongoing capacity challenges, including long waiting lists and deteriorating report turnaround times. At the end of January 2025, over 27,000 patients (excluding children and screening participants) were waiting for gastrointestinal (GI) endoscopy appointments. None of the laboratories in Ireland's eight designated cancer centres met turnaround time targets for GI endoscopic biopsies or cancer resection cases in 2023 (the latest available data). The recommended report turnaround time targets for MRI, CT, ultrasound and X-ray were not met by 22 of 41 radiology services in 2023.

Lowering the starting age of BowelScreen from 55 to 50 would increase the eligible population by approximately 27%. Compared to offering screening to those aged 55 to 74 only, this age extension would require approximately 2,000, 2,400 and 2,300 additional colonoscopies (index, additional planned procedures and surveillance) as part of the BowelScreen programme in year one, year five, and year ten, respectively, as well as increasing the demand on histopathology and diagnostic radiology services.

BowelScreen operates within the general symptomatic services; colonoscopy and CT colonography procedures are performed in units that also provide services to symptomatic patients, while samples taken at colonoscopy are processed by laboratories that also process samples from symptomatic cases. As such, pressures on the general symptomatic services can impact the programme's ability to deliver screening in line with its quality assurance standards and requirements. Waiting times for BowelScreen colonoscopy and CT colonography appointments have to date not reached the minimum performance threshold specified in the programme quality assurance standards.

Minimum experience levels and performance quality indicators for screening colonoscopies limit the number of endoscopists who meet the BowelScreen quality assurance criteria. Screening colonoscopies are generally performed by consultant gastroenterologists or general surgeons, while samples removed at colonoscopy are reported on by histopathologists. Workforce shortages have been highlighted across all three specialties. The National Doctors Training and Planning unit has estimated the number of consultants in gastroenterology and hepatology, general surgery and histopathology that will be required by 2038, outlining the required increase in the annual number of higher specialist training places to meet the projected demand. Training for these roles typically spans a period of five to eight years, with constraints on a potential expansion of training programmes including the supply of trainees, sufficient training capacity, and availability of funding for training posts.

The Programme for Government 2025 outlined a commitment to the building of four new elective treatment centres, which, once operational, could provide capacity for up to 128,100 additional endoscopy procedures annually. This additional endoscopy capacity could help meet existing unmet demand, the increased demand from future demographic changes, the planned BowelScreen expansion to those aged 55–74 years, and potentially support the extension to those aged 50–54. According to Sláintecare 2025+, the two new elective treatment centres in Cork and Galway are expected to become operational in 2030. Operational dates for the two Dublin treatment centres have not been reported. If endoscopy capacity were to remain constrained at the time of implementation of an age extension, one additional endoscopy room may be sufficient to support expansion of the programme to include those aged 50–54, assuming that up to 3,050 procedures may be conducted per room annually.

Delivering both the infrastructure and resourcing for the new facilities will be challenging. Given a finite number of endoscopists with the required level of experience and expertise to perform screening colonoscopies, as well as capacity constraints in histopathology and radiology services, the potential additional capacity impact of the new elective treatment centres is unclear.

Capacity may be impacted by many factors. Developments and advances in screening and diagnostic techniques and treatment, such as advanced endoscopic techniques, molecular testing and total neoadjuvant therapy, will continue to increase demands for endoscopy, histopathology and radiology resources. The estimates from the modelling work conducted for this HTA are therefore likely to underestimate the future demand on these services that will result from an extension of CRC screening.

The services required by BowelScreen are experiencing significant ongoing capacity challenges. Extending the programme without coordinated efforts to address the existing constraints is likely to negatively impact the ability of both BowelScreen and symptomatic services to provide care in accordance with quality assurance standards and KPI targets; this could potentially lead to longer waiting lists and worsening turnaround times.

Ethical, patient and social considerations

The ethical, patient, and social implications that the proposed age extension of the BowelScreen programme to those aged 50 to 54 years may have for patients, families, the general public and the healthcare system in Ireland were explored. Compared to those aged 55–74, the benefit of screening may be lower in those aged 50–54 due to lower incidence and mortality rates in this age group. This reduced benefit, however, should be considered in the context of reduced harms from screening. Screening for colorectal cancer is likely to be cost-effective in those aged 50–54, and may therefore be considered an efficient use of healthcare resources.

There was limited data available to address specific elements of the HTA, such as clinical and cost effectiveness, as well as test accuracy. As a result, the benefits and harms of extending BowelScreen to those aged 50–54 are subject to a degree of uncertainty, as data relating to the 50–54 age group specifically were limited.

Considering autonomy, it is important that individuals are aware of the benefits and harms of screening, to ensure that they can make informed decisions at each stage of the screening process. In terms of justice and equity, underserved groups are the least likely to benefit from colorectal cancer screening as a result of reduced uptake, but are often more likely to have a higher incidence and poorer outcomes relating to the disease. Lowering the screening age is likely to strain healthcare resources, including financial resources, staffing, endoscopy, histopathology and radiology services and screening infrastructure. It is important to consider the ethical implications of the potential diversion of resources from symptomatic services, and to ensure that the benefits of expanded screening justify the additional costs and resources.

Conclusion

There is consistent evidence, based on a range of screening modalities and study designs, that screening from age 50 reduces CRC mortality compared to no screening, with a reduced risk of adverse events among younger screening participants. The available evidence also suggests that screening from 50–74 is likely to be cost-effective compared to screening from 55–74. Lowering the screening age would increase the size of the population eligible for screening by 27%, and is estimated to incur additional costs of between approximately €45 million and €66 million over 10 years compared to screening those aged 55–74, depending on the pace of implementation. Once established, the overall incremental cost would be expected to decline over time as a result of earlier cancer detection, which reduces the need for more costly advanced-stage treatments.

While a commitment to screen those aged 55–74 is in place, as of May 2025, this has not been achieved. Ongoing developments in novel, non-invasive screening tests may lead to changes in the screening pathway prior to or in tandem with the planned expansion of the programme to those aged 55–74, increasing the uncertainty in the estimates presented in this report.

The services required for screening, including endoscopy, histopathology and diagnostic radiology, are experiencing significant, ongoing capacity constraints, including workforce shortages. Extending the programme without coordinated efforts to address the existing constraints is likely to negatively impact the ability of both BowelScreen and symptomatic services to provide care in accordance with quality assurance standards and KPI targets, which could lead to longer waiting lists and worsening turnaround times. Significant investment and planning would be required to ensure the necessary resources are in place to support a potential extension of the programme to include those aged 50 to 54.

1 Introduction

1.1 Background to the request

In 2019, the National Screening Advisory Committee (NSAC) was established by the Minister for Health as an independent advisory committee to play a significant strategic role in the development and consideration of population-based screening programmes in Ireland. At the request of the Department of Health, the Health Technology Assessment (HTA) Directorate within the Health Information and Quality Authority (HIQA) undertakes evidence synthesis and provides evidence-based advice to NSAC on behalf of the Minister for Health.

Following submissions received by NSAC as part of the 2021 and 2022 Calls for Submissions, NSAC requested that HIQA undertake a HTA of extending the BowelScreen colorectal cancer screening programme to those aged 50 to 54 years. This would be in addition to the planned expansion of BowelScreen to those aged 55 to 74, which was outlined in The National Cancer Strategy 2017–2026 and the 2020 Programme for Government.^(1, 2)

The NSAC outlines 20 criteria for appraising the viability, effectiveness and appropriateness of a screening programme.⁽³⁾ The purpose of this HTA is to systematically synthesise the evidence in relation to expanding the BowelScreen programme to those aged 50 to 54 years, with reference to the NSAC criteria for appraising the viability, effectiveness and appropriateness of a screening programme, in order to support the NSAC in its recommendation to the Minister for Health on this topic.

1.1.1 Decision context

Colorectal cancer, also called bowel cancer, refers to cancer that occurs in the lower part of the bowel, that is, the colon and rectum. Colorectal cancer usually develops from benign polyps (growths of tissue that commonly occur on the mucous membrane) in the lining of the colon or rectum. These polyps, or adenomas, may become cancerous over time. The progression of adenomas from benign to cancerous is referred to as the adenoma-carcinoma sequence. The removal of adenomas interrupts this sequence, and has the potential to impact the subsequent development of colorectal cancer.⁽⁴⁾

Globally, colorectal cancer (CRC) is the third most commonly diagnosed cancer, accounting for approximately 10% of all cancers diagnosed in 2020, with over 1.8 million new cases.⁽⁵⁾ In Ireland, colorectal cancer is the second most frequently occurring cancer (excluding non-melanoma skin cancer) in males and the third most common cancer in females, with an annual average of 2,750 new cases between

2021 and 2022.⁽⁶⁾ Similarly, CRC represents the third most common category of cancer deaths, accounting for an average of approximately 1,000 deaths a year between 2012 and 2020.⁽⁷⁾ While the age-standardised CRC incidence rate in Ireland decreased by an average of 2.5% a year in men between 2012 and 2019, and by an average of 0.3% a year in women between 1994 and 2019,⁽⁸⁾ the absolute number of CRC cases is projected to continue to increase as a result of population growth.⁽⁹⁾ Risk factors for colorectal cancer include increasing age, male sex, a family or personal history of colorectal cancer, personal history of inflammatory bowel disease, sedentary lifestyle, obesity, a diet high in red and processed meats, smoking, and alcohol consumption.^(10, 11)

The BowelScreen programme

In January 2010, following due consideration of the evidence from two HIQA HTAs,^(12, 13) a decision was made to introduce a national population-based colorectal cancer screening programme. BowelScreen, the National Bowel Screening Programme, commenced in October 2012 with the aim of offering free screening to people aged 55 to 74 years on a two-yearly cycle. The first round of screening (2012 to 2015) invited those aged 60 to 69. As of April 2025, BowelScreen invites people aged 59 to 70 years for screening. The National Cancer Strategy 2017–2026 and the 2020 Programme for Government outlined a commitment to expand BowelScreen to those aged 55 to 74, as per the original aim of BowelScreen.^(1, 2) The 2025 Programme for Government similarly included a commitment to extend BowelScreen,⁽¹⁴⁾ while the 2025 HSE National Service Plan outlined that a key area of focus includes the expansion of the programme to include those aged 58 to 70 years on an incremental basis by 2026.⁽¹⁵⁾

BowelScreen uses a faecal immunochemical test (FIT) as its primary screening tool to detect occult (hidden) blood in stool, with a decision threshold of 45µg haemoglobin/g faeces (225ng haemoglobin per mL buffer). Screening participants with a FIT result above this threshold are referred for colonoscopy, or, in some cases, computed tomography (CT) colonography, for further investigation.

The scope of this HTA is limited to consideration of extending the BowelScreen programme to people aged 50 to 54 years. The HTA will not consider alternative testing modalities (for example, a primary screening tool other than FIT) or specifications (for example, an alternative FIT threshold for test positivity, or an alternative screening interval, other than two-yearly).

1.2 Terms of reference

Based on the available evidence, this HTA will inform a recommendation of NSAC to the Minister for Health.

The terms of reference for this HTA, which were agreed between HIQA and the Chair of NSAC, on behalf of the NSAC, are to:

- describe the epidemiology and burden of disease of colorectal cancer in Ireland
- describe the care pathway for patients with colorectal cancer in Ireland, including screening and diagnosis, and the proposed age extension to include people aged 50 to 54 years
- describe international policy and guidelines on screening for colorectal cancer
- review the clinical effectiveness and safety of colorectal cancer screening in people aged 50 to 54 years
- review the methods and results of published economic evaluations reporting on the cost effectiveness of extending FIT-based colorectal cancer screening to people aged 50 to 54 years
- assess the cost effectiveness and budget impact of extending the age of eligibility of the BowelScreen programme to include people aged 50 to 54 years in the context of the Irish public healthcare system
- assess the potential resource and organisational implications of a BowelScreen age extension in Ireland
- consider any ethical or social implications that the proposed age extension to the BowelScreen programme may have for patients, families, the general public or the healthcare system in Ireland.

1.3 Overall approach

A multidisciplinary EAG was convened by HIQA, comprising representation from relevant stakeholders and scientific experts. Stakeholders included patient and public representation from the Irish Cancer Society and Patients for Patient Safety, as well as representation from the Department of Health, BowelScreen, the National Screening Service (NSS), the HSE Endoscopy Programme, the National Cancer Control Programme (NCCP), the National Clinical Programme for Gastroenterology and Hepatology, the HSE Laboratory Services Reform Programme, the Faculty of Radiologists and Radiation Oncologists, and the National Cancer Registry Ireland (NCRI).

The role of the EAG was to inform and guide the process, provide expert advice and information, and to provide access to data where appropriate. A full list of the membership of the EAG is available in the acknowledgements section of this report.

The terms of reference of the EAG were to:

- contribute to the provision of high quality research and considered advice by HIQA to NSAC on behalf of the Minister for Health
- contribute to the work of the group by providing expert guidance, as appropriate
- be prepared to provide expert advice on relevant issues outside of group meetings, as requested
- provide advice to HIQA regarding the scope of the analysis
- review the project plan outline and advise on priorities, as required
- support the Evaluation Team during the assessment process by providing expert opinion and access to pertinent data, as appropriate
- review the draft report from the Evaluation Team and recommend amendments, as appropriate
- contribute to HIQA's development of its approach to HTA by participating in an evaluation of the process on the conclusion of the assessment
- notify the project lead if a nominee can no longer participate or contribute to the process, as non-participation may require alternative EAG membership to be sought.

HIQA appointed an Evaluation Team, comprising staff from the team within the HTA Directorate designated to support NSAC, to carry out the assessment.

The HTA protocol, including the terms of reference of the HTA, was reviewed by the EAG prior to the first meeting. Draft versions of the assessment were circulated to the EAG for review and discussion at three formal meetings of the group, with amendments made, where appropriate. A draft version of the report has been made available for targeted and public consultation. The feedback received during the consultation and HIQA's responses to the issues raised, including any changes made to the report, will be summarised in a Statement of Outcomes report. After the consultation, a final draft of the report, including the advice to NSAC, will be circulated to the EAG for review.

Consistent with HIQA governance processes, the final draft of the HTA and associated Statement of Outcomes report arising from the consultation will be submitted to the Board of HIQA for approval. Following its approval, the final HTA will be submitted to NSAC for consideration and published on the HIQA website.

DRAFT

2 Description of technology

2.1 Key points

- Colorectal cancer screening aims to reduce mortality through the earlier detection of cancer and the removal of pre-cancerous lesions, and has been recommended by the Council of the European Union for those aged 50 to 74 years since 2003.
- The most commonly-used screening tests for colorectal cancer are either stool-based, that is, testing of a person's stool sample, or visualisation tests, in which the examiner obtains a visual image or representation of the colon to identify potential abnormalities.
- Stool-based tests include faecal occult blood tests (FOBT), which detect hidden (occult) blood in stool, a potential indication of adenomas or colorectal cancer. A positive stool-based test result is typically followed up with a confirmatory visualisation test such as colonoscopy.
- Quantitative faecal immunochemical tests (FIT) are a type of FOBT that quantify the concentration of haemoglobin (Hb) in stool, measured in microgram (μg or mcg) of Hb per gram of faeces, or nanogram (ng) of Hb per ml of buffer solution. The concentration of Hb at or above which an individual is considered to have a positive screening test result is referred to as the FIT threshold. FIT thresholds are linked to the effectiveness of screening and to resource requirements and constraints of individual programmes.
- Visualisation tests, such as colonoscopy, are considered more accurate than stool-based tests as they allow for the direct visualisation of the colon and rectum to identify abnormalities. Colonoscopy is considered the reference standard and is highly sensitive and specific in detecting both cancer and pre-cancerous polyps. However, it is an invasive procedure and, in the context of screening, is primarily carried out following a positive indication on a non-invasive test, such as FIT.
- BowelScreen, Ireland's national colorectal cancer screening programme, commenced in 2012. As of April 2025, people aged 59 to 70 are invited for screening every two years. Screening uptake rates have ranged from 38% in those aged 60–64 to just below 50% in those aged 65–69.
- The primary screening test for BowelScreen is FIT, with a positivity threshold of $45\mu\text{g}$ Hb/g faeces. Individuals who receive a positive FIT result

are referred for colonoscopy. Depending on the results of the colonoscopy, individuals are either returned to routine screening, enter a surveillance pathway, or, if cancer is detected, are referred for treatment.

- Since the introduction of BowelScreen, approximately 2.4 million invitations for screening have been issued, with approximately 1 million satisfactory FIT tests returned between 2012 and 2023.
- FIT positivity rates have ranged from 3.0% to 4.0% in those aged 60–64 years, and from 3.2% to 5.4% in those aged 65–69.
- The colonoscopy rate, based on the number of positive FIT tests, has ranged from 79.2% to 82.4% in the younger age group, and from 77.0.% to 82.2% in the older age group.
- The cancer detection rate in those aged 60–64 years decreased from 2.36 per 1,000 screened in the first screening round (2012–2015) to 1.54 per 1,000 screened in those aged 59–64 in 2022–2023. In those aged 65–69, the cancer detection rate decreased from 2.71 per 1,000 in 2012–2015 to 1.57 in 2022–2023. Adenoma detection rates have consistently exceeded 55% in each round of the programme, with similar adenoma detection rates in both age groups.
- With the planned expansion of the programme to those aged 55 to 74 years, participating individuals will be eligible for up to 10 rounds of screening. Under the proposed extension of lowering the starting age to 50, participating individuals would be eligible for up to 13 rounds of screening.
- Eight international colorectal cancer screening guidelines were reviewed. Seven guidelines recommended colorectal cancer screening from the age of 50, of which two included additional 'grade B' or 'conditional' recommendations for screening in those aged 45 to 49.
- Of the 22 countries included in a review of international practice, 20 were found to have a national or regional colorectal cancer screening programme in place. Most of the countries reviewed use FIT as the primary screening test, though there is variation in FIT positivity thresholds between countries. Across European countries examined, the age of eligibility for screening ranged from 50 to 75, though some countries had a later starting age and or an earlier stopping age. Considering non-European countries, Australia was noted to have lowered the starting age of screening from 50 to 45 as of 2024.

2.2 Introduction

Colorectal cancer screening aims to reduce mortality through the earlier detection of cancer and the removal of pre-cancerous lesions, and has been recommended for those aged 50 to 74 years by the Council of the European Union since 2003.⁽¹⁶⁾ In Ireland, BowelScreen, the National Bowel Screening Programme, commenced in October 2012. As of April 2025, BowelScreen invites people aged 59 to 70 years for screening, with a commitment to expand to those aged 55 to 74. In line with the request received from the National Screening Advisory Committee (see Chapter 1, section 1.1), the focus of this HTA is on extending BowelScreen to those aged 50 to 54 years.

The purpose of this chapter is to describe the key elements of the technology under consideration; that is, screening for colorectal cancer in average-risk populations. The chapter will outline the screening tests available for colorectal cancer (section 2.3), followed by a description of the BowelScreen programme (section 2.4). In addition, an overview of international guidance on screening (section 2.5), as well as colorectal cancer screening programmes internationally (section 2.6), is presented.

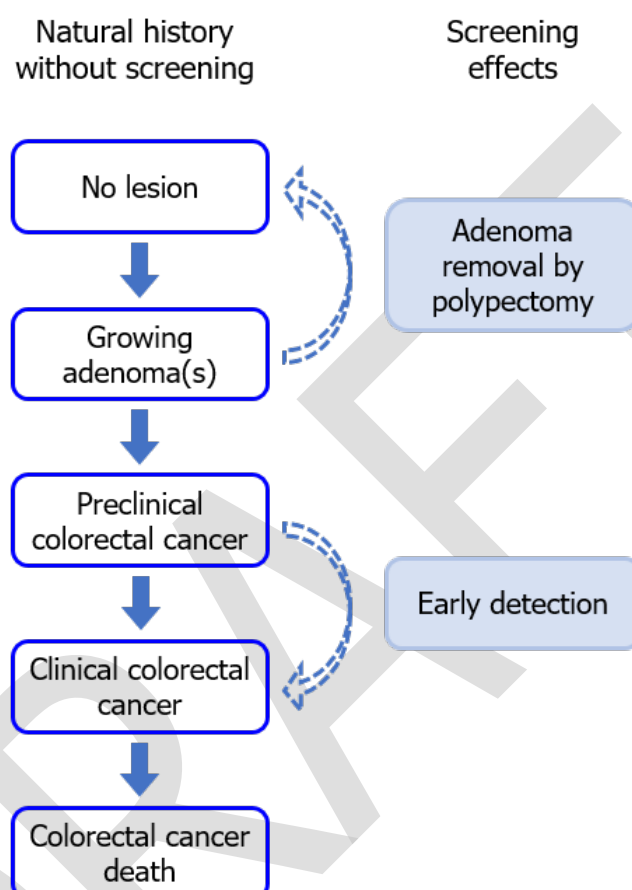
2.3 Screening for colorectal cancer

The natural history of colorectal cancer, diagnosis and treatment, as well as the epidemiological patterns associated with colorectal cancer, are described in detail in Chapter 3. Briefly, colorectal cancer usually develops from benign polyps (growths of tissue that commonly occur on the mucous membrane) in the lining of the colon or rectum. These polyps, or adenomas, may become cancerous over time. The progression of adenomas from benign to cancerous is referred to as the adenoma-carcinoma sequence. Adenomas can be removed through polypectomy performed during a colonoscopy.⁽¹⁷⁾ The removal of cancerous or pre-cancerous adenomas reduces the likelihood of developing cancer in future,⁽¹⁷⁾ while earlier detection of colorectal cancer has the potential to improve treatment outcomes.⁽¹⁸⁾ Screening aims to interrupt the natural history of colorectal cancer through the removal of adenomas and the earlier detection of cancer.^(4, 19) Figure 2.1 demonstrates the interaction between screening and the natural history of colorectal cancer.

Screening for colorectal cancer has been recommended by various international agencies and professional bodies, including, but not limited to, the German Guideline Program for Oncology,⁽²⁰⁾ Spain's Sociedad Española de Oncología Médica,⁽²¹⁾ and the United States Preventive Services Task Force.⁽²²⁾ At a European level, the European Commission has recommended screening for colorectal cancer for those aged 50 to 74 years since 2003, based on published principles for screening as a tool for preventive medicine from the World Health Organization in 1968⁽²³⁾ and the

European Council in 1994,⁽²⁴⁾ as well as the burden of colorectal cancer and evidence of the efficacy of screening from randomised trials.⁽¹⁶⁾

Figure 2.1 The interaction of screening and the natural history of colorectal cancer



Adapted from the United States Preventive Services Task Force (USPSTF) technical report, *Colorectal Cancer Screening: An Updated Decision Analysis for the U.S. Preventive Services Task Force*.⁽⁴⁾

2.3.1 Forms of colorectal cancer screening

The most commonly-used screening tests for colorectal cancer are either stool-based, that is, testing of a person's stool sample, or visualisation tests, in which the examiner obtains a visual image or representation of the colon in order to identify potential abnormalities.^(25, 26) A brief summary of available tests and alternative testing methods is presented below, with a focus on the screening modalities used by the BowelScreen programme in Ireland.

Stool-based tests

Colorectal cancer screening has undergone significant changes over the last 20 years, particularly in the development and adoption of stool-based screening tests. These include faecal occult blood tests (FOBT), such as guaiac-based faecal occult blood tests (gFOBT) and faecal immunochemical tests (FIT), as well as stool DNA tests.⁽²⁶⁾ Faecal occult blood tests are based on the premise that blood vessels within larger colorectal polyps or cancers are fragile and easily damaged.⁽²⁷⁾ As a result, blood in the stool is a potential indication of polyps, advanced adenomas or colorectal cancer.⁽²⁷⁾ A positive result on a stool-based test is typically followed up with a confirmatory visualisation test, such as colonoscopy.

Guaiac-based faecal occult blood test (gFOBT)

Guaiac-based faecal occult blood tests were one of the earliest methods employed to screen for colorectal cancer. Guaiac paper contains a chemical compound that can facilitate the identification of blood in a sample. When a stool sample placed on guaiac paper is exposed to hydrogen peroxide, the presence of haem (an iron containing molecular component of haemoglobin within blood cells) in the sample reacts, resulting in a blue colour change, thereby serving as a qualitative test to signal whether or not there is blood present.⁽²⁸⁾ Sample collection can be carried out at home.⁽²⁹⁾ Certain medications, supplements, and foods may interfere with the results of the test and lead to inaccurate results, including false positives from the presence of non-human haem. Therefore, a specific diet (avoiding certain fruits and vegetables such as broccoli, as well as red meats) is required prior to testing to ensure the validity of the test, with adherence to this diet required for a week leading up to sample collection.⁽²⁹⁾ Guaiac-based faecal occult blood tests are not used by BowelScreen, and have largely been superseded by faecal immunochemical tests (see below).

Faecal immunochemical test (FIT)¹

Similar to gFOBT, faecal immunochemical tests aim to identify blood in the stool, in this case using an antibody to detect haemoglobin (Hb).⁽³⁰⁾ The sample can be collected at home, and, as FIT is selective in its detection of human haemoglobin originating from the colon and rectum, does not require any dietary restrictions.⁽²⁹⁾ Compared to gFOBT, FIT is superior in detecting advanced adenomas and colorectal cancer, with higher sensitivity and specificity for lower gastrointestinal bleeding and

¹ Faecal immunochemical tests are sometimes referred to as immunochemical faecal occult blood tests (iFOBT).

improved uptake.⁽³¹⁾ FITs can be qualitative or quantitative. Qualitative FITs require visual interpretation and cannot be subjected to automated analysis.^(32, 33) Quantitative FITs quantify the concentration of blood detected in stool, measured in micrograms (μg or mcg) of haemoglobin per gram of faeces (or ng Hb/mL buffer). As the analysis of samples is automated, interpretation of results is less subjective. This has led to the increased adoption of FIT, gradually replacing gFOBT in many screening programmes internationally.^(31, 34, 35)

Two of the major considerations in FIT-based screening are the intervals at which screening is carried out, and, for quantitative FIT tests, the decision threshold applied to determine a positive result.⁽³⁶⁾ The interval refers to the time between screenings; common intervals used in FIT-based screening are one or two years.⁽²⁵⁾ The decision threshold (that is, the concentration of Hb required for the test to be considered 'positive', commonly referred to as the FIT threshold or FIT cut-off) can be adjusted, with higher thresholds for test positivity implying greater concentrations of haemoglobin. In the context of a screening programme, the FIT threshold determines whether or not an individual is noted as screen positive, and therefore determines whether that individual receives further testing as part of the screening pathway.^(25, 37) FIT thresholds differ across screening programmes in Europe, ranging from 15 to $120\mu\text{g Hb/g}$. Programme variations in other countries are further outlined in section 2.6.1.

The BowelScreen programme in Ireland uses a quantitative FIT as the primary screening test, with a decision threshold of $45\mu\text{g Hb/g}$ faeces. FIT testing with a lower threshold ($10\mu\text{g Hb/g}$) is used as part of the symptomatic referral pathway, to facilitate the prioritisation of symptomatic patients for investigation for colorectal cancer, high-risk adenomatous polyps or inflammatory bowel disease.⁽³⁷⁻³⁹⁾ The test accuracy of FIT for detecting colorectal cancer (Chapter 4) and the clinical effectiveness of CRC screening (Chapter 5) will also be reviewed as part of this assessment.

Multi-target FIT (mtFIT)

While faecal immunochemical tests are superior to guaiac-based faecal occult blood tests, FIT sensitivity for pre-cancerous lesions remains low, with a reported sensitivity for advanced adenomas of 18–31%.⁽⁴⁰⁾ This has prompted ongoing research to improve sensitivity while maintaining high levels of specificity. One example is a multi-target FIT (mtFIT), which targets haemoglobin and two additional protein biomarkers (calprotectin, and serpinF2).⁽⁴¹⁾ A 2021 study reported an increase in sensitivity for advanced adenomas from 28% with FIT (at a threshold of $15.3\mu\text{g/g}$) to 38% with mtFIT; however, this study included stool samples from a referral population to increase the number of cases,⁽⁴¹⁾ and may not reflect test performance in an average-risk population. A Dutch study published in March 2024

found that, compared with FIT at a threshold of 47µg/g, mtFIT detected a greater number of advanced neoplasia (colorectal cancer, advanced adenomas or advanced serrated polyps [see Chapter 3, section 3.3]) and advanced adenomas.⁽⁴²⁾ However, the test positivity rate was also higher.

Stool DNA tests

Stool DNA testing aims to identify certain abnormal sections of DNA from cancer or polyp cells that have shed into the stool, through transportation of DNA in the bloodstream or through direct contact with the colorectal tissue.⁽⁴³⁾ Methylated DNA markers and DNA mutations in the genes of these cells form the basis of these tests.⁽⁴³⁾ Similar to FIT sample collection, stool DNA testing does not require any dietary restrictions or fasting, and the sample can be collected at home.⁽⁴³⁾ Stool DNA testing has seen many developments, such as the multi-target stool DNA test (mtsDNA),⁽⁴⁴⁾ which was approved by the US Food and Drug Administration in 2014. Compared with FIT, the collection and diagnostic process for mtsDNA is more complex, requiring a larger stool sample, liquid preservative, and two additional molecular assays.⁽⁴⁵⁾ Analyses are not performed in traditional pathology laboratories; rather, the samples are returned directly to the manufacturer.^(45, 46) More recently, in 2024, a next-generation multi-target stool DNA test featuring a new panel of biomarkers selected to increase specificity has demonstrated high sensitivity for detecting colorectal cancer and high specificity for advanced neoplasia.⁽⁴⁷⁾ While the next-generation mtsDNA has been found to be more sensitive for detecting CRC and advanced pre-cancerous lesions compared with FIT, it is also less specific, with specificity further decreasing with increasing age.⁽⁴⁷⁾ In the context of a screening programme, lower specificity leads to an increased number of false positive test results and unnecessary colonoscopies,⁽⁴⁷⁾ which in turn increases healthcare costs and the risk of complications.⁽⁴⁶⁾ Stool DNA tests have to date not been widely adopted by population-based colorectal cancer screening programmes. Quantitative FITs are considered the preferred screening test by the majority of international CRC screening programmes for referring individuals for follow-up colonoscopy.⁽⁴⁸⁾

A summary of the main stool-based CRC screening tests is provided in Table 2.1.

Table 2.1 Summary of stool-based CRC screening tests

Test	Target	Notes
gFOBT	Protein: haemoglobin	May detect haem from any part of the gastrointestinal tract, as well as non-human haem from red meat. Has largely been replaced by newer FIT tests.
FIT (qualitative)	Protein: haemoglobin	Uses an antibody specific to human haemoglobin. Results are reported as either positive or negative.
FIT (quantitative)	Protein: haemoglobin	Uses an antibody specific to human haemoglobin. The cut-off determining a positive result can be adjusted.
mtFIT	Protein: - haemoglobin - calprotectin - serpin family F member 2	Developed to improve sensitivity of FIT for advanced neoplasia (colorectal cancer and advanced adenomas).
mtsDNA	DNA: - aberrantly methylated BMP3 and NDRG4 promoter regions - KRAS mutations - reference gene (β-actin) Protein: - haemoglobin	Approved by the US Food and Drug Administration in 2014. Included in the United States Preventive Services Task Force 2021 and American College of Gastroenterology 2021 guidelines on colorectal cancer screening (see section 2.5.2)
Next generation mtsDNA	DNA: - methylated DNA markers (LASS4, LRRC4, PPP2R5C) - reference marker (ZDHHC1) Protein: - haemoglobin	Developed to improve specificity and reduce false positive results of the first generation mtsDNA.

Key: FIT – faecal immunochemical test, gFOBT – guaiac faecal occult blood test, mtFIT – multi-target FIT, mts-DNA – multi-target stool DNA test.

Visualisation tests

Visualisation tests for colorectal cancer screening include colonoscopy, flexible sigmoidoscopy, and computed tomography (CT) colonography. These tests are considered more accurate than stool-based tests as they allow for the direct visualisation of potential cancerous adenomas or pre-cancerous polyps. Visualisation

tests are often carried out following a positive result on a stool-based test or other symptomatic indications.

Colonoscopy

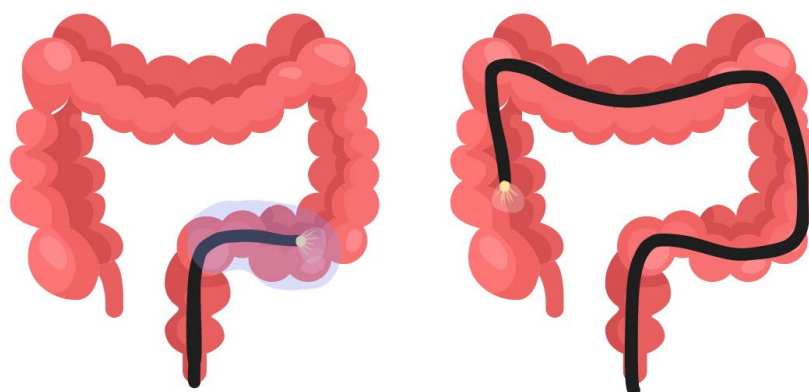
Colonoscopy is a visual exam of the structure of the colon and rectum to identify any abnormal areas.⁽⁴⁹⁾ It involves the use of a flexible, narrow tube with a camera and light at the end, called a colonoscope, which is inserted through the rectum into the colon. This allows the endoscopist to examine the entire colon and remove polyps through polypectomy if necessary, as well as take samples for biopsy.⁽⁴⁹⁾

Colonoscopy is considered the reference standard, that is, the most effective method of detection of colorectal cancer and adenomas, being highly sensitive and specific in detecting both cancer and pre-cancerous polyps.⁽⁴⁹⁾ However, colonoscopy is an invasive procedure that usually occurs while the patient is sedated, and is associated with additional risks such as perforation and bleeding.⁽⁴⁹⁾ In the context of screening, colonoscopy is primarily carried out following a positive indication on another non-invasive test, such as FIT.⁽⁴⁹⁾ As part of the BowelScreen programme in Ireland, screening participants who receive a positive FIT result (that is, haemoglobin concentration above the BowelScreen decision threshold) are referred for colonoscopy (see section 2.4.1).

Flexible sigmoidoscopy

Flexible sigmoidoscopy is another method of visualisation of the colon for the detection of colorectal cancer. Similar to colonoscopy, it involves the insertion of a scope to visualise the internal structure of the colon. However, flexible sigmoidoscopy focuses primarily on the rectum and sigmoid colon, rather than the entire large intestine (Figure 2.2).⁽⁴⁹⁾ It is considered less thorough in the detection of colorectal cancer when compared to colonoscopy, as it does not provide visualisation of the entire colon.⁽⁴⁹⁾ Therefore, abnormalities indicative of changes associated with colorectal cancer in areas beyond the reach of the scope would not be detected.⁽⁴⁹⁾ Flexible sigmoidoscopy may be used in BowelScreen surveillance if clinically indicated.

Figure 2.2 The area of the colon and rectum reached by flexible sigmoidoscopy (left) and colonoscopy (right)



Computed Tomography (CT) colonography

Computed tomography is a diagnostic imaging procedure that uses X-ray technology (ionising radiation) to create detailed images of any part of the body, including the bones, muscles and blood vessels. CT colonography, also referred to as virtual colonoscopy, is a visualisation test that uses a CT scan with oral contrast to create an image of the colon and rectum.⁽⁴⁹⁾ The examination can detect polyps and cancers, but unlike colonoscopy, it usually requires a follow-up colonoscopy if abnormalities are found.⁽⁴⁹⁾ The examination involves the preparation of the colon through fasting, laxatives and fluids. During the examination, carbon dioxide is pumped into the colon to allow for clearer imaging. CT colonography may be used in individuals for whom more invasive visual examination is deemed inappropriate for screening purposes due to factors such as age or poor health.⁽⁴⁹⁾ The rate of referral for CT colonography following a positive FIT result in the BowelScreen programme was 2.1% in the period 2022–2023 (see section 2.4).

CT colonography involves exposure to ionising radiation. While the risks are generally considered to be low, all exposures to ionising radiation carry some risk. One of the main risks associated with exposure to ionising radiation in the medical setting is the elevated risk of developing cancer. This risk may exist even at low doses, can persist for decades due to the latent period associated with developing cancer, and increases as a person's cumulative radiation dose increases. In order to ensure the safety of participants, BowelScreen adheres to a standard for the CT colonography radiation dose for participants as part of its quality assurance processes and to monitor exposures to ionising radiation.

Capsule endoscopy

Capsule endoscopy is a method of visualisation of the colon wherein a small camera contained within a capsule is swallowed, capturing images of the internal structures of the colon and rectum.⁽⁴⁹⁾ A 2023 HSE clinical guidance document suggests that capsule endoscopy should be considered in the following situations:⁽⁵⁰⁾

- Non-urgent symptomatic patients
- Patients who have undergone an incomplete colonoscopy
- Patients who have declined a colonoscopy, despite suitability
- For high-risk patients where diagnostic delay due to colonoscopy capacity may be an issue
- As an alternative for polyp surveillance where access to surveillance colonoscopy is prolonged.

While the capsule does provide visualisation of the colon, this may not be complete, as the capsule may fail to capture the entire surface. Factors such as bowel motility, capsule retention, and incomplete transit can lead to areas being missed.⁽⁵¹⁾ Other limitations include patient acceptability, as some individuals may find it difficult to swallow the capsule.⁽⁵¹⁾ Capsule endoscopy is not currently used by the BowelScreen programme.

Future developments and alternative tests

While the stool-based and visualisation tests mentioned above are the key modalities in use or under consideration for colorectal cancer screening, there are ongoing developments of alternative colorectal cancer screening modalities. For example, increasing evidence suggests a role of the gut microbiome in the development of colorectal cancer, which may serve as a biomarker for early diagnosis.⁽⁴⁹⁾ Testing for blood-based biomarkers, referred to as liquid biopsy, involves a non-invasive blood test to detect circulating tumour cells or other tumour-related components in the blood. A 2024 analysis of the comparative effectiveness and cost effectiveness of a hypothetical blood-based test with a sensitivity of 74% for colorectal cancer (CRC) and specificity of 90% (the thresholds set by the US Centers for Medicare and Medicaid Services), and a cost assumed equal to that of multi-target stool DNA, found that, while screening with a blood-based test could reduce colorectal cancer incidence and mortality compared with no screening, it was more costly and less effective than screening with FIT or colonoscopy.⁽⁵²⁾ A 2023 systematic review of non-invasive diagnostics for colorectal cancer concluded that while many blood-based biomarkers have been evaluated, few have advanced past the discovery stage, with a need for larger, prospective studies in screening populations.⁽⁵³⁾ Developments in non-invasive or minimally invasive screening modalities in the future may improve colorectal cancer screening uptake rates as they may prove

more acceptable to patients, and could reduce patient harms that may be associated with more invasive screening tests.

A growing body of research has also explored the potential role of risk-based screening tools. Risk-based screening involves the combination of several risk factors and or biomarkers into a risk prediction score, model or algorithm,⁽⁵⁴⁾ with the aim of tailoring screening strategies according to an individual's risk of colorectal cancer.⁽⁵⁵⁾ While risk-based strategies have the potential to improve the diagnostic yield of screening, they also increase the complexity of a screening programme and may affect participation rates.⁽⁵⁵⁾ More research is needed on the feasibility, cost-effectiveness and impact on outcomes of risk-based screening tools in the context of established screening programmes.^(54, 55)

While alternative testing modalities may have benefits such as reduced invasiveness, some studies have suggested that they may not be cost-effective and may be less sensitive and specific than other screening options.^(56, 57) For example, FIT has been shown to be more cost-effective than alternative tests such as virtual colonoscopy and multi-target stool DNA testing.⁽⁵⁸⁾ The cost effectiveness of other non-invasive colorectal cancer screening methods may require further evaluation.⁽⁵⁹⁾ As further evidence emerges, alternative tests may play a more prominent role in colorectal cancer screening in future, either in isolation or in tandem with existing tests. Section 2.6 provides an overview of the screening tests used internationally.

2.4 Colorectal cancer screening in Ireland: the BowelScreen programme

Colorectal cancer screening has been in place in Ireland since 2012 in the form of the BowelScreen programme,⁽¹⁸⁾ which is delivered operationally by the HSE National Screening Service (NSS). BowelScreen was introduced following the publication of two HIQA reports in 2009 and 2010, which examined colorectal cancer screening and resource use in cancer screening programmes.^(12, 13) These reports evaluated the feasibility as well as the optimal approach to colorectal (as well as general) cancer screening in Ireland.^(12, 13) The 2009 HTA focused on various colorectal cancer screening scenarios for people aged between 55 and 74 years (as well as for various screening methods, including FIT, gFOBT, and flexible sigmoidoscopy).⁽¹²⁾ This HTA concluded that FIT-based colorectal cancer screening for people aged 55 to 74 years was the optimal screening option.

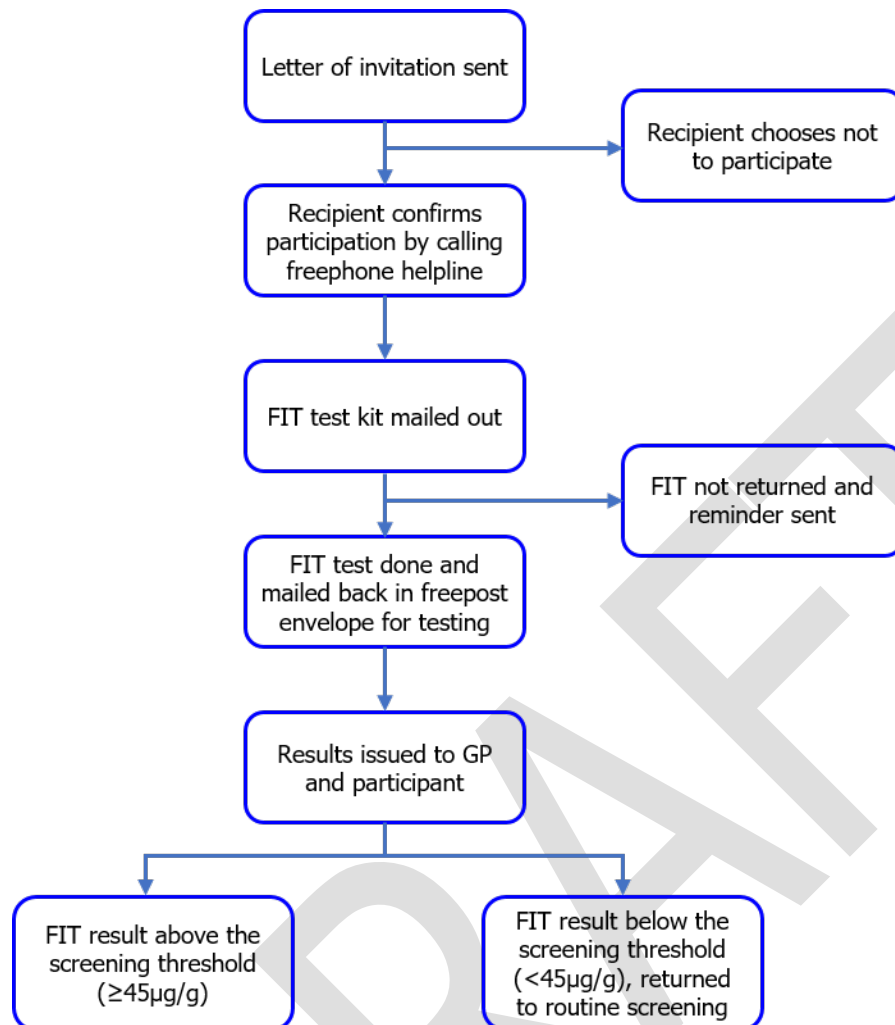
BowelScreen initially commenced screening people aged 60 to 69 years in October 2012 using FIT as the primary screening test, with participants who received a positive FIT result (that is, haemoglobin concentration above the BowelScreen decision threshold) being referred for colonoscopy. In 2014, the FIT threshold was increased from 20µg to 45µg Hb/g faeces to ease pressure on endoscopy capacity

within the programme.^(18, 37, 60) As of April 2025, BowelScreen invites adults aged 59 to 70 years for screening every two years, with an expansion to those aged 55 to 74 years committed to in the 2020 Programme for Government and the National Cancer Strategy 2017–2026.^(1, 2) The expansion of the programme to include those aged 58 to 70 on an incremental basis by 2026 was highlighted as a key area of focus in the 2025 HSE National Service Plan.⁽¹⁵⁾ Since its introduction in 2012, the BowelScreen programme has carried out over one million screening tests for colorectal cancer.

2.4.1 BowelScreen screening pathway

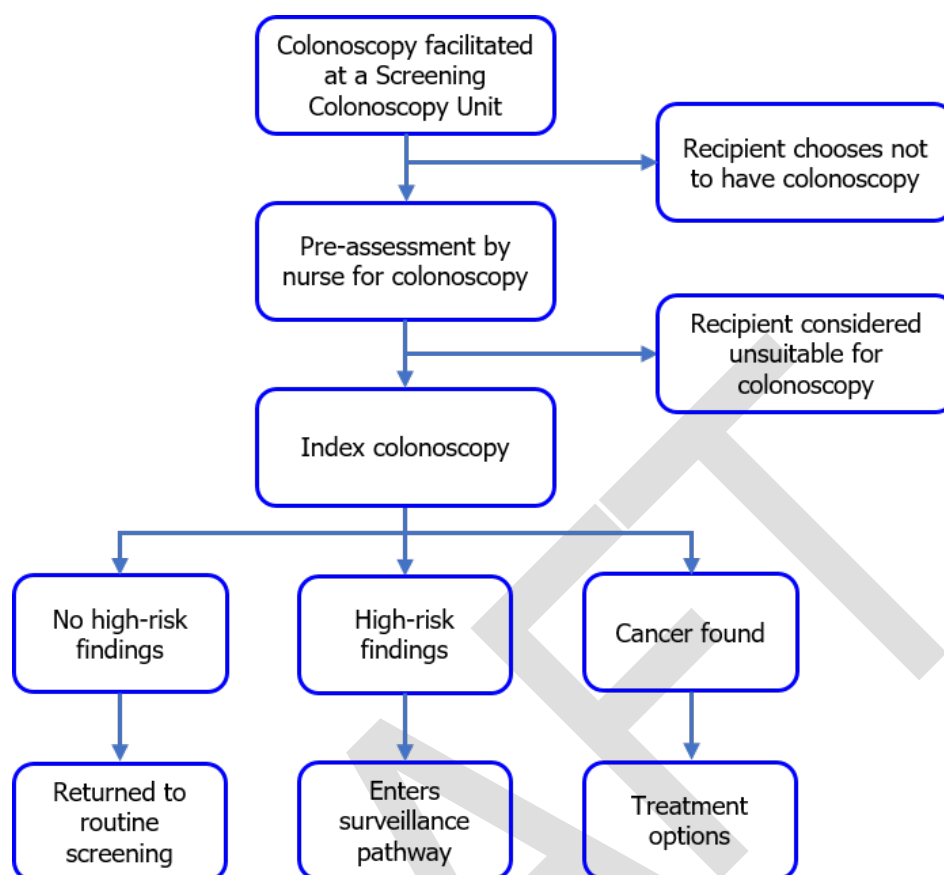
The BowelScreen programme uses a quantitative FIT (OC-Sensor™ as of January 2025) to screen for colorectal cancer. Eligible individuals are identified through the NSS database using information provided by the Department of Social Protection, and invited by mail to participate in the screening programme.⁽⁶¹⁾ Once an individual has agreed to participate, a test kit is sent to their home, which is then returned by post and sent to a contracted laboratory for analysis. Results of the test are issued to both the individual and their general practitioner (GP). If the concentration of haemoglobin detected is less than 45µg Hb/g faeces (the threshold used by BowelScreen), the person is returned to the regular screening pathway. Participants with a FIT result of 45µg Hb/g faeces or higher are invited for a colonoscopy in one of 15 colonoscopy screening units throughout the country.^(61, 62) For those deemed unsuitable for colonoscopy (for example, those in poor health or at higher risk of perforation), those who refuse colonoscopy, as well as in the event of incomplete colonoscopy, CT colonography is carried out in line with European Society of Gastrointestinal and Abdominal Radiology practice guidelines.⁽⁶³⁾ If no abnormalities are detected during colonoscopy, the individual is returned to routine screening. If polyps are identified, these are removed during the colonoscopy and sent for testing. All samples taken during colonoscopy are examined by BowelScreen histopathologists in one of eight designated cancer centers.⁽⁶¹⁾ The individual is then either returned to routine screening or is followed up in a surveillance programme (see section 2.4.2), or, the individual is referred for treatment (see Chapter 3, section 3.6). Figure 2.3 and Figure 2.4 detail the BowelScreen screening pathway. Section 2.4.2 provides further information on participant follow-up post colonoscopy.

Figure 2.3 Flow diagram of the BowelScreen FIT screening pathway



Adapted from BowelScreen.⁽⁶⁴⁾

Figure 2.4 Flow diagram of the BowelScreen colonoscopy pathway



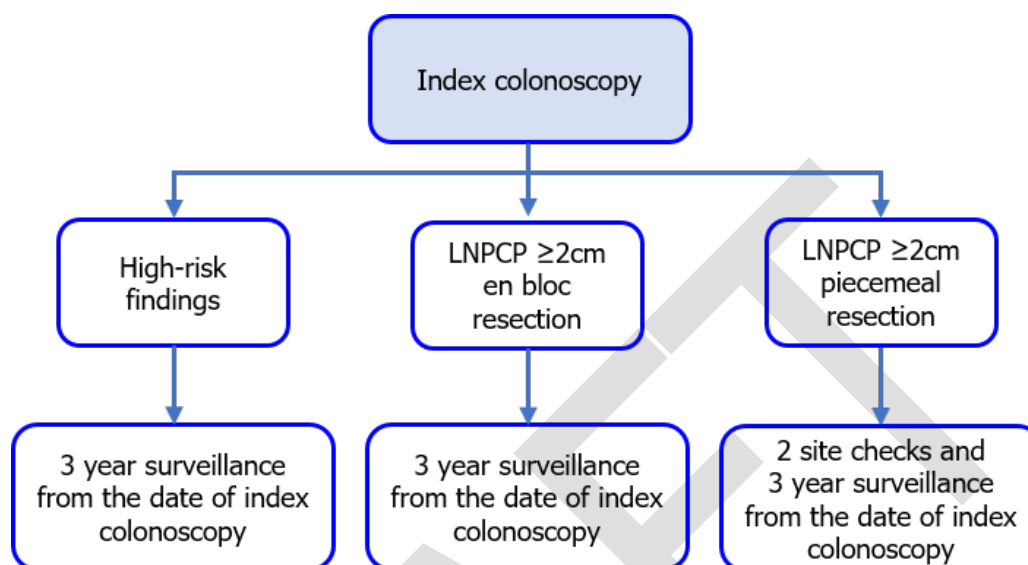
Adapted from BowelScreen.⁽⁶⁴⁾

2.4.2 BowelScreen surveillance

In December 2022, the BowelScreen programme updated its surveillance pathway by implementing the British Society of Gastroenterology, the Association of Coloproctology of Great Britain and Ireland and Public Health England (BSG/ACPGBI/PHE) guidelines for colorectal cancer surveillance.⁽⁶⁵⁾ An overview of these guidelines was subsequently published by BowelScreen.⁽⁶⁶⁾ According to the guidelines, individuals who are found to have high-risk indications (two or more premalignant polyps including one or more advanced colorectal polyp, or five or more premalignant polyps), or for whom large non-pedunculated colorectal polyps (LNPCPs) are identified (and resected), will enter a surveillance pathway. This pathway is designed to monitor those at potentially increased risk of developing colorectal cancer based on the results of the index colonoscopy. Those with high-risk findings and those with LNPCPs ≥ 2 cm who received 'en bloc' resection (polyps removed in one piece), will undergo colonoscopic surveillance three years from the date of the original colonoscopy. For those with LNPCPs ≥ 2 cm who received 'piecemeal' resection (polyps removed in multiple pieces), two site checks will be carried out in addition to colonoscopic surveillance three years from the date of the

original colonoscopy. The BowelScreen surveillance pathway is demonstrated in Figure 2.5.

Figure 2.5 BowelScreen surveillance pathway



Adapted from BowelScreen Surveillance Overview.⁽⁶⁶⁾

Key: LNPCP – large non-pedunculated colorectal polyp.

2.4.3 BowelScreen programme 2012–2023

For reporting purposes, the programme has been broadly separated into five rounds, encompassing the years 2012–2015, 2016–2017, 2018–2019, 2020–2021, and 2022–2023. BowelScreen has seen fluctuations in the number of eligible individuals invited, with the highest, being 606,275 people invited in 2022–2023. Lower numbers of participants were invited and screened during round four of the programme (2020–2021) as a result of the COVID-19 pandemic and the cyber-attack on the HSE.⁽¹⁸⁾

Since 2012, BowelScreen has issued over 2.4 million invitations for colorectal cancer screening. The uptake rate of FIT has ranged from 38.1% among those aged 60–64 to 49.9% among those aged 65–69 (Table 2.2). Across screening rounds, uptake among women and those aged 65–69 years has consistently been higher than in men and those aged 60–64, with the highest uptake among women aged 65–69 and the lowest uptake among men aged 60–64 (Figure 2.6).

The FIT positivity threshold for the first 14 months of the programme was 20µg Hb/g faeces, resulting in a positivity rate of 8.6%. To ease pressure on colonoscopy capacity, the threshold was subsequently raised to 45µg/g, reducing the positivity

rate to 4.1%.⁽⁶¹⁾ FIT positivity rates have ranged from 4.9% in 2012–2015 to 3.1% in 2022–2023. In those aged 65 to 69, positivity rates have ranged from 5.4% (2012–2015) to 3.2% (2022–2023), while rates in the younger age group have ranged from 4.0% (2012–2015) to 3.0% (2022–2023). The number of index colonoscopies (that is, the initial colonoscopy following a positive FIT) carried out has ranged from 7,333 in 2012–2015 to 3,727 in 2020–2021. Considering surveillance, a total of 12,018 surveillance colonoscopies were performed as part of the BowelScreen surveillance pathway between 2013 and 2023.

The colonoscopy rate, based on the number of positive FIT tests, has ranged from 79.2% (2018–2019) to 82.4% (2022–2023) in the younger age group, and from 77.0% (2016–2017) to 82.2% (2020–2021) in the older age group (Table 2.2). Colonoscopy rates have ranged from 79.4% (2018–2019) to 82.2% (2020–2021) in males and from 76.7% (2016–2017) to 80.6% (2020–2021) among females. Colonoscopy rates by screening round, age and sex are displayed in Figure 2.7.

In the younger age group, the cancer detection rate per 1,000 screened decreased from 2.36 in the first round of the programme (2012–2015, n=140) to 1.54 in the most recent round (2022–2023, n=237). In those aged 65 to 69, the detection rate decreased from 2.71 per 1,000 in the first screening round (2012–2015, n=334) to 1.24 in the third round (2018–2019, n=120), with a detection rate of 1.57 in the most recent round (2022–2023, n=196). Detection rates have been consistently higher in males than females (Figure 2.8).

Adenoma detection rates have consistently exceeded 55% in each round of the programme, with similar adenoma detection rates on index colonoscopy in both age groups (Table 2.2). As with cancer detection rates, the adenoma detection rate has been consistently higher in males (Figure 2.9).

Table 2.2 BowelScreen data by screening round and age group

	2012–2015		2016–2017		2018–2019		2020–2021		2022–2023	
	60–64	65–69	60–64	65–69	60–64	65–69	60–64	65–69	59–64	65–69
No. eligible invited	151,660	298,792	303,880	240,269	327,412	205,706	144,287	146,463	355,403	250,872
No. FIT satisfactory	59,395	123,346	115,714	109,645	126,929	96,707	62,340	73,043	153,901	124,810
Uptake	39.2%	41.3%	38.1%	45.6%	38.8%	47.0%	43.2%	49.9%	43.30%	49.80%
No. FIT positive	2,354	6,628	4,009	4,152	3,917	3,453	2,009	2,561	4,619	4,054
FIT positivity rates	4.0%	5.4%	3.5%	3.8%	3.1%	3.6%	3.2%	3.5%	3.0%	3.2%
No. index colonoscopy	1,898*	5,443	3,187	3,198	3,101	2,670	1,622	2,105	3,673	3,010
Colonoscopy rate based on FIT positive	80.6%	82.1%	79.5%	77.0%	79.2%	77.3%	80.7%	82.2%	82.4%	77.5%
No. with adenomas	1,059*	2,993	1,832	1,753	1,713	1,470	951	1,208	2,251	1,818
Adenoma detection rate (on index colonoscopy [‡])	56.0%	55.0%	57.5%	54.8%	55.2%	55.1%	58.6%	57.4%	59.2%	57.9%
No. cancer detected	140	334	198	191	183	120	101	98	237	196
Cancer detection rate (per 1,000 screened with satisfactory FIT)	2.36	2.71	1.71	1.74	1.44	1.24	1.62	1.34	1.54	1.57

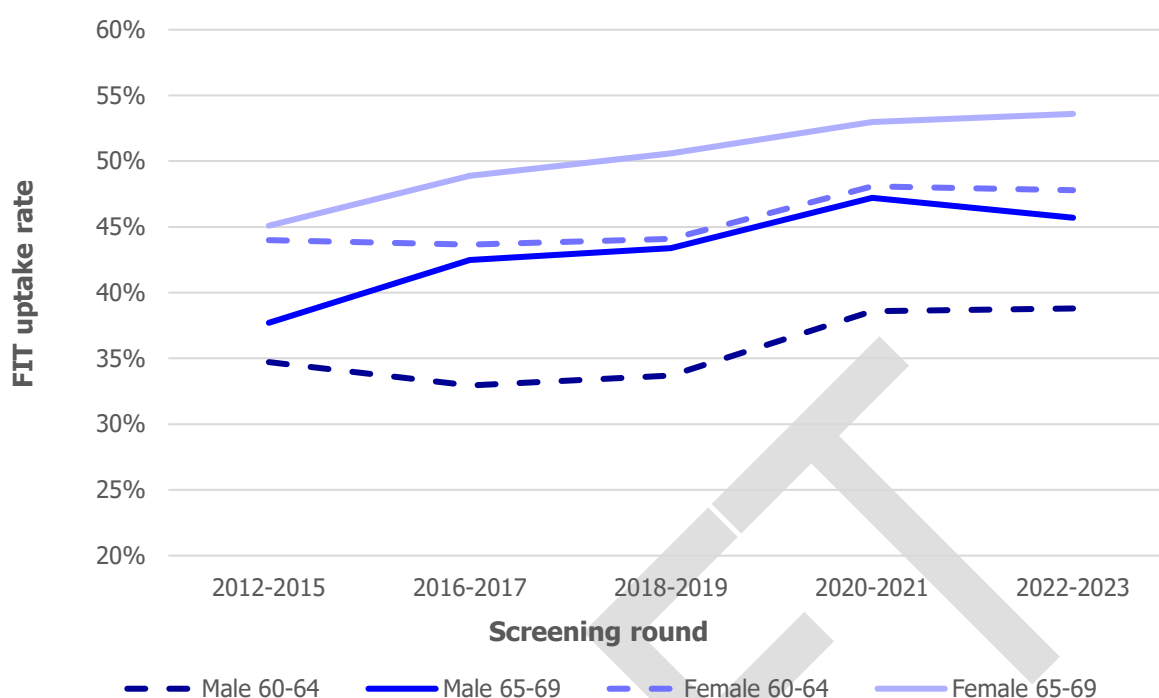
Source: BowelScreen.

* Numbers between one and five were aggregated. The upper range five was used to calculate the number of colonoscopies and adenomas in the 60–64 age group in 2012–2015.

‡ Colonoscopy after a positive result on a FIT test.

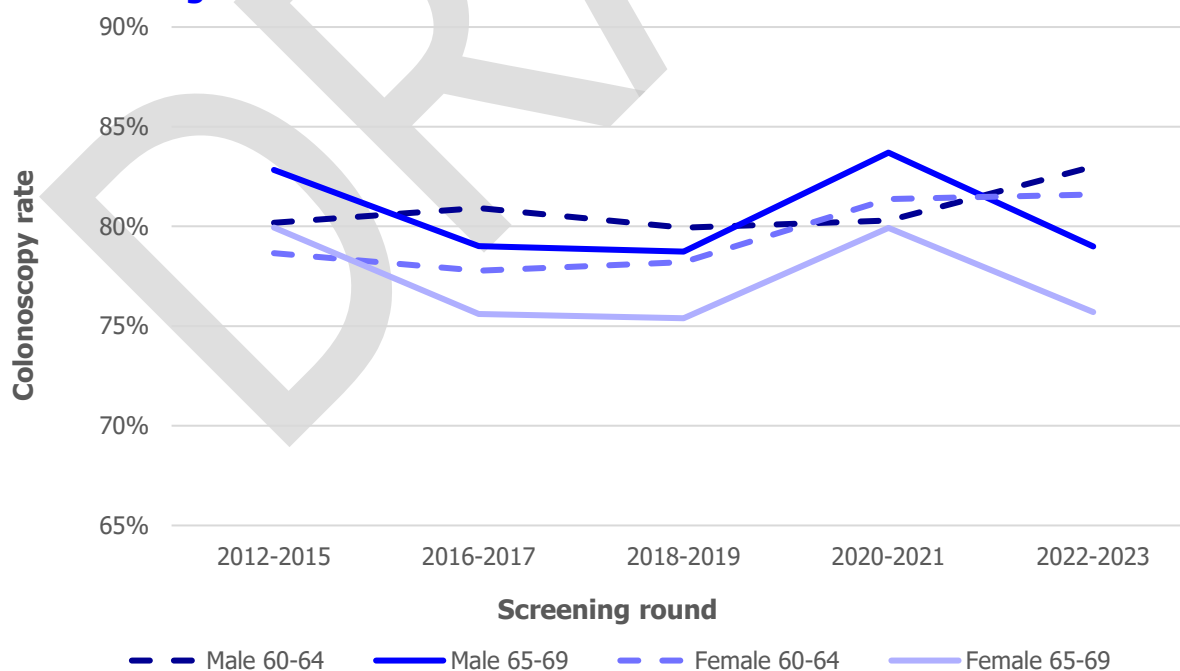
Note: Data may vary slightly from figures presented in published BowelScreen programme reports as data presented here were re-run on a yearly (rather than screening round) basis.

Figure 2.6 FIT uptake rates by screening round, age and sex



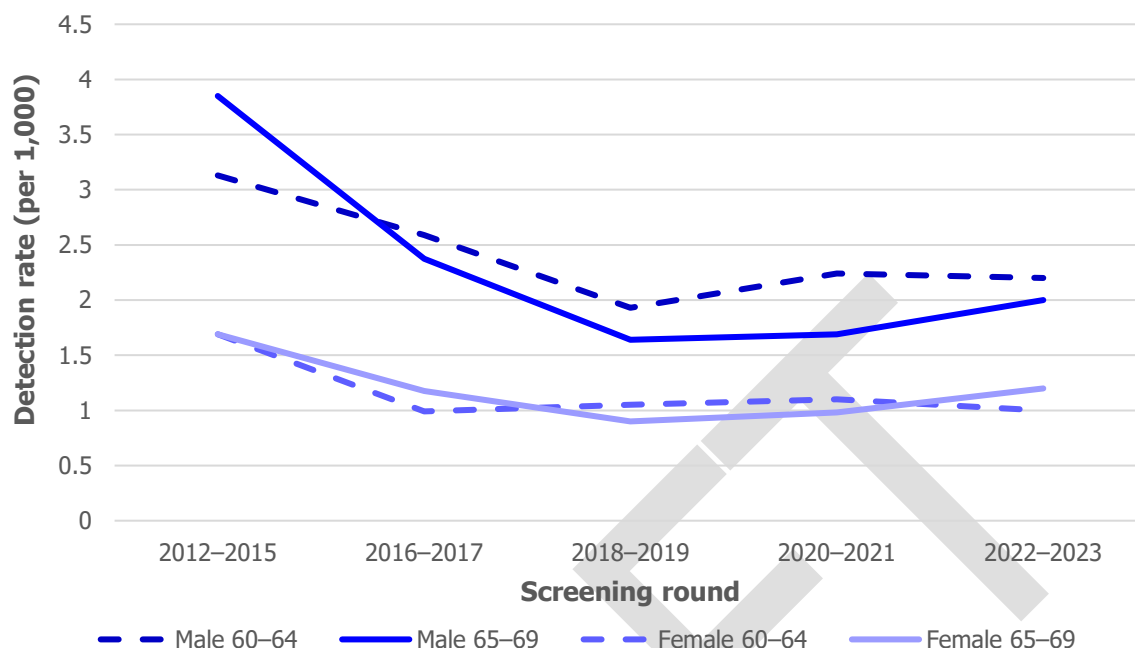
Source: BowelScreen. Note: 2022–2023 data for the younger age group (60–64) include a small number of people aged 59 years.

Figure 2.7 Colonoscopy rates based on positive FITs* by screening round, age and sex



Source: BowelScreen. Note: 2022–2023 data for the younger age group (60–64) include a small number of people aged 59 years.*FIT results above the screening threshold.

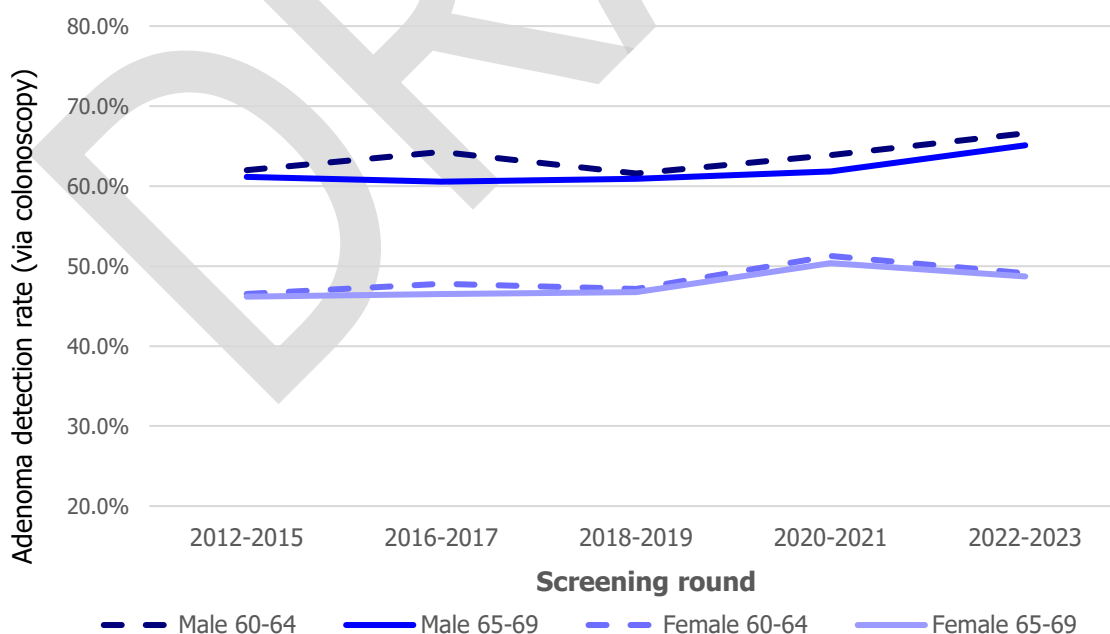
Figure 2.8 Cancer detection rates per 1,000* by screening round, age and sex



Source: BowelScreen.

* Per 1,000 people screened with satisfactory FIT.

Figure 2.9 Adenoma detection rate on index colonoscopy* by screening round, age and sex



Source: BowelScreen. Note: 2022-2023 data for the younger age group (60-64) include a small number of people aged 59 years.

* Colonoscopy after a FIT result above the screening threshold.

2.4.4 Proposed modification to the BowelScreen programme

As of April 2025, BowelScreen invites those aged 59 to 70 years for screening, with a commitment to screening those aged 55 to 74 years in the future. Under the proposal received by HIQA for evaluation, the age at which screening commences would be reduced to 50 years. This would be a substantial increase in the population eligible for screening, and will be described further in the budget impact analysis and organisational considerations chapters of the report (see Chapters 7 and 8).

As of April 2025, individuals who participate in all screening rounds (that is, every two years) will undergo FIT screening six times as part of the BowelScreen programme during their lifetime. With the planned expansion of the programme to those aged 55 to 74 years, participating individuals will receive up to 10 rounds of screening. Under the current proposed age extension, which would lower the starting age to 50, participating individuals would receive up to 13 rounds of screening if they were to participate in each screening round for which they were eligible (Table 2.3). Therefore, the current proposal would constitute an increase of three rounds of screening, when compared to the age range to which expansion has already been committed.

Table 2.3 Outline of the potential screening rounds for BowelScreen based on the proposed age ranges

	Starting age	Finishing age	Interval	Rounds
April 2025	59	70	2 years	6
Commitment	55	74	2 years	10
Proposed extension	50	74	2 years	13

2.5 Colorectal cancer screening guidelines

2.5.1 European Commission recommendations and initiatives on colorectal cancer screening

In 2003, the European Council recommended 'screening with faecal occult blood test in men and women aged 50–74 years'.⁽¹⁶⁾ These recommendations were in turn based on recommendations published in 2000 by the Advisory Committee on Cancer Prevention,⁽⁶⁷⁾ together with experience gathered under the Europe against Cancer programme. The European Council recommendations noted, however, that important factors must be assessed before a population-wide implementation of the

recommendations is decided; these include the frequency and interval to be used in screening and national epidemiological specificities, and ethical, legal, social, medical, organisational and economic aspects.⁽¹⁶⁾ Furthermore, the recommendations stated that the indicated age ranges are to be understood as maximum ranges, subject to national epidemiological evidence and prioritisation, and that smaller age ranges may be appropriate.

More recently, in 2021, the initiative *Europe's Beating Cancer Plan* was announced, which aimed to support member states to ensure that 90% of the EU population who qualify for breast, cervical, and colorectal cancer screenings are offered screening by 2025.⁽⁴⁸⁾ The 2022 updated European Council recommendation stated that FIT is considered the preferred screening test for referring individuals for follow-up colonoscopy between 50 and 74 years old; and also noted the potential for implementation of risk-tailored strategies, such as introducing thresholds defined according to sex, age, or results of earlier screening rounds.⁽⁶⁸⁾ This recommendation was based on the scientific opinion of the Commission's Group of Chief Scientific Advisors, which was in turn informed by the evidence review 'Improving cancer screening in the European Union' by the consortium Science Advice for Policy by European Academies.⁽⁶⁹⁾

2.5.2 Guidelines for colorectal cancer screening

Colorectal cancer screening guidelines serve to provide evidence-based recommendations for the early identification of cancer in asymptomatic patients. These guidelines often outline aspects such as the most effective screening methods and the appropriate age and frequency for screening, with the ultimate goal of reducing the incidence and mortality of colorectal cancer. They may also serve to inform healthcare providers and policy-makers in designing and implementing effective screening programmes.

Guidelines for colorectal cancer screening have been published by multiple international organisations. Only guidelines that focused on average-risk populations were considered as part of this review. In addition to a guideline published by the European Commission Initiative on Colorectal Cancer,⁽⁷⁰⁾ a total of eight guidelines were selected. These were identified from a 2018 systematic review of colorectal cancer screening guidelines, supplemented by a search to identify subsequent publications from each of the organisations included in the review.⁽⁷¹⁾ Of these, seven were at an individual country level,^(20, 72-77) while one guideline made recommendations at a European level.⁽⁷⁸⁾ Six of the guidelines made a recommendation on both a starting and end age for screening, while one recommended screening at age 50 and above. It is important to note that a 2016 US publication, *Updated Evidence Report and Systematic Review for the US Preventive Services Task Force*,⁽⁷⁹⁾ was referred to by four other guidelines (including the

updated 2021 publication from the USPSTF), and was likely used to support the recommendations made in each. A brief summary of each of the guidelines is provided below, with a summary of the recommendations presented in Table 2.4.

Colorectal cancer screening guidelines in Europe

At EU level, in 2023, the European Commission Initiative on Colorectal Cancer, which produces guidance on CRC screening and care, examined whether screening or no screening should be recommended for those aged 50 to 69 at average risk of colorectal cancer.⁽⁷⁰⁾ A strong recommendation, based on moderate quality evidence, was issued in favour of screening in this age group. The guideline working group judged that the balance between desirable and undesirable effects favours screening; that there is no important uncertainty or variability in how much people value the main outcomes; and that the intervention is probably cost-effective and acceptable. These judgments applied to all screening tests considered (FIT, colonoscopy, flexible sigmoidoscopy), and it was noted that the balance between desirable and undesirable effects, cost-effectiveness, and acceptability considerations may vary according to the different strategies adopted. The working group also considered that organised screening would probably increase equity, and is feasible to implement.⁽⁸⁰⁾

The European Society of Medical Oncology (2020) recommends FIT for individuals aged 50 to 74 years, but without specifying thresholds or intervals.⁽⁷⁸⁾ The Scottish Intercollegiate Guidelines Network recommends the use of FIT set to a cut-off that is 'appropriate for investigative capacity', but which is not lower than the analytical sensitivity of FOBT.⁽⁷⁷⁾ The German Guideline Program in Oncology specifies that individuals in Germany aged 50 and above should undergo colonoscopy every ten years, with sigmoidoscopy as an alternative for those who refuse.⁽²⁰⁾ Annual gFOBT is reserved for those not undergoing colonoscopy, with FIT used as an alternative if it has a high specificity (>90%) and sensitivity.⁽²⁰⁾ In Spain, Sociedad Española de Oncología Médica advises a range of screening modalities for individuals aged 50 to 69, including FIT, colonoscopy, flexible sigmoidoscopy, faecal DNA analysis, and CT colonography.⁽²¹⁾ The intervals vary: two years for FIT, ten years for colonoscopy, five years for flexible sigmoidoscopy and CT colonography, and three years for faecal DNA analysis.⁽²¹⁾

US colorectal cancer screening guidelines

In the US, the American College of Gastroenterology (ACG),⁽⁷⁶⁾ American College of Physicians (ACP),⁽⁸¹⁾ and United States Preventive Services Task Force (USPSTF),^(82, 83) offer comprehensive recommendations for a range of screening options.

Screening for average-risk individuals is recommended from age 50 to 75 by the ACG, USPSTF and ACP guidelines. The ACG and USPSTF include additional

conditional or 'grade B' recommendations to screen from age 45 to 49, based on very low-quality evidence or moderate certainty that screening in this age group has a moderate net benefit, respectively. In contrast, the 2023 ACP guidance states that clinicians should consider not screening asymptomatic, average-risk patients between 45 and 49 years old. Reasons for this recommendation from the ACP included: lack of sensitivity and specificity data for CRC in this age group; the potential for the exacerbation of health disparities; concerns over assumptions used in modelling studies; and a reduced net benefit of screening in those aged 45 to 49 when compared to older age groups.⁽⁸¹⁾ The guidelines cover a number of screening modalities including colonoscopy, FIT, flexible sigmoidoscopy, CT colonography, and capsule endoscopy, with intervals ranging from one to ten years depending on the modality. Both the USPSTF and ACP guidelines additionally include the multi-target stool DNA test as a potential screening option. While the ACP guideline recommends colonoscopy and FIT as the primary screening modalities, a 'conditional' recommendation, based on 'very low' quality evidence, suggests that mtsDNA could be considered for individuals who are unable or unwilling to undergo colonoscopy or FIT-based screening.⁽⁷⁶⁾ In contrast, the ACP 2023 guidance statement recommended against the use of stool DNA tests for colorectal cancer screening, citing a lack of evidence of clinical effectiveness compared to other stool-based tests, as well as long-term costs when compared to more effective screening such as colonoscopy.⁽⁸¹⁾

Canadian Guidelines

In 2016, guidelines from the Canadian Task Force on Preventive Health Care made a strong recommendation for the screening of those aged 60 to 74 years using gFOBT or FIT every two years, or flexible sigmoidoscopy every ten years, with a weak recommendation for screening in those aged 50 to 59.⁽⁷⁴⁾ Both recommendations were based on moderate-quality evidence. In the first instance, the task force supported the use of FIT/gFOBT or flexible sigmoidoscopy as reasonable tests for screening those aged 50 to 74, based on the accuracy of the tests. The weak recommendation for screening those aged 50 to 59 was based on lower absolute benefit expected from screening in people in this age group compared to those aged 60 to 74, based on data from two randomised controlled trials (RCTs).^(84, 85) The task force additionally made weak recommendations against the screening of those aged 75 and above and the use of colonoscopy as a primary screening test, based on low-quality evidence.⁽⁷⁴⁾ The clinical effectiveness of colorectal cancer screening is considered in more detail in Chapter 5.

Table 2.4 Overview of international guideline recommendations

Organisation (year) Country/Region	Age range	Recommended screening modalities (intervals)
Scottish Intercollegiate Guidelines Network (2016), ⁽⁷⁷⁾ Scotland	Not specified	FIT (interval unspecified)
German Guideline Program in Oncology (2019), ⁽²⁰⁾ Germany	≥50 (strong expert consensus)	- Colonoscopy (sigmoidoscopy for those refusing colonoscopy) (10 years) - gFOBT (only for those not undergoing colonoscopy) (1 year) - FIT (with a proven high specificity and sensitivity may be used alternatively to the guaiac test) (1 year)
Sociedad Española de Oncología Médica (2019), ⁽²¹⁾ Spain	50 – 69 (grade 1A recommendation)	- FIT (2 years) - Colonoscopy (10 years) - FSIG (5 years) - Faecal DNA (5 years) - CT colonography (5 years)
European Society of Medical Oncology (2020), ⁽⁷⁸⁾ Europe	50 – 74 (grade B recommendation)	- Colonoscopy (10 years) - FSIG (5–10 years) - FIT (not specified)
American College of Gastroenterology (2021), ⁽⁷⁶⁾ United States	50 – 75 (strong recommendation) 45 – 49 (conditional recommendation)	- FIT (1 year) - Colonoscopy (10 years) Conditional (for those refusing or unwilling to undergo FIT or colonoscopy): - FSIG (5–10 years) - CTC (5 years) - mtsDNA (3 year) - Capsule Endoscopy (5 years)
American College of Physicians (2023), ⁽⁸¹⁾ United States	50 – 75*	- FIT or high sensitivity gFOBT (2 years) - FSIG (10 years) plus FIT (2 years) - Colonoscopy (10 years)
United States Preventive Services Task Force (2021), ^(82, 83) United States	50 – 75 (grade A recommendation) 45 – 49 (grade B recommendation)	- gFOBT (1 year) - FIT (1 year) - mtsDNA (1 year) - FSIG + FIT (10 years + 1 year) - FSIG (5 year) - Colonoscopy (10 years) - CTC (5 years)
Canadian Task Force on Preventive Health Care (2016), ⁽⁷⁴⁾ Canada	50 – 59 (weak recommendation) 60 – 74 (strong recommendation)	- gFOBT or FIT (2 years) - FSIG (10 years)

Key: CTC – computed tomography colonography, FIT – faecal immunochemical test, FOBT – faecal occult blood test, FSIG – flexible sigmoidoscopy, gFOBT – guaiac faecal occult blood test, mtsDNA – multi target stool DNA test.

* Recommendations by the American College of Physicians were not subject to formal grading.

2.6 Colorectal cancer screening: international practice

This section reviews colorectal cancer screening internationally. Countries selected for review were those that were considered particularly relevant in terms of transferability or applicability to the Irish context, and are listed in the [protocol](#) accompanying this review.

2.6.1 Colorectal cancer screening programmes

Colorectal cancer screening programmes vary across European countries. As of 2020, national or regional population-based screening programmes had been implemented, or were in the process of being implemented, by 20 member states (including the UK).⁽⁶⁹⁾ The majority of EU and EEA countries considered within the present review (Belgium, Denmark, Finland, France, Germany, Italy, Ireland, the Netherlands, Norway, Slovenia, Spain, Sweden, and Switzerland) have structured, predominantly FIT-based national or regional screening programmes in place (Table 2.5). Screening in Portugal is recommended by the Portuguese National Health Service;⁽⁸⁶⁾ however, it is carried out at a regional rather than national level through a combination of regional pilot programmes and initiatives, as well as opportunistically via general practitioners.⁽⁸⁷⁾ Colorectal cancer screening in Austria is opportunistic, based on the information obtained in this review. Screening in Germany commenced in 2002 (albeit on an opportunistic basis until 2019), while Finland began screening in 2019.

Screening uptake

Colorectal cancer screening uptake has varied across countries. Screening uptake in the Netherlands has consistently been around 70%, with a rate of 68.4% in 2022.⁽⁸⁸⁾ In Sweden, 70.9% of those invited returned a valid FIT test between 2017 and 2019.⁽⁸⁹⁾ In the UK, uptake rates were 70.2% in England (2022–2023),⁽⁹⁰⁾ 66.1% in Scotland (2021–2023),⁽⁹¹⁾ and 61.5% in Wales (2019–2020).⁽⁹²⁾ Lower uptake rates have been reported in France (28.9% in 2019–2020),⁽⁹³⁾ and Spain (45.9% in 2016–2017).⁽⁹⁴⁾ In Ireland, screening uptake rates have ranged from 38.1% in those aged 60 to 64 years to 49.9% in those aged 65 to 69.

In Canada, between January 2017 and June 2019, programme participation rates ranged from 18.3% (New Brunswick) to 54.8% (Saskatchewan).⁽⁹⁵⁾ In the US, 72.2% of individuals aged 50 to 74 were considered 'up-to-date' on colorectal cancer screening in 2021.⁽⁹⁶⁾

Screening interval

For most of the EU and EEA countries with a national programme in place, the screening interval is every two years. Germany is an exception, where screening

intervals in the German programme vary based on both age and sex. Outside the EU and EEA, the screening interval ranges from one to two years in Canada and is two years in other non-EU countries. Table 2.5 provides an overview of colorectal cancer screening in the countries included in this review.

Screening age

An important consideration for colorectal cancer screening is the age range during which screening is performed. There is evidence to suggest that colorectal cancer incidence increases with age (see Chapter 3, section 3.9.1); however, the age at which screening is undertaken varies between countries, and is often set at a regional or country level, rather than according to international consensus. As of April 2025, those aged 59 to 70 are eligible to participate in the BowelScreen programme.⁽⁹⁷⁾ Countries such as the US provide screening to younger individuals, and have published recommendations that include screening from age 45.⁽²²⁾ In Australia, the screening age was lowered from 50 to 45 in July 2024.⁽⁹⁸⁾ In England, the colorectal cancer screening programme has recently expanded to screen those aged 50–74 as part of a gradual four-year initiative that started in April 2021.⁽⁹⁹⁾ EU and EEA countries were found to generally screen between the ages of 50 and 74. Screening in Italy was found to take place from age 50 to 69, with some regions screening to age 74.⁽¹⁰⁰⁾ The Finnish colorectal cancer screening programme, as of January 2025, screens those aged 60 to 70;⁽¹⁰¹⁾ however, the programme plans to expand screening to those aged 56 to 74 by the year 2031.⁽¹⁰²⁾

FIT thresholds

FIT thresholds differ across screening programmes in EU and EEA countries, ranging from 15 to 80µg Hb/g. Only the Swedish colorectal cancer screening programme was found to employ differing FIT thresholds for men (80µg) and women (40µg).^(103, 104) Notably, Germany presents a unique case where men aged 50 to 54 can choose between FIT or colonoscopy, whereas women at this age are only offered FIT, with the interval being two years for FIT and ten years for colonoscopy.⁽¹⁰⁵⁾ For those aged 55 and above (both male and female), the interval for colonoscopy remains every ten years, but the frequency for FIT changes to yearly for both men and women.⁽¹⁰⁵⁾

Outside the EU and EEA, Australia, Canada, New Zealand, England, Northern Ireland, Scotland, and Wales also predominantly use FIT, with age ranges generally between 50 to 74 years. Canada has multiple local programmes with varying thresholds of between 10–50µg Hb/g,⁽¹⁰⁶⁾ while thresholds in the UK range from 80µg Hb/g in Scotland to 120µg Hb/g in England, Wales and Northern Ireland (Table 2.5).⁽¹⁰⁷⁾

Colonoscopy capacity

Challenges with colonoscopy capacity have been experienced by multiple screening programmes. For example, in Slovenia, initial difficulties with the provision of sufficient colonoscopy capacity were reported following an increase of the upper age limit from 69 to 74 in 2015.⁽¹⁰⁸⁾ Some countries have acted to mitigate these challenges; for example, in the Netherlands, similar to Ireland, the FIT threshold was increased from 15 to 47µg Hb/g in an effort to relieve pressure on colonoscopy capacity within the Dutch colorectal cancer screening programme.⁽¹⁰⁹⁾ This change resulted in a reduction in the screen positivity rate of the programme from 10.6% to 6.7%, and by extension, a reduction in the number of colonoscopies required.^(109, 110) Colonoscopy capacity and other organisational implications of extending BowelScreen will be discussed in more detail in Chapter 8 of this HTA.

2.6.2 Summary

This review of international colorectal cancer screening programmes indicates the widespread use of FIT with a two-yearly screening interval, although there is variability in the age range and thresholds for a positive result. These variations reflect differing national policies, healthcare practices and resources. While different thresholds, intervals, and ages may be applied in different colorectal cancer screening programmes, there is no clear consensus available on the best practice for these parameters, and it is likely that factors such as population demographics, colorectal cancer incidence and colonoscopy capacity play a key role in determining the best approach at an individual programme level.⁽²⁵⁾ This is reflected in the 2022 European Council recommendations, which invite member states to consider the disease burden and healthcare resources available at a regional and national level when implementing screening programmes.⁽⁶⁸⁾

Table 2.5 Overview of colorectal cancer screening international practice

Country	Year programme started	Eligible age	Current screening method±	Threshold (for positive result)	Interval
EU and EEA Countries					
*Belgium ^(111, 112)	2009	50 to 74	FIT	15µg Hb/g	2 years
Denmark ^(113, 114)	2014	50 to 74	FIT	100µg/L faeces	2 years
Finland ^(101, 102)	2019	60 to 70	FIT	25µg Hb/g	2 years
France ^(115, 116)	2008	50 to 74	FIT	30µg Hb/g	2 years
Germany ⁽¹⁰⁵⁾	2002 (opportunistic) 2019 (organised)	50 to 54 (female)	FIT	<i>Not found during search</i>	1 year
		50 to 54 (male)	Colonoscopy (alternatively FIT)	<i>Not found during search</i>	10 years (colonoscopy) 1 year (FIT)
		≥55 (male and female)	Colonoscopy (alternatively FIT)	<i>Not found during search</i>	10 years (colonoscopy) 2 years (FIT)
*Italy ⁽¹⁰⁰⁾	Varied by region [†]	50 to 69 (74 in some regions)	FOBT (unspecified)	<i>Not found during search</i>	2 years
Ireland ⁽¹¹⁷⁾	2012	59 to 70	FIT	45µg Hb/g	2 years
The Netherlands ⁽¹¹⁸⁾	2013	55 to 75	FIT	47µg Hb/g	2 years
Norway ^(119, 120)	2022	55 to 65	FIT	15µg Hb/g (in trial)	2 years
Slovenia ⁽¹⁰⁸⁾	2009	50 to 74	FIT	100ng Hb/mL buffer	2 years
Spain ⁽¹²¹⁾	2009	50 to 69	FIT	<i>Not found during search</i>	2 years
Sweden ^(103, 104)	2008	60 to 74	FIT	40µg Hb/g (women) 80µg Hb/g (men)	2 years
*Switzerland ^(122, 123)	Varied by region since 2013	50 to 69	FIT Colonoscopy	<i>Not found during search</i>	2 years (FIT) 10 years (colonoscopy)
Non-EU Countries					
Australia ⁽¹²⁴⁾	2006	45 to 74 (from July 2024)	FIT	<i>Not found during search</i>	2 years
*Canada ⁽¹⁰⁶⁾	Varied by region since 2007	50 to 74 or 75	FIT	Varied by region	1–2 years

Country	Year programme started	Eligible age	Current screening method±	Threshold (for positive result)	Interval
10–50µg Hb/g					
New Zealand ^(125, 126)	2017	60 to 74	FIT	200ng Hb/ml buffer	2 years
England ⁽¹⁰⁷⁾	2006	50 to 74	FIT	120µg Hb/g	2 years
Northern Ireland ⁽¹⁰⁷⁾	2010	60 to 74	FIT	120µg Hb/g	2 years
Scotland ⁽¹⁰⁷⁾	2007	50 to 74	FIT	80µg Hb/g	2 years
Wales ^(107, 127)	2008	50 to 74	FIT	120µg Hb/g	2 years

Key: FIT – faecal immunochemical test, FOBT – Faecal occult blood test, µg Hb/g – microgram haemoglobin per gram of faeces.

*Countries screening at a regional level and may have some degree of additional regional variation. Screening in both Austria and Portugal was found to be regional or opportunistic only.

±Positive FIT tests are followed up with colonoscopy in all countries. The threshold used to determine a positive screen result is presented using the unit of measurement reported by the individual programmes.

¥In Italy, a national formal screening programme was introduced in the 2003–2005 and 2005–2007 national health programmes.

2.7 Discussion

Colorectal cancer screening aims to interrupt the natural history of CRC through the removal of pre-cancerous adenomas, and prevent colorectal cancer deaths through earlier detection and the potential for earlier access to treatment. A variety of screening tests are available to screen for CRC, including stool-based faecal occult blood tests and visualisation tests such as colonoscopy. Stool-based tests aim to identify blood or DNA in the stool, which can act as an indicator of colorectal cancer and pre-cancerous lesions. Visualisation tests enable the visualisation of the internal structures of the colon and rectum, and in the context of screening, are usually carried out following positive indication on a stool-based test. Colonoscopy is considered the reference standard for colorectal cancer visualisation and detection, providing visualisation of the entire colon. Additionally, polypectomy can be performed during colonoscopy to remove adenomas, and samples can be taken for biopsy.

The BowelScreen programme in Ireland commenced in 2012, and as of April 2025 invites people aged 59 to 70 years for screening, with a commitment to screening those aged 55 to 74 in the future. The current proposal would extend the age further to include those aged 50 to 74, increasing the number of people being screened, as well as the number of screening rounds for each eligible participant in the programme. As a result, the number of FIT tests issued and processed, and the number of colonoscopies required, would also increase. Endoscopy capacity and other organisational and budget implications associated with the proposed extension of BowelScreen will be further discussed in Chapters 7 and 8.

Of the countries included in the review of international practice, the included screening programmes generally employed a screening age range of 50 to 75 years, with some variation between countries. The Finnish programme, which started in 2019, is the most comparable to the Irish BowelScreen programme in terms of age range, screening those aged 60 to 70 using a FIT threshold of 25µg Hb/g, with a planned expansion to include those aged 56 to 74 by the year 2031.^(101, 102) Outside of the countries included in this review, other organised colorectal cancer screening programmes generally use FIT as the primary screening test, with a similar range of starting and stopping ages.⁽¹²⁸⁻¹³⁰⁾ In Japan and South Korea, FIT-based screening is offered on an annual basis with no upper age limit, with Japan screening from age 40 and South Korea from age 50.⁽¹³⁰⁾

While the countries reviewed generally use FIT as the primary screening test, the threshold used to determine a positive result varies between countries, and is likely determined by a number of factors, including epidemiological considerations such as local cancer incidence and prevalence, as well as organisational factors such as budget and endoscopy capacity. In terms of similarity with the Irish programme, the

Dutch colorectal cancer screening programme has the most comparable FIT threshold of the countries reviewed, with a positivity threshold of 47µg Hb/g.

FIT threshold affects positivity rates, which increase at lower FIT thresholds. FIT positivity rates also vary depending on the underlying burden of disease, age and sex of screening participants, with positivity rates increasing in older age groups and being higher in men than women. FIT positivity rates in Ireland have ranged from 3% to 4% in those aged 60–64 years, and from 3% to 5% in those aged 65–69. In Denmark, FIT positivity rates have ranged from 4% in those aged 50–54 to 10% in those aged 70 and above, and from 6% for females to 8% for males, at a threshold of 20µg Hb/g.⁽¹³¹⁾

The FIT threshold denoting a positive result was originally set at 20µg Hb/g in Ireland; however, in 2014, in response to endoscopy capacity challenges, the programme increased this threshold to 45µg Hb/g. The increased threshold resulted in lower positivity rates (from 8.6% to 4.1%) and fewer overall colonoscopy referrals.⁽⁶¹⁾ Colonoscopy capacity has been identified as a challenge by other colorectal cancer screening programmes. In the Netherlands, the threshold for positivity was raised from 15µg Hb/g to 47µg Hb/g to relieve colonoscopy capacity, resulting in a reduction in the positivity rate from 10.6% to 6.7%.^(109, 132) In Slovenia, initial challenges with delivering sufficient capacity were noted following an extension of the eligibility for screening from an upper age limit of 69 to 74.⁽¹⁰⁸⁾ However, a lower proportion of positive tests resulting from the inclusion of people who had already been screened, combined with additional staff, resulted in fewer organisational challenges and shorter waiting times for participants in the subsequent screening round.⁽¹⁰⁸⁾

While increasing the FIT threshold reduces positivity rates (including false positives), cancer and adenoma detection rates are also reduced. In Ireland, the CRC detection rate per 1,000 people screened decreased from 3.8 per 1,000 at a FIT threshold of 20µg Hb/g to 2.3 per 1,000 at a threshold of 45µg Hb/g.⁽⁶¹⁾ During implementation, BowelScreen initially focused on screening participants in the upper age range (65 to 69), which may have impacted CRC detection rates in the early years of the programme due to higher incidence rates in this age group. In the Netherlands, age-adjusted detection rates (based on the number of positive FIT tests) decreased from 5.8% for CRC and 30.8% for advanced adenomas at a threshold of 15µg Hb/g, to 4.4% and 20.6%, respectively, at a threshold of 47µg Hb/g.⁽¹³²⁾ Analyses of subsequent screening rounds of the Dutch colorectal cancer screening programme indicated that some of the advanced neoplasia missed due to the increase in FIT threshold during the first screening round were detected in the subsequent screening round,⁽¹⁰⁹⁾ somewhat reducing the impact of the lower detection rates.

Since its introduction in 2012, the uptake rate of BowelScreen has been below 50% (ranging from 38.1% in those aged 60–64 to 49.9% in those aged 65–69). A report reflecting on the achievements and challenges of the programme highlighted the low uptake of 40.2% in the first round.⁽⁶¹⁾ Participation increased over the subsequent rounds of the programme, reaching 46.6% in 2020–2021. A 2010 European Commission guideline document stated that the desirable uptake for CRC screening is 65%, with an acceptable rate of 45%.⁽¹³³⁾ As of January 2025, the BowelScreen target uptake rate is $\geq 50\%$, with an achievable standard of $\geq 60\%$.⁽¹⁸⁾ A systematic review of FIT-based colorectal cancer screening programmes reported a pooled participation rate of 52.7% in European studies, with higher programme-wide participation rates for programmes that started screening from around the age of 55 years, compared to programmes that commenced screening around the age of 50 (63.5% vs 50.3%).⁽¹³⁴⁾ A 2017 report on the implementation of cancer screening in the European Union similarly suggested that participation rates tended to be lower in those aged 50–59 compared to those aged 60–69.⁽¹³⁵⁾ In Denmark, uptake rates between January 2018 and January 2020 ranged from 54.3% in those aged 50–54 to 67.2% in those aged 65–69.⁽¹¹³⁾ When considering uptake by sex, women consistently participate in colorectal cancer screening at a higher rate than their male counterparts. The reasons for this increased participation rate are nuanced and multifaceted, and include factors such as health-seeking behaviours, perceptions of risk, and previous interactions with cancer screening programmes, among others.⁽¹³⁶⁻¹³⁹⁾ These factors will be discussed further in the ethics chapter of this report (Chapter 9).

While guidelines for colorectal cancer screening have been published by multiple organisations at both national and European level, recommendations provided in these guidelines are not always consistent with international practice. Deviation from these guidelines at a programme level is evident in areas such as the age range of those eligible for screening (with starting ages ranging from 50 to 60, and stopping ages from 68 to 74), the method of screening (FIT versus colonoscopy), and the interval at which screening is carried out (1–2 years for FIT, 10 years for colonoscopy). In 2023, the European Commission Initiative on Colorectal Cancer working group made a strong recommendation in favour of screening those aged 50 to 69 years who are at average risk of colorectal cancer, based on moderate certainty of evidence; this recommendation was for screening in general.⁽⁷⁰⁾ The European Council separately states that FIT is the preferred screening test for referring individuals for follow-up colonoscopy between 50 to 74 years old; however, the Council also acknowledges that decisions made at national and regional level are likely to depend on the disease burden and healthcare resources available, as well as the benefit-harm balance and cost effectiveness of screening.⁽⁶⁸⁾ The following chapter (Chapter 3) presents the epidemiology of colorectal cancer in Ireland, with a focus on the age group of interest to this HTA in comparison to the presently

screened population. The clinical and cost effectiveness of extending colorectal cancer screening in Ireland to include people aged 50 to 54, as well as the organisational and resource implications of extending BowelScreen, are considered in subsequent chapters.

Considering future developments, in the US, a multi-target stool DNA (mtsDNA) test for colorectal cancer screening was approved by the Food and Drug Administration (FDA) in 2014, with a multi-target stool RNA test receiving approval in May 2024. While the USPSTF includes mtsDNA in its list of recommended screening options,⁽⁸²⁾ the 2021 American College of Gastroenterology clinical guideline includes a 'conditional' recommendation, based on 'very low' quality evidence, suggesting that mtsDNA could be considered for individuals who are unable or unwilling to undergo colonoscopy or FIT-based screening.⁽⁷⁶⁾ Stool DNA testing was not recommended by the American College of Physicians (ACP) in its 2023 guidance statement, with the ACP citing a lack of comparative evidence as well as costs when compared with colonoscopy as justification for its decision.⁽⁸¹⁾ Specificity for colorectal cancer and advanced neoplasia is lower in stool DNA tests than in FIT,^(44, 140) leading to an increased false positive rate. In July 2024, a cell-free DNA blood-based test, with a sensitivity of 83% for colorectal cancer, received approval by the FDA.^(141, 142) Further developments in colorectal cancer screening methodologies, such as improvements in the accuracy of stool DNA tests and other novel approaches, may present alternative screening options in future.

2.7.1 Conclusion

Similar to the BowelScreen programme in Ireland, the majority of countries reviewed rely on FIT as the primary colorectal cancer screening test, with FIT-positive individuals referred for colonoscopy. The age at which screening starts varies across countries, generally falling within the range of 50 to 60 years, and is recommended by the European Council subject to national considerations regarding epidemiology and resource implications. While screening uptake and positivity rates tend to be lower in the younger age groups, extending the programme to those aged 50–54 will substantially increase the number of people eligible for screening, which will in turn increase the absolute number of positive FIT tests and colonoscopy referrals.

3 Epidemiology

3.1 Key points

- Colorectal cancer (CRC), otherwise known as bowel cancer, occurs in the lower part of the bowel; that is, the colon and the rectum. CRC typically develops from benign polyps or adenomas, which may become cancerous over time.
- Modifiable risk factors, such as smoking, processed meat consumption, alcohol intake, obesity and physical inactivity can increase the risk of CRC.
- Symptoms may include rectal bleeding, abdominal pain, abdominal mass, unexplained weight loss, and a change in bowel habits, such as increased bowel movement frequency, persistent diarrhoea and constipation. However, symptoms are often subtle, absent, or lack specificity at the earlier stages of cancer development.
- Diagnosis of CRC is carried out through a biopsy, typically taken during a colonoscopy, and is supplemented by imaging studies to allow for cancer staging. Cancer stage, which assesses the size and spread of cancer, is a key determinant of treatment plans and patient survival. Treatment plans may include a combination of surgery, chemotherapy, and or radiotherapy.
- CRC is the third most commonly diagnosed cancer and the second leading cause of cancer death globally, with high-income countries, including Ireland, at elevated risk.
 - The population burden of CRC, both in terms of incidence and mortality rate, is generally higher in older people, as well as in men compared to women.
 - Survival following diagnosis has generally improved over the years worldwide, including in Ireland, as a result of advances in diagnosis and treatment.
 - In Ireland, there are on average 2,750 new CRC cases and 1,000 CRC-related deaths annually.
- In those aged 50–54, for whom an extension to the BowelScreen programme is under consideration, the CRC incidence rate has remained relatively stable, with an average annual incidence rate of 47.3 per 100,000 (between 2013

and 2021). This is comparable to the European-average incidence rate of 48.4 per 100,000.

- The incidence rate of CRC is rising in people aged 50 or younger around the world, including in Ireland, despite decreasing incidence rates in older populations. This increasing burden in the younger cohort raises the possibility of an increase in CRC incidence in older cohorts, most imminently for those aged 50–54, as the cohort matures.
- Due to the increasing and ageing population in Ireland, the number of CRC cases overall is projected to roughly double by 2045 (compared to 2015). Nonetheless, National Cancer Registry Ireland projections suggest that the incidence rate is expected to remain constant over the same timeframe.
- Colorectal cancer mortality in age groups older than 60 in Ireland has declined over time, while it has remained stable in younger age groups.
- Cancer screening programmes allow removal of pre-cancerous lesions and earlier CRC detection at less advanced cancer stages, leading to better survival prognosis. BowelScreen was introduced in Ireland in 2012 for people aged between 60 and 69.
- Currently, screen-detected CRC accounts for almost one quarter of all CRC reported in Ireland in the population eligible for screening. Most screen-detected cancers were found at early stages (stages I or II, 62%).
- The percentage of symptomatically-detected CRC cases occurring between 2012 and 2020 that were diagnosed at advanced stages (Stages III and IV), by age group, was:
 - 50–54 year-olds: 67%
 - 55–59 year-olds: 65%
 - 60–64 year-olds: 63%
 - 65–69 year-olds: 62%.
- Colorectal cancer typically develops slowly and may present with subtle symptoms, underscoring the need for early detection and intervention. The BowelScreen programme has been effective in identifying cancers at an early stage. However, CRC incidence is rising overall in Ireland, particularly in individuals under 50. As the age cohorts mature, a similar increase is anticipated in older groups, especially those aged 50–54.

3.2 Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in the world, with over 1.8 million new cases in 2020 accounting for 10% of all cancers diagnosed.⁽⁵⁾ It is also the second leading cause of cancer death internationally, with CRC estimated to claim over 900,000 lives annually, accounting for 9.4% of all cancer deaths.⁽¹⁴³⁾ The number of new cases worldwide is projected to increase to 3.2 million by 2040, with deaths projected to increase to 1.6 million.⁽¹⁴⁴⁾ People living in high-income settings, including Ireland, are at particular risk of developing CRC.⁽⁵⁾ While the ageing population is a major contributor to the increased overall burden of disease, the increasing burden of CRC has also been attributed to changing risk factors, for example, lifestyle factors such as diet and sedentary behaviour, which could impact the entire population.⁽¹⁴⁵⁾

In the following sections, this chapter describes the natural history (3.3), symptoms (3.4), diagnosis (3.5), treatment (3.6), quality of life of CRC survivors (3.7), risk factors (3.8), and epidemiology of CRC in Ireland including future projections (3.9), and the international context (3.10). This chapter draws on both the international literature and national data provided by the National Cancer Registry Ireland (NCRI) and the BowelScreen programme. The focus of this chapter is the epidemiological context for the age group (50–54) of the proposed BowelScreen expansion. Evaluation of the performance of BowelScreen is outside the scope of this HTA; performance figures for BowelScreen are published in the BowelScreen Programme Reports.^(18, 146-149)

3.3 Natural history of colorectal cancer

The colon, or large intestine, is an organ that plays a vital part in the human digestive system.⁽¹⁵⁰⁾ It is responsible for the absorption of water and electrolytes, compaction of faeces, and the movement of waste material towards the rectum (that is, the last 12 to 15 centimetres of the colon) for elimination.⁽¹⁵⁰⁾

Cancer that occurs in the lower part of the bowel, that is, the colon and the rectum, is referred to as colorectal cancer (CRC), or bowel cancer.⁽¹⁵¹⁾ It is worth noting that the definition of CRC has evolved over the years. Historically, anal cancer was classified together with rectal cancer in the International Classification of Diseases-9th Revision (ICD-9: code 154), which came into effect in 1979.⁽¹⁵²⁾ Since the introduction of the 10th revision (ICD-10) in 1993, anal cancer has been independently classified as code C21, separate from rectal cancer (codes C19–C20). Due to this historical convention, however, cancers of the colon (coded as C18 in ICD-10), rectum (C19–20) and anus (C21), are still sometimes collectively grouped as CRC in the literature and by cancer registries around the world.⁽¹⁵³⁾ Throughout

this chapter, CRC refers to C18–20 (that is, excluding anal cancer) unless otherwise stated.

Cancers of the colon and rectum are further categorised based on the specific type of cell from which the cancer starts its growth pattern.^(154, 155) Adenocarcinoma, which is found in the glands that line the organs, is the most common type, accounting for about 95% of all CRCs.⁽¹⁵⁶⁾ The remaining fraction comprises squamous cell tumours, carcinoid tumours, sarcomas, lymphomas, and melanomas.⁽¹⁵⁷⁾ Adenocarcinoma in the lining of the colon or rectum develops from benign polyps or growths of tissue on the mucous membrane.⁽¹⁵¹⁾ These polyps, or adenomas, may become cancerous over time.⁽¹⁵¹⁾ The process is usually slow and may take several years: mathematical models predict the progression from low-risk adenoma to CRC to take between 8 to 29 years.⁽¹⁵⁸⁾ Distinct pathways of polyp development are recognised. In the conventional pathway, adenomas can be tubular, tubulovillous, or villous in shape. In contrast, the serrated neoplasia pathway begins with the formation of serrated adenomas, which have a flatter, saw-toothed profile.⁽¹⁵⁹⁾ This lower morphology makes serrated adenomas more challenging to detect. However, recent advancements in colonoscopy technology have improved detection rates.⁽¹⁶⁰⁾ Serrated adenomas were once believed to have no malignant potential; however, it is now estimated that the serrated pathway accounts for as much as 15–40% of CRCs, while the conventional pathway is considered responsible for 60–85%.^(159–161) Adenomas are categorised as either low, intermediate, or high risk according to their likelihood of developing into cancer.^(151, 158, 162)

3.4 Symptoms of colorectal cancer

Symptoms of CRC may include rectal bleeding, abdominal pain, abdominal mass, unexplained weight loss and a change in bowel habits, such as increased bowel movement frequency, persistent diarrhoea and constipation.⁽¹⁶³⁾ In the early stages, these symptoms may be subtle, absent or lack specificity, meaning that alternative underlying causes may produce similar symptoms.⁽¹⁶⁴⁾ However, persistent and characteristic symptoms necessitate further investigation to rule out the possibility of CRC.⁽¹⁵¹⁾ While the majority of pre-cancerous adenomas do not result in severe symptoms,⁽¹⁵¹⁾ they may result in blood in the stool, which is sometimes hidden (occult).⁽¹⁶⁵⁾ The presence of such blood in the stool is the principle of detection of cancer and pre-cancerous lesions via stool-based tests (see Chapter 2, section 2.3.1).

3.5 Diagnosis of colorectal cancer

Diagnosis of CRC is primarily done through a biopsy, typically taken during a colonoscopy.⁽¹⁵¹⁾ With a biopsy, a tissue sample is taken and tested to determine if

cells are cancerous.⁽¹⁵¹⁾ In addition, these tests can provide detailed characteristics of the cancer if present, such as the size and shape of the cells and their nuclei, as well as the arrangement of the cancerous cells.^(166, 167) In particular, these tests look for specific biomarkers such as RAS and BRAF mutation status,² which are tumour characteristics that may impact the treatment options available to a patient.^(168, 169) Following diagnosis, additional testing may be performed, such as magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and ultrasound.^(151, 165, 166) These tests allow for grading and staging of the cancer. Pre-cancerous adenomas are also removed during diagnostic and screening colonoscopies (polypectomy).⁽¹⁵¹⁾

3.5.1 Staging

Cancer diagnosis includes a process in which the cancer is measured and categorised based on its size and spread.⁽²⁷⁾ This categorisation typically follows the American Joint Committee on Cancer (AJCC) TNM staging system.⁽²⁷⁾ In this system, T refers to the size and extent of the main tumour, N indicates the involvement of nearby lymph nodes, and M describes whether the cancer has spread to distant organs (Table 3.1).⁽²⁷⁾

The TNM staging system can be simplified to provide a numeric score from zero to four, with higher numbers indicating increasingly severe forms:⁽¹⁷⁰⁾

- Stage 0: an in situ carcinoma, which means it is not yet classified as cancerous, although it has the potential to develop into cancer (Tis, N0, M0)
- Stage I: a small, localised cancer (T1–T2, N0, M0)
- Stage II: a cancer that has grown, but has not spread (T2–T4, N0, M0)
- Stage III: cancer that is larger and may have spread to the surrounding tissues and or the lymph nodes (T1–T4, N1–N3, M0)
- Stage IV: cancer that has spread from where it started to at least one other organ in the body (T1–T4, N1–N3, M1).

² The RAS gene family makes proteins involved in cell signaling pathways that control cell growth and cell death. The BRAF gene makes a protein that is involved in sending signals in cells and in cell growth. Mutated (changed) forms of these genes may be found in some types of cancer.

Table 3.1 TNM colorectal cancer staging guideline according to the TNM classification of malignant tumours, 5th and 7th edition

Tumour (T)	Size of primary tumour
T0	There is no evidence of primary tumor.
Tis	Carcinoma in situ. It is in the mucosa but no further.
T1	The tumour is in the inner layer of the bowel (submucosa).
T2	The tumour has grown into the muscle layer of the bowel wall but no further.
T3	The tumour has grown through the muscle layer of the bowel and into the tissues that surround the bowel, but not through the membrane covering the outside of the bowel (peritoneum).
T4	The tumour has grown through the outer layer of the bowel wall (serosa) and the peritoneum.
Nodes (N)	The extent of spread to nearby lymph nodes
N0	No lymph nodes contain cancer cells.
N1	There are cancer cells in up to three nearby lymph nodes, or there are cancer cells in the tissues around the bowel.
N2	There are cancer cells in four or more nearby lymph nodes.
Metastasis (M)	Spread to distant sites
M0	The cancer has not spread to distant organs.
M1	The cancer has spread to distant organs such as the liver, or lungs.

Source: TNM classification of malignant tumours, 5th and 7th edition.^(171, 172) The TNM 5th and 7th editions were used from 2000–2013 and from 2014–2021 in the data provided, respectively. The 7th edition further details sub-stages for T4, N1, N2 and M1.

3.6 Treatment of colorectal cancer

The primary methods of CRC treatment are surgery, chemotherapy, and radiotherapy.⁽¹⁵¹⁾

Surgery aims to physically remove the cancerous cells (resection), which may be done through open or laparoscopic (keyhole) surgeries.

Chemotherapy involves the use of drugs to target cancerous cells. However, the target of these drugs is not specific to cancer cells and therefore other cells in the body may also be affected during the treatment.⁽¹⁵¹⁾ Chemotherapy may sometimes be augmented with biological drug treatments when the cancer has spread beyond the bowel (that is, metastatic CRC). Biological treatments are a category of drugs that target specific proteins and gene changes responsible for cancer growth.⁽¹⁵¹⁾

The National Cancer Control Programme publishes systemic therapy regimens of chemotherapy and biological treatments that are used in colorectal cancer;⁽¹⁷³⁾ these regimens, and those for other cancers, are developed in order to support safe, evidence-based and cost-effective treatment for all cancer patients in Ireland.

Radiotherapy uses ionising radiation to damage or destroy cancer cells. Radiotherapy can be delivered externally (such as by x-ray) or internally (using radioactive implants).⁽¹⁵¹⁾

The choice of treatments and the combination in which they are administered vary based on several factors. These include the cancer location, patient age, stage, appropriateness and accessibility of the treatment options, any other existing health conditions, the patient's capacity to withstand the treatment, and the patient's priorities (for example, extending life or reducing suffering).^(151, 174-176)

Specific treatment patterns and regimens differ across international centres but several principles are common.⁽¹⁷⁷⁾ For localised colorectal cancer, surgical resection is the mainstay of treatment. Other than palliative resection (for example, for obstruction), the aim of surgery is to physically remove the cancerous cells (resection). The earliest stage of CRC, pT1 CRC (a tumour that grows inside a polyp and invades the submucosa, but does not extend beyond the submucosa), may be treated using advanced endoscopic or minimally invasive surgical techniques. These techniques include endoscopic mucosal resection (EMR), endoscopic mucosal dissection (ESD), and transanal minimally invasive surgery, and may not require more invasive surgery (laparoscopic or open resection).⁽¹⁷⁸⁾ Surgery should be avoided when the risks are thought to outweigh the potential benefits: for example, when the patient is unfit for major surgery due to underlying comorbidities, or when resection of advanced disease (Stage IV) may not alter survival or quality of life.

3.6.1 Resectable colon cancer

For patients with colon cancer without metastases, the primary treatment is colectomy (removal of part or all of the colon) with removal of the regional lymph nodes. Such patients with Stage III, and, in some cases, Stage II disease, may be offered adjuvant chemotherapy (chemotherapy given following surgery in order to help prevent relapse). Patients with Stage IV colon cancer that is resectable may receive preoperative or postoperative chemotherapy and may receive biological treatments.⁽¹⁷⁷⁾

3.6.2 Resectable rectal cancer

Patients with Stage I rectal cancer who have a resectable tumour are offered surgery to remove the cancer. The treatment for patients with Stage II and III rectal cancer typically involves preoperative radiotherapy or chemoradiotherapy

(chemotherapy combined with radiotherapy), followed by surgery. Preoperative cancer-directed treatment in this setting is 'neoadjuvant', that is, performed with the aim of reducing the tumour burden before surgery. Adjuvant chemotherapy may also be used in some cases.

The combination of neoadjuvant radiotherapy and systemic chemotherapy, known as total neoadjuvant therapy (TNT), is now considered the standard of care for locally advanced rectal cancers.⁽¹⁷⁹⁾ In December 2024, the National Cancer Control Programme (NCCP) published an updated guideline on neoadjuvant treatment of patients with locally advanced rectal cancer, recommending that 'all patients diagnosed with locally advanced operable rectal cancer should be considered for neoadjuvant therapy.'⁽¹⁸⁰⁾ This recommendation supersedes that included in the 'Treatment: Patients receiving neoadjuvant therapy' section within the Department of Health (2020) Diagnosis, staging and treatment of patients with rectal cancer (NCEC National Clinical Guideline No. 25).⁽¹⁷⁵⁾

Patients with Stage IV rectal cancer may receive surgery or radiotherapy directed at the primary tumour with a view to controlling symptoms. They may also have metastases in, for example, the liver, lung and peritoneum; in such patients surgery may also be performed to try to control the cancer in these sites.⁽¹⁷⁷⁾

3.6.3 Unresectable colorectal cancer

For patients with unresectable cancer, the goal of treatment is not curative but to prolong overall survival and maintain quality of life. The mainstay of treatment is systemic drug therapy including chemotherapy and biological treatments.⁽¹⁷⁷⁾

3.6.4 Receipt of treatment in Ireland

The National Cancer Registry Ireland (NCRI) collects information on whether or not a patient has received surgery, chemotherapy or radiotherapy in the first year following diagnosis; here, the term 'chemotherapy' also includes treatment with targeted drugs such as biological treatments. For the purposes of this HTA, a high-level view of treatment received is presented in order to understand the extent to which patients diagnosed with colorectal cancer undergo broad treatment modalities (for example, receipt of surgery, or receipt of both surgery and chemotherapy) following diagnosis. Time trends in treatment from the year 2000 are presented in Appendix A (section A.1), while a snapshot of trends for a recent year (2019) is presented below. This year was chosen as the most recent year for which data were available and which did not fall within the COVID-19 pandemic period. The timing and nature of treatment within a modality, for example, neoadjuvant versus adjuvant chemotherapy, is not discussed in this chapter.

Receipt of treatment by site, age group, stage and mode of detection

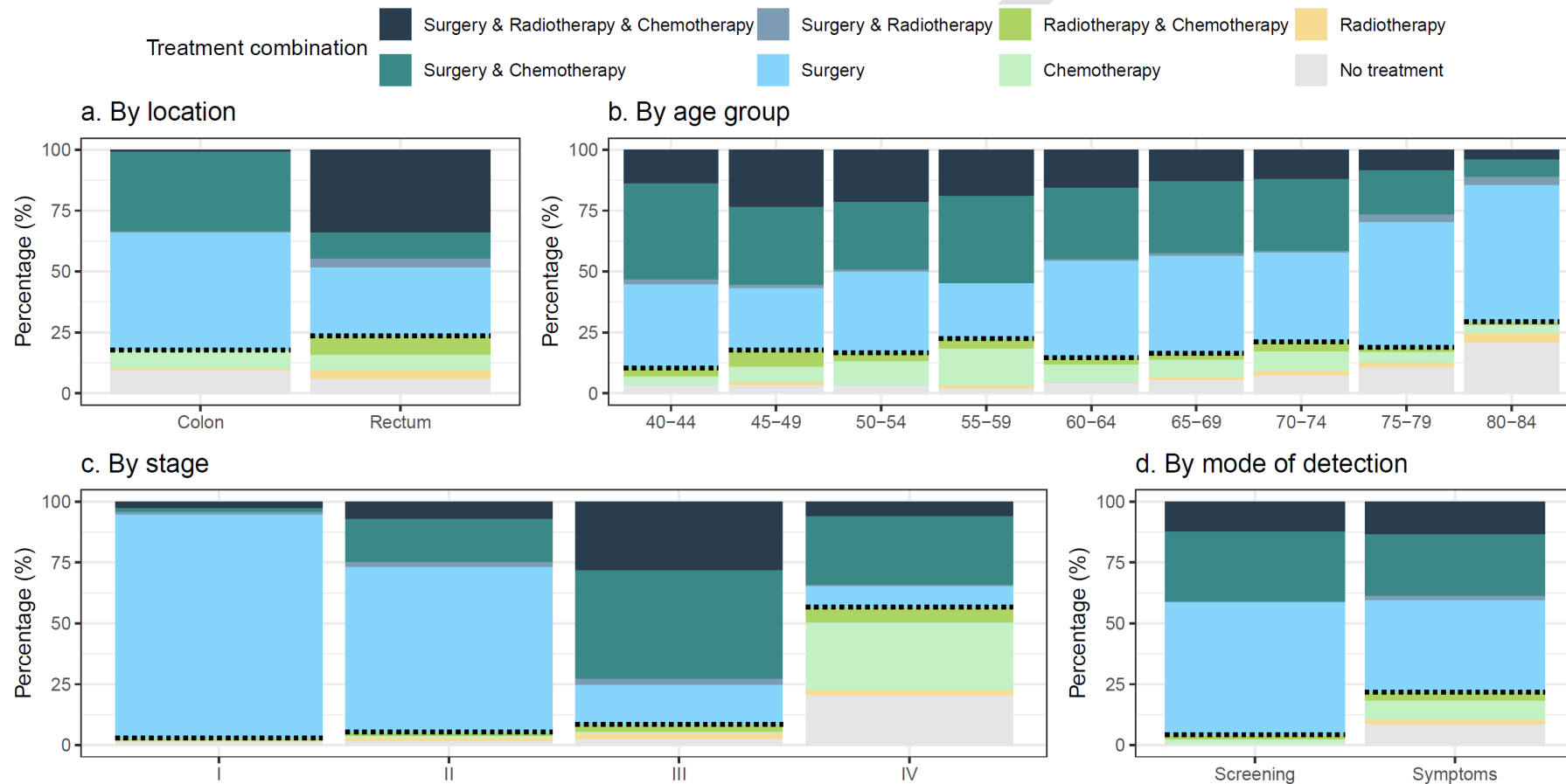
In Ireland, in 2019, 82.2% of colon cancer patients and 76.4% of rectal cancer patients underwent surgery within 12 months of CRC diagnosis (Figure 3.1a). Additionally, as described above, rectal cancer patients were more likely to receive chemotherapy and radiotherapy. NCRI data show that 59.1% of rectal cancer patients underwent chemotherapy and 48.1% underwent radiotherapy in 2019. In contrast, only 41.5% of colon cancer patients received chemotherapy, and fewer than 2% underwent radiotherapy. These differences reflect the National Clinical Guidelines for cancer treatments, which more broadly recommend the use of chemotherapy and radiotherapy for rectal than colon cancer.^(175, 176) Treatment plans vary across age groups because many of the factors that influence treatment decisions, such as tolerance and existing health conditions, often change with age.⁽¹⁷⁴⁾ Generally, a smaller proportion of older patients received treatment, and older patients also received fewer categories of treatments (Figure 3.1b).

As noted above, cancer stage, particularly its spread, informs the goals and plans of CRC treatment. The majority of Stage I CRCs in Ireland (91.9%) were surgically removed without further intervention in 2019 (Figure 3.1c). Treating more advanced CRC increasingly involves chemotherapy to minimise or manage the cancer spread. However, some patients with advanced CRC may not be medically suitable for some treatments or may choose to forego cancer-directed treatment in the interest of preserving quality of life.⁽¹⁷⁴⁾ In Ireland in 2019, 20.6% of Stage IV CRC patients received no tumour directed treatment in their first year of diagnosis (Figure 3.1c).

Related to the stage of detection is the mode of detection: as screening allows for earlier detection of CRCs than those symptomatically presented (discussed below in section 3.9.3), the treatment receipt of screen-detected cases resembles that of early CRC stages (in particular, Stage II). In contrast, symptomatically presented cases undergo surgery less frequently and are more likely to receive chemotherapy on its own or to receive no tumour-directed therapy (Figure 3.1d).

Specifically in the 50–54 age group, in 2019, 83.3% of CRC patients overall underwent surgery, while 62.7% and 25.3% received chemotherapy and radiotherapy, respectively. In comparison, 77.6%, 74.0% and 24.0% of those aged 55–59 underwent surgery, chemotherapy and radiotherapy, respectively.

Figure 3.1 Breakdown of treatment combinations carried out within one year of colorectal cancer diagnosis in Ireland in 2019, presented by location (a), age group (b), stage (c) and mode of detection (d)



Source: NCRI. Data displayed are of patients between 40 and 84 years old. Note that data collection for cases diagnosed in 2019 was 98% complete at the time of data download (02/09/2023). Each listed treatment combination is a mutually exclusive category, that is, patients are counted under one category only. Dotted lines split the proportion of patients receiving categories of treatment involving surgery (above dotted line) and not involving surgery (below dotted line).

Key: NCRI – National Cancer Registry Ireland.

3.7 Quality of life of colorectal cancer survivors

Cancer survivors face numerous challenges that adversely affect their quality of life. In Ireland, a 2022 study of 304 CRC survivors found that 54% are dissatisfied with their life quality, citing concerns such as negative body image (74%), fatigue (68%), sexual dysfunction (66%), and sleep disturbances (59%).⁽¹⁸¹⁾ Colorectal cancer treatments, including surgery, chemotherapy and radiotherapy, frequently lead to physical impairments.⁽¹⁸²⁾ Patients often report the experience of pain, bowel dysfunction, and fatigue, which can persist long after treatment.⁽¹⁸²⁾ A study of 496 CRC survivors in Ireland found that 99% of participants had frequently experienced at least one of the 11 most commonly cited symptoms, which included fatigue, insomnia, flatulence, constipation, diarrhoea, bloating, appetite loss and frequent urination.⁽¹⁸³⁾ While abdominal and buttock pain were reported less frequently overall, they were more common in CRC survivors under the age of 55 years.⁽¹⁸³⁾

In addition to physical symptoms, CRC survivors may also experience psychosocial challenges and difficulties with relationships,⁽¹⁸⁴⁾ with two-thirds of CRC survivors in Ireland reporting social difficulties.⁽¹⁸⁵⁾ Both social difficulty and lower satisfaction with continuity of care have been found to predict poorer quality of life.⁽¹⁸⁵⁾ A systematic review of 53 international studies further identified critical factors that negatively impact the quality of life in CRC survivors.⁽¹⁸⁶⁾ These included the presence of a stoma (an opening on the surface of the abdomen that has been surgically created to divert the flow of faeces; this may be required following removal of part or all of the bowel to remove the tumour, and poses physical and psychological challenges), comorbidities, high body mass index (BMI), fatigue, psychological stress, low levels of physical and social activity, low income, perceived poor quality of cancer care, and adverse personal circumstances.⁽¹⁸⁶⁾ The patient, social and ethical considerations for extending colorectal cancer screening will be discussed in more detail in Chapter 9 of this assessment.

3.8 Risk factors for colorectal cancer

Several demographic characteristics have been linked to a higher risk of CRC, such as:

- increasing age
- male sex
- taller height.⁽¹⁰⁾

Disparities in incidence have also been observed by ethnicity; for example, in the United States, African-Americans have experienced higher incidences of CRC, particularly late-stage CRC, with this disparity considered to be multifactorial in cause.^(10, 187)

Certain pre-existing medical histories, both familial and personal, are also indicative of heightened CRC risk. These include:

- previous CRC case in family
- diabetes
- inflammatory bowel disease (ulcerative colitis and Crohn's disease)⁽¹⁰⁾

Additionally, rare hereditary conditions – most notably, Familial Adenomatous Polyposis (FAP) and Lynch Syndrome (LS) – predispose to CRC development.⁽¹⁶³⁾ Lynch syndrome (also known as hereditary nonpolyposis colorectal cancer (HNPCC)) is the most common known cause of hereditary CRC, and results from germline mutations in mismatch repair genes. LS increases the risk of CRC and other cancers, with an estimated cumulative incidence for any cancer at age 70 of 75% in females and 58% in males.⁽¹⁸⁸⁾ Estimates of the prevalence of Lynch syndrome in CRC vary, with a 2022 systematic review reporting an overall pooled estimate of 2.2%, rising to 5.1% in studies of universal germline testing of all patients.⁽¹⁸⁹⁾ The majority of people with LS may be unaware they have the condition. CRC develops at a younger age among patients with LS, although the age at onset varies depending on genotype.^(188, 190) The median age of diagnosis of any LS-associated cancer was calculated in one Irish study as 44.5 years, ranging from 23 to 81; this study included LS patients attending two cancer genetics services in Ireland between 2000 and 2018.⁽¹⁹¹⁾

Familial adenomatous polyposis (FAP) is an autosomal dominant condition that occurs as a result of mutations in the adenomatous polyposis coli (*APC*) gene. FAP is characterised by hundreds to thousands of adenomatous polyps in the colon and rectum,⁽¹⁹²⁾ developing from an average age of 16 years.⁽¹⁹³⁾ Individuals with FAP have an almost 100% lifetime risk of CRC, with an average age of 39 years at diagnosis if untreated.⁽¹⁹⁴⁾ FAP is estimated to account for approximately 1% of all CRCs.^(195, 196) Attenuated FAP (AFAP) is a less severe form of FAP characterised by less than one hundred colon polyps, with the onset of polyposis and cancer occurring later than in FAP, with an estimated lifetime CRC risk of 70%.^(192, 193)

3.8.1 Modifiable risk factors of colorectal cancer

A systematic review by the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) in 2017 identified several modifiable factors as having an established or convincing risk of CRC.⁽¹¹⁾ These include:

- smoking
- the consumption of processed meat
- alcohol intake
- adiposity
- physical inactivity.

The WCRF/AICR review also identified red meat consumption as a probable risk factor, while the consumption of wholegrain foods, dairy products, a high fibre diet and calcium supplements were considered 'probably protective'.⁽¹¹⁾ Furthermore, a meta-analysis of 20 studies identified familial history of CRC, hyperlipidemia, obesity and alcohol consumption as significant risk factors of early-onset CRCs.⁽¹⁹⁷⁾

In Ireland, the NCRI estimated, based on 2016 data, that 25% to 39% of CRC cases were preventable through changes in modifiable risk factors.⁽¹⁹⁸⁾ Of note, overweight and obesity were estimated to account for 11% of colon cancers; processed meat intake 5.8% (female) and 9.4% (male) of CRCs; and physical inactivity 3% of colon cancers.⁽¹⁹⁸⁾

A growing body of literature focuses on the existence of novel, emerging risk factors. In particular, recent studies have suggested an increased risk due to environmental and occupational chemical exposures. Potentially CRC risk-elevating chemicals (for example, pesticides⁽¹⁹⁹⁾ and benzene⁽²⁰⁰⁾) are hypothesised to enter the gastrointestinal tract via contaminated water and food. However, the mechanisms through which these chemical exposures affect colorectal carcinogenesis remain an open question.⁽¹⁴⁵⁾ Additionally, the timing of exposure has been spotlighted in recent years, as early-life exposures to risk factors likely elevate the risk of CRC later in life. Examples of reported adverse early exposures include:

- in-utero exposure to synthetic hormones⁽²⁰¹⁾
- childhood obesity⁽²⁰²⁾
- early-to-mid-life chronic antibiotic use.⁽²⁰³⁾

3.9 Epidemiology of colorectal cancer

This section describes the incidence, mortality, mode and stage of detection, and five-year net survival of CRC in Ireland, and concludes with estimation of future projections of the burden of disease. Data from the NCRI are presented, with a focus on the time period since the introduction of colorectal cancer screening in Ireland in 2012. The introduction of BowelScreen serves as a useful reference point for consideration of recent trends and also serves to suggest potential trends that may be observed following implementation of screening, which may be informative for considering the impact of age extension.

The present assessment focused on the crude and age-specific rates to specifically allow consideration of the burden of disease in the overall population and for specific age groups of interest. Age-standardised estimates, in contrast, allow for overall population rates to be compared (for example, over time) while accounting for both changes in population size and age structure. Age-standardised rates are particularly useful for identifying whether additional factors (for example, increased use of diagnostic testing) might be contributing to differences in epidemiological measures.

Age-standardised CRC incidence and mortality rates are published by the NCRI and are referred to at points within the following sections to provide additional context.⁽⁸⁾

3.9.1 Incidence of colorectal cancer in Ireland

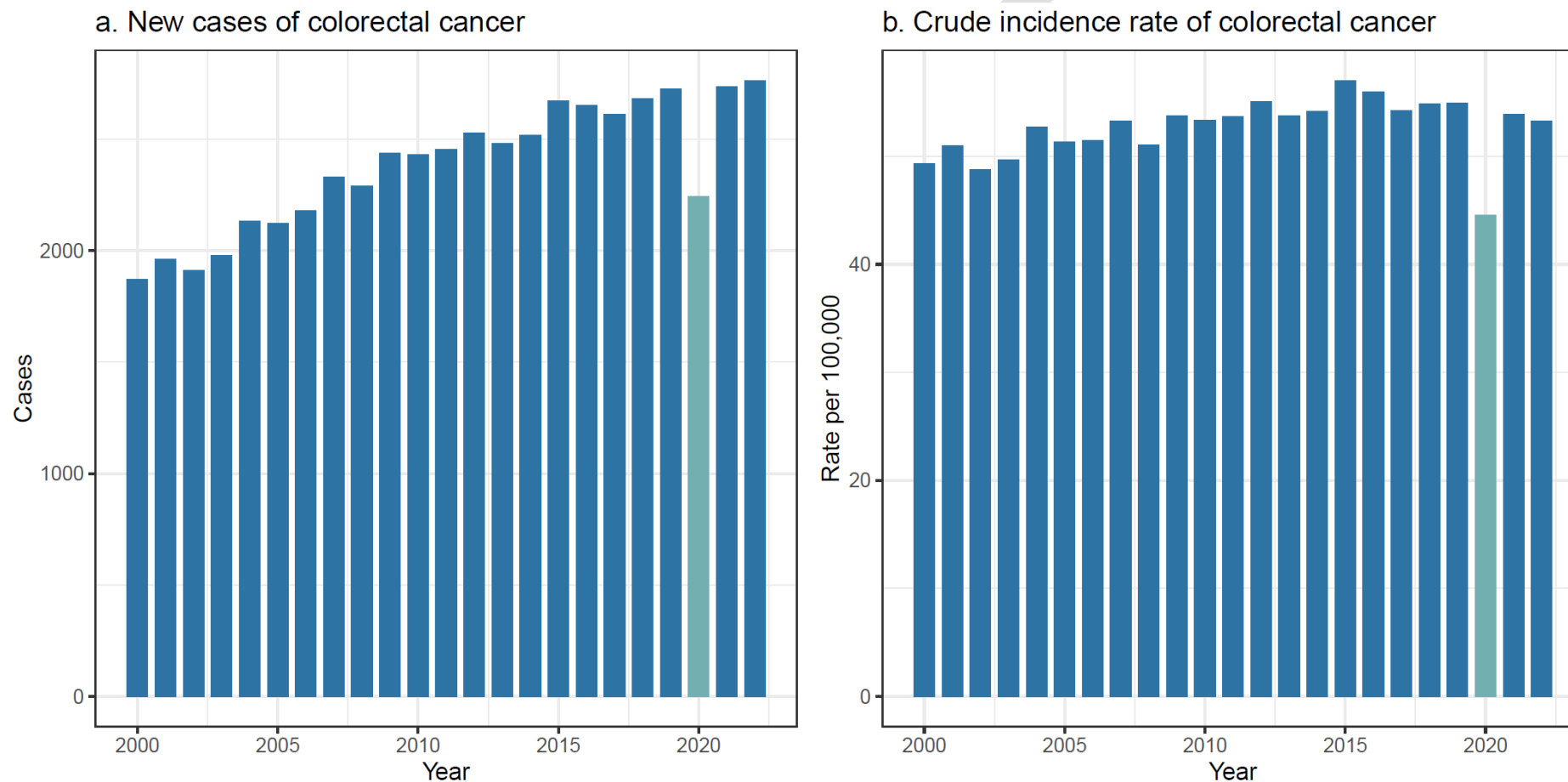
In 2021–2022, an average of 2,750 new cases were recorded each year, which translates to 53.6 cases per 100,000 in the population (Figure 3.2). The CRC case number has increased in the last two decades in Ireland, while the crude incidence rate per 100,000 people peaked in 2015 and has since remained stable (Figure 3.2). The increasing case number is linked to the age-specific risk of CRC and the ageing population in Ireland. Specifically, the crude CRC incidence rate increases with age (Figure 3.3) and the proportion of the population that is older is increasing over time: for example, people under 50 years of age have the lowest CRC incidence rate; similarly the proportion of people under 50 is decreasing in the population (Figure 3.4; Appendix A, section A.2). In the years following the introduction of BowelScreen (2013 to 2021, excluding 2020), approximately two-thirds of reported CRC cases (66.5%, ranging from 64.0% to 67.6%) involved colon cancer (C18) rather than rectal cancer (C19 and C20). During the same period, the overall CRC incidence rate averaged 46.0 (min = 43.4; max = 46.7) and 64.5 (min = 62.4; max = 68.3) per 100,000 in females and males, respectively. Considering overall trends, NCRI reports that, since 2012, the age-standardised CRC incidence rate in men has significantly decreased by 2.5% annually, while there has been a smaller but continuous decline of 0.3% per year since 1994 in women.⁽⁸⁾ During the COVID-19 pandemic, there was an 18% drop in reported CRC cases in 2020, compared to the preceding year.⁽²⁰⁴⁾ The registered CRC numbers were subsequently restored to the pre-pandemic level by 2021, according to an NCRI analysis of projected and registered cases.⁽²⁰⁵⁾

Age-specific colorectal cancer incidence

The BowelScreen programme was introduced in October 2012 for people aged 60 to 69 years, initially focusing on older individuals who were nearing the upper age limit in 2012–2013. In the years following the introduction of BowelScreen (2013 to 2021, excluding 2020), the annual CRC incidence rate among 60 to 64-year-olds has ranged from 115 to 170 per 100,000, with an average of 125 per 100,000. The corresponding incidence rate for 65 to 69 year-olds has ranged from 149 to 230 per 100,000, with an average of 181 per 100,000 (Figure 3.3). In age groups 50–54 and 55–59, there were on average 141 (ranging from 129 to 167) and 210 (ranging from 186 to 238) cases per year (between 2013 and 2021, excluding 2020). The corresponding average incidence rate was 47.3 per 100,000 (ranging from 44.4 to 50.9) and 78.3 per 100,000 (ranging from 70.1 to 84.1) during the same period (Figure 3.3).

Breakpoint regression analysis was used to summarise trends over the period 2000 to 2019, with trends expressed in terms of the average annual percent change (AAPC) for a given period. The incidence rate has declined since 2000 for those aged 55–59 (AAPC: -0.5%); from 2014 for those aged 65–69 (AAPC: -5.3%); from 2008 for those aged 70–74 (AAPC: -3.4%); and from 2009 for those aged 75 and older (AAPC: -1.5% from 2009–2019; -6.5% since 2019). (Figure 3.3; Appendix A, section A.2). The incidence rate has largely remained consistent since 2000 in those aged 50–54 and 60–64 (Figure 3.3; Appendix A, section A.2). For those younger than 50, incidence has increased (AAPC: +1.8%) in the same timeframe (Figure 3.3; Appendix A, section A.2); however, the absolute incidence in this age group remains low (Figure 3.3).

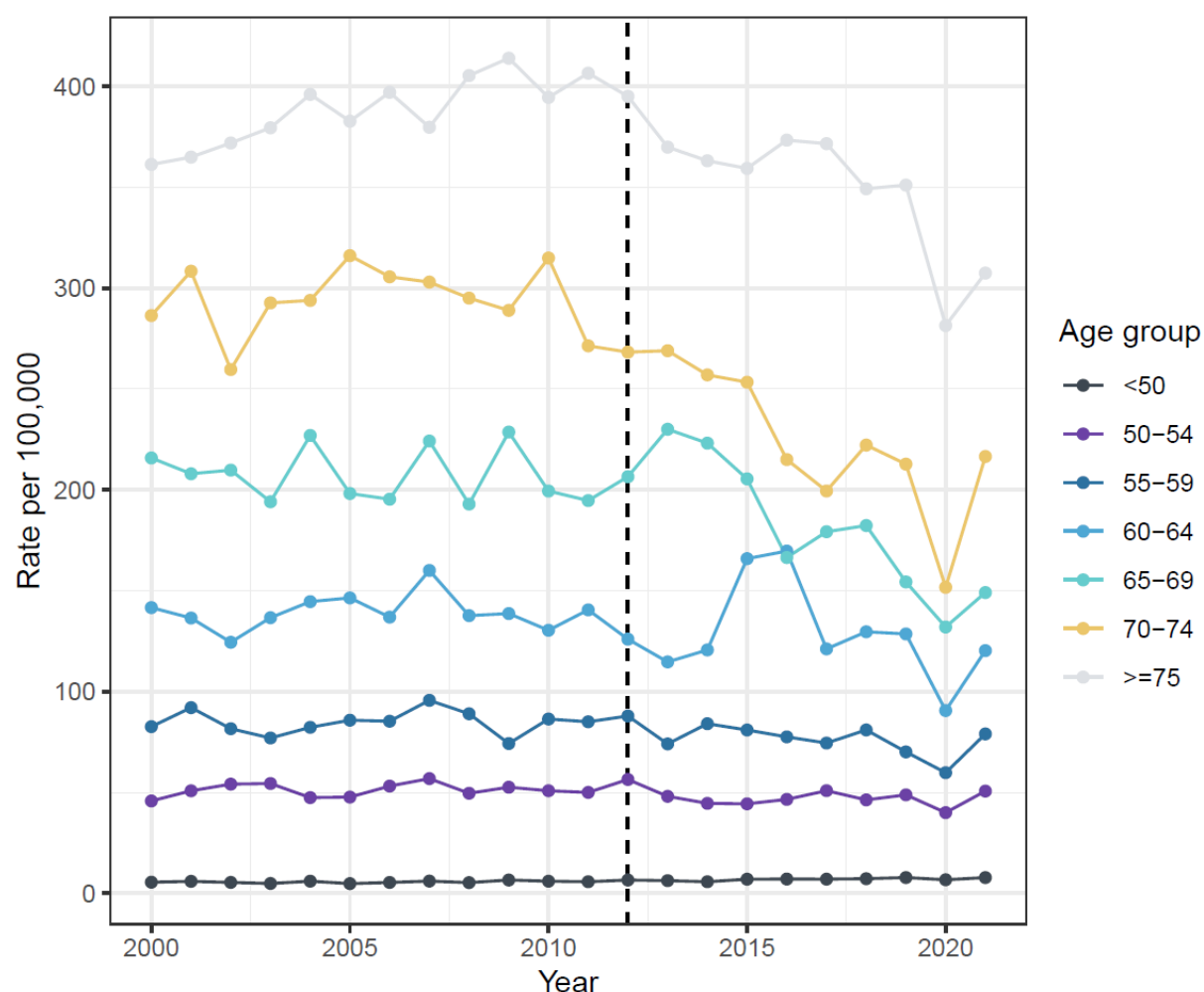
Figure 3.2 (a) Number of new cases, and (b) crude incidence rate of colorectal cancer per 100,000 people, across all age groups, in Ireland from 2000 to 2022



Source: NCRI incidence statistics. The crude rates were calculated using the CSO PEA01 population data.⁽²⁰⁶⁾ Cancer diagnoses were impacted by the COVID-19 pandemic in the year 2020 (marked in green).⁽²⁰⁵⁾

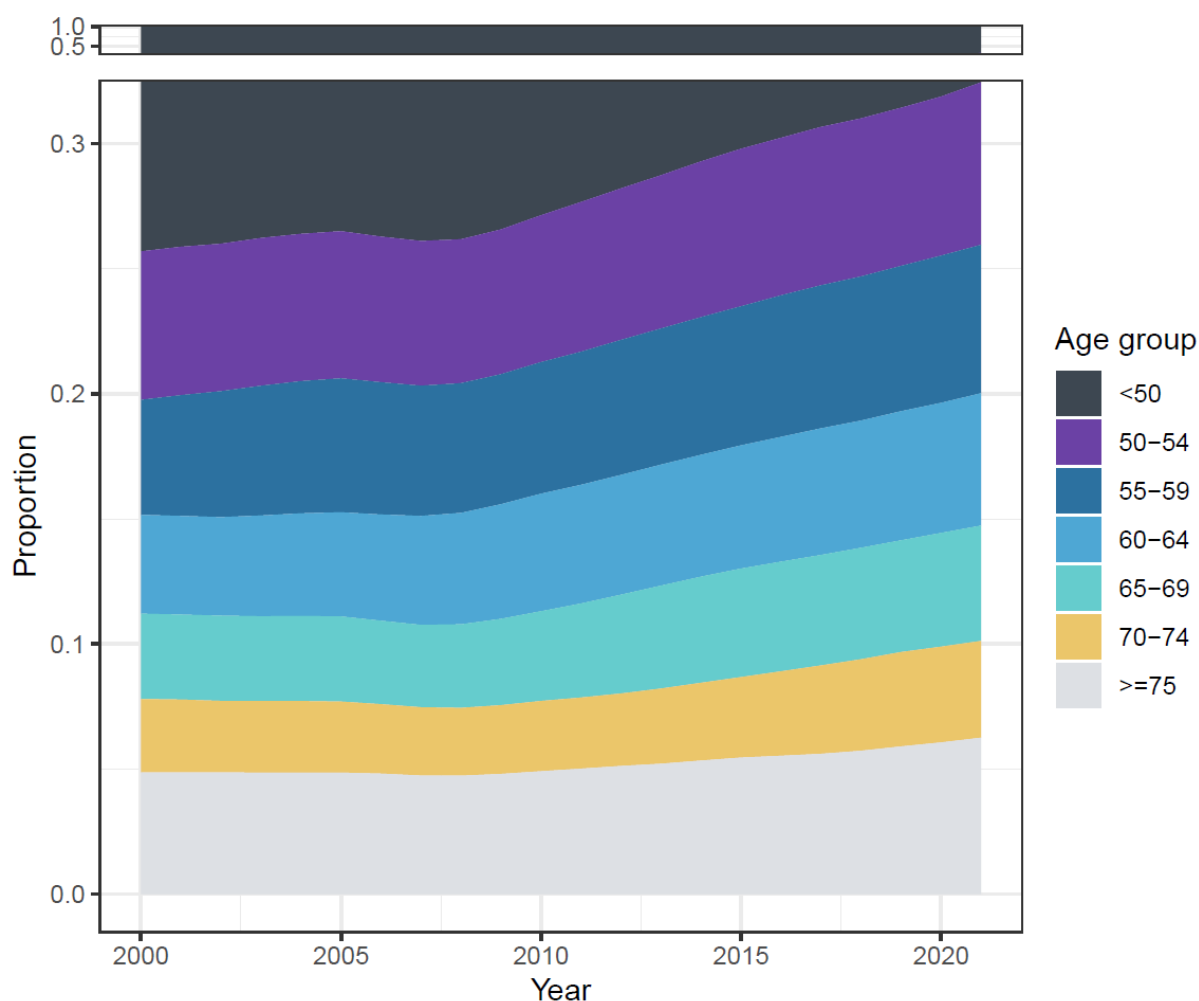
Key: CSO – Central Statistics Office, NCRI – National Cancer Registry Ireland.

Figure 3.3 Incidence rate of colorectal cancer per 100,000 by age group



Source: NCRI and CSO.⁽²⁰⁷⁾ Age-specific rates are calculated using denominators derived from CSO PEA01 population data.⁽²⁰⁶⁾ BowelScreen has been available since 2012 (indicated by the vertical dashed line) for people aged 60 to 69 years old. The age groups outside the scope of screening in Ireland (which are, <50 and >=75) are shown in grey scales (dark and light grey, respectively). Key: CSO – Central Statistics Office, NCRI – National Cancer Registry Ireland.

Figure 3.4 Proportion of the population in Ireland by age groups



Source: CSO.⁽²⁰⁷⁾ The age groups outside the scope of screening in Ireland (which are, <50 and ≥75) are shown in grey scales (dark and light grey, respectively). Note that there is a break in the y-axis and the values (between 0.35 and 1) in the top panel are visually compressed.
Key: CSO – Central Statistics Office Ireland.

3.9.2 Mortality

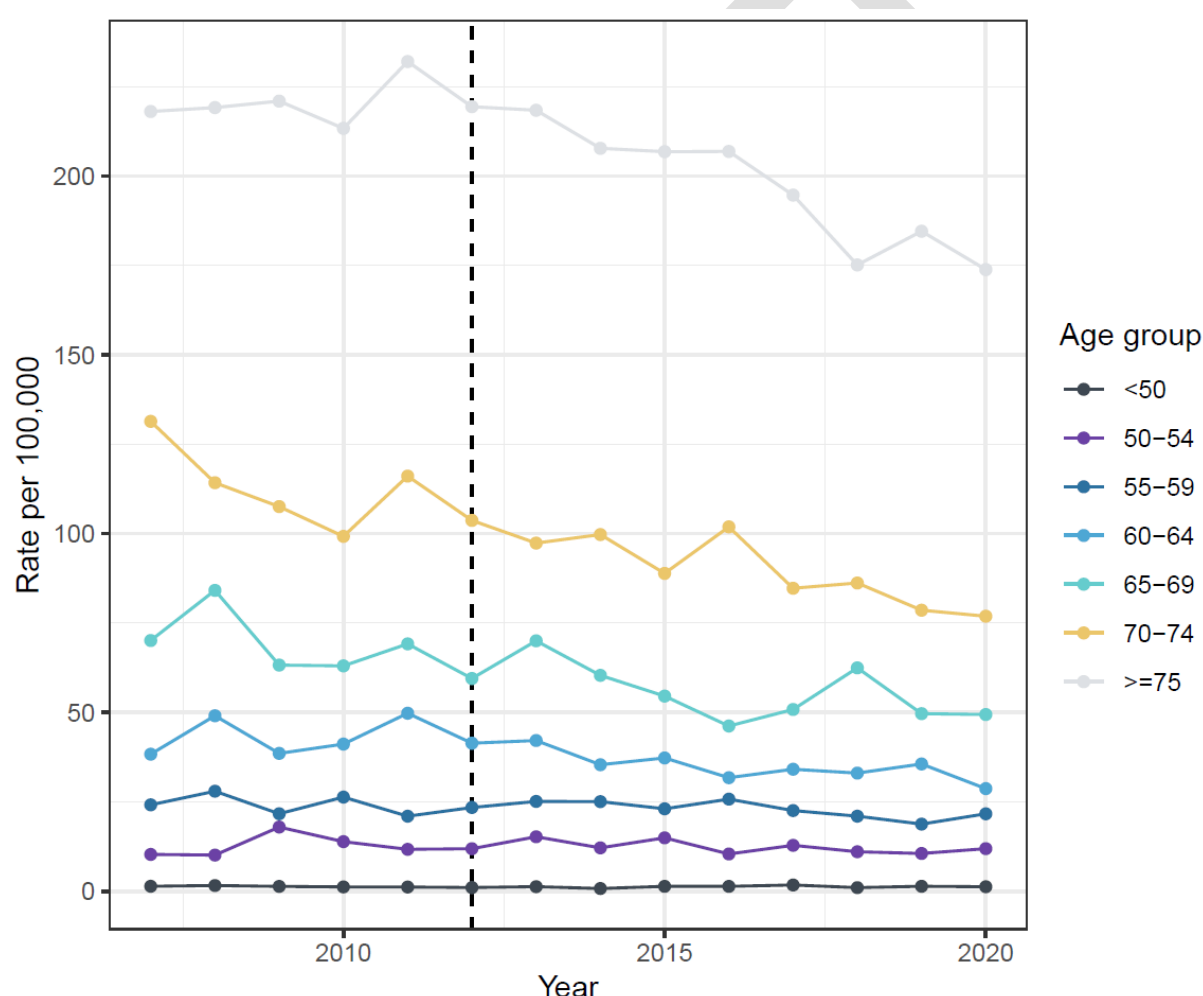
Between 2012 and 2020, there have been, on average, 1,014 deaths annually attributable to CRC (min = 981; max = 1,034). Colon and rectal cancers accounted for 47.0% and 53.0% of the deaths, respectively.⁽²⁰⁶⁾ Of all CRC deaths, 41.9% occurred in females and 58.1% in males. The age-standardised CRC mortality rates per 100,000 population (including anal cancers, ICD-10 C21) were estimated at 21.9 for females and 38.7 for males for the same period.⁽²⁰⁵⁾

Age-specific colorectal cancer mortality

Older people experience a higher CRC mortality rate (Figure 3.5). The median mortality rates per 100,000 since 2012 in the age groups 50–54, 55–59, 60–64 and

65–69 were 11.87 (min = 10.08; max = 17.92), 23.21 (min = 18.74; max = 27.94), 37.77 (min = 28.67; max = 49.75), and 61.39 (min = 46.18; max = 84.11), respectively. The mortality rate among those aged under 60 has remained stable since 2007 (that is, the beginning of availability of ICD-10 coded data from the Central Statistics Office (CSO)).⁽²⁰⁸⁾ In older age groups, however, the mortality rate has declined in the same time frame (Figure 3.5; Appendix A, section A.2; declining since 2012 for those aged 75 and older). Trends in net survival of CRC patients are separately described in section 3.9.4.

Figure 3.5 Age-specific mortality rate per 100,000 people due to colorectal cancer



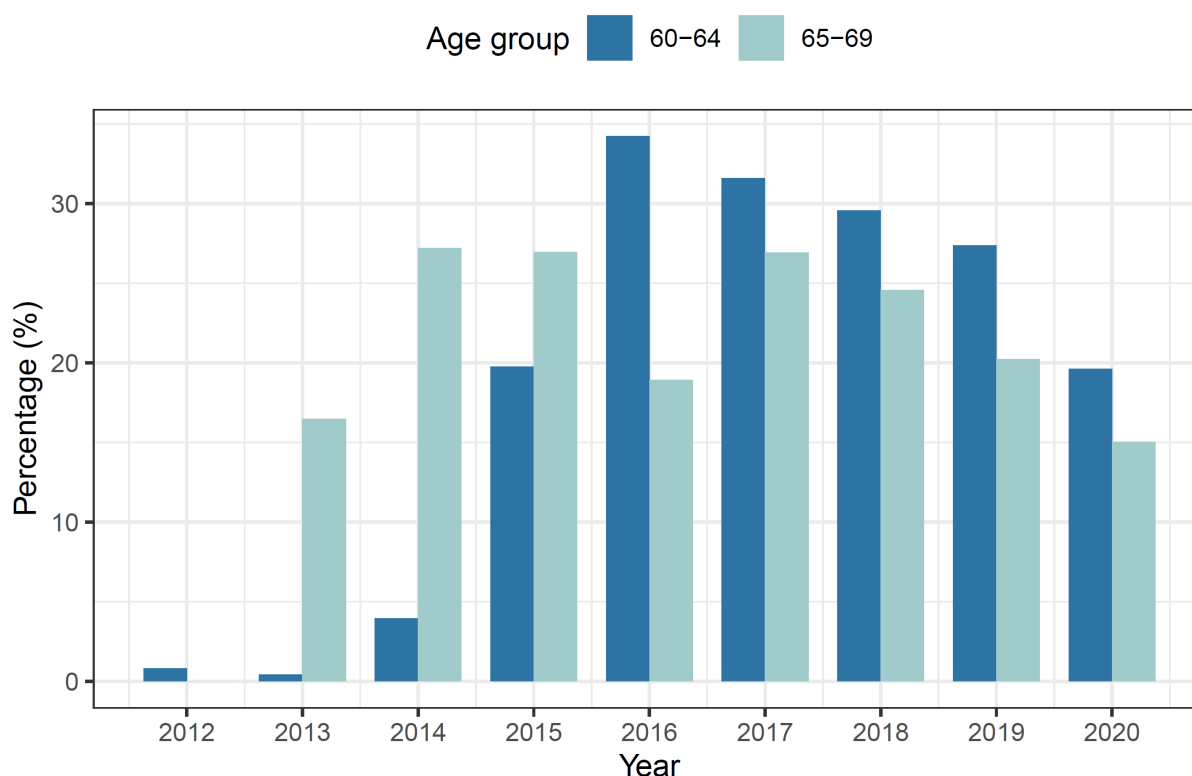
Source: CSO: VSA35.⁽²⁰⁸⁾ Rates are standardised to the CSO PEA01 population data.⁽²⁰⁶⁾ BowelScreen was introduced in 2012 (indicated by the vertical dashed line) for people aged 60 to 69 years old. The age groups outside the scope of screening in Ireland (which are, <50 and ≥75) are shown in grey scales (dark and light grey, respectively).

Key: CSO – Central Statistics Office.

3.9.3 Mode of detection and stage at detection

Following the rolling out of the BowelScreen programme from October 2012 to people aged 60 to 69, the proportion of CRC cases detected by organised screening increased over time, reaching roughly a quarter of all cases by 2013–2014 and 2015–2016 in the older (65–69) and younger (60–64) cohorts, respectively (Figure 3.6; Appendix A, section A.2). After the initial increase, the proportion of cases detected by organised screening remained stable, with no statistically significant trend over time (Appendix A, section A.2).

Figure 3.6 Percentage of colorectal cancer cases detected in Ireland through screening between 2012 and 2020 among people aged 60 to 64 and 65 to 69 years old

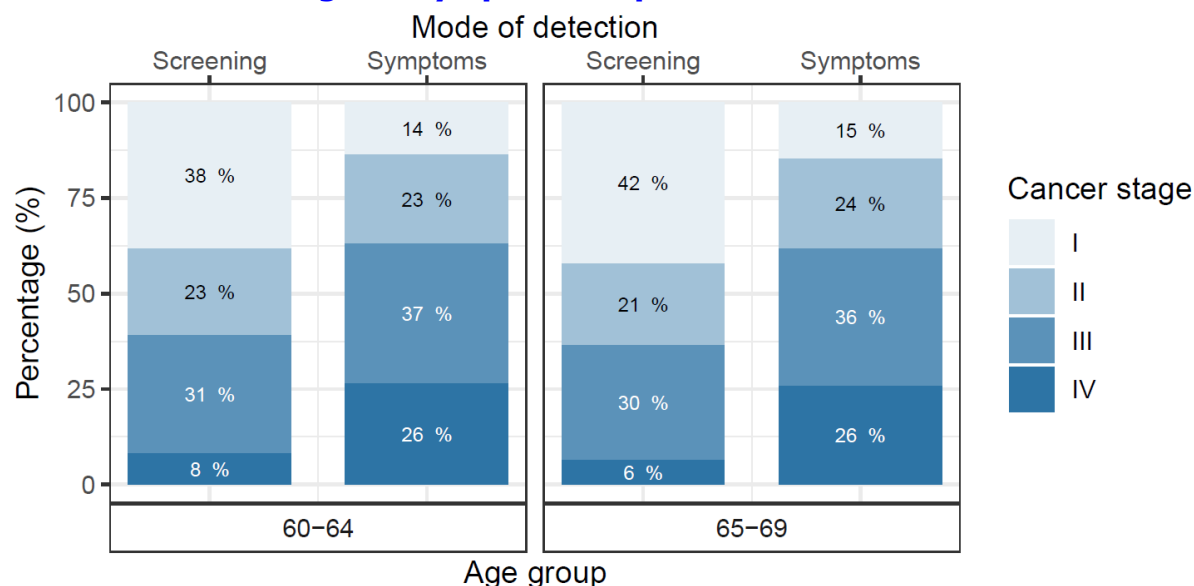


Source: NCRI. BowelScreen was introduced to people aged 60 to 69 years old in October 2012. Screening includes organised screening only and excludes opportunistic or unspecified screening. Key: NCRI – National Cancer Registry Ireland.

CRC cases detected by BowelScreen have been less likely to be diagnosed at advanced cancer stages (Figure 3.7). Up to 38 to 42% of CRC detected through screening have been found in the least advanced Stage I, while only 14 to 15% of

symptomatically detected cases were classified as such. Conversely, 26% of those that presented symptomatically were detected in the most advanced Stage IV, while only 6 to 8% of those discovered through screening were in Stage IV.

Figure 3.7 Stage distribution of colorectal cancers detected in Ireland by screening and symptomatic presentation from 2012 to 2020

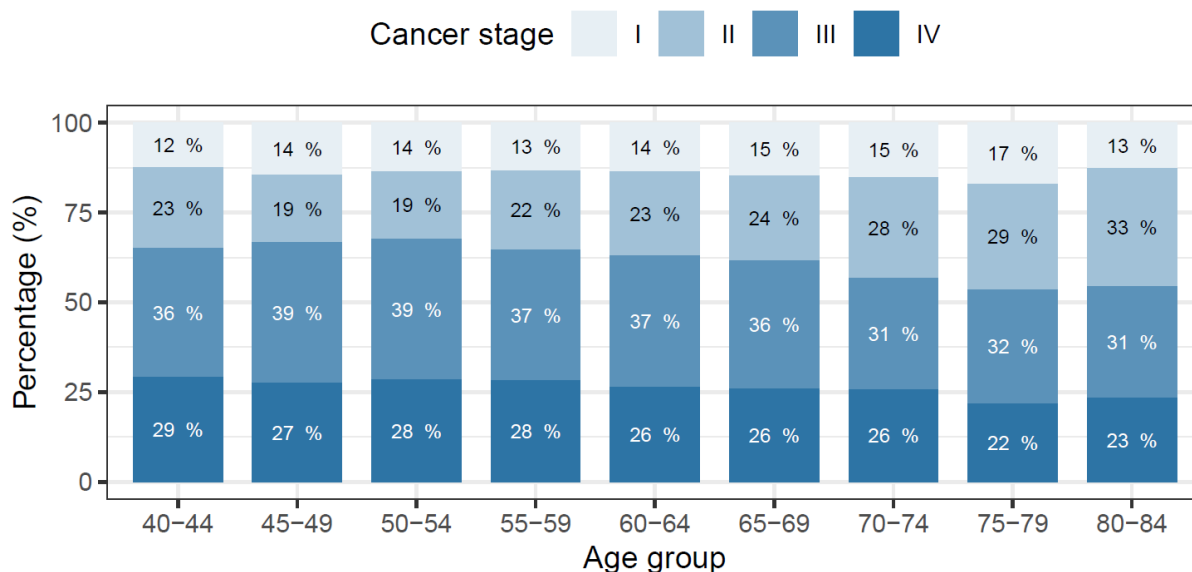


Source: NCRI. BowelScreen has been available since 2012 for people aged 60 to 69 years old, initially focusing on older individuals who were nearing the upper age limit in 2012–2013.

Key: NCRI – National Cancer Registry Ireland.

Among symptomatically presented CRCs, the proportion of Stage II CRCs increased with age from 45–49 years upwards, while the proportion of Stage III CRCs was found to generally decrease with age (Figure 3.8). It is notable that the proportion of CRC detected at advanced stages (that is, Stage III or IV) since 2012 was the highest in those aged 50–54 (Figure 3.8; 67% among 50–54, compared with 65% in those aged 55–59, 63% in those aged 60–64, and 62% in those aged 65–69).

Figure 3.8 Stage distribution of symptomatically detected colorectal cancers in Ireland from 2012 to 2020 by age group



Source: NCRI. BowelScreen has been available since 2012 for people aged 60 to 69 years old, initially focusing on older individuals who were nearing the upper age limit in 2012–2013.

Key: NCRI – National Cancer Registry Ireland.

3.9.4 Five-year net survival rate

CRC survival prognosis is typically expressed as the net survival rate, which represents the probability of surviving CRC for a particular follow-up duration after diagnosis (for example, five years).⁽²⁰⁹⁾ The net survival may be interpreted as the chance of survival in a hypothetical scenario where CRC is the only possible cause of death.⁽²⁰⁹⁾ In other words, the net survival estimates are cause-specific, meaning that competing causes of death are factored out by incorporating life tables that contain the expected survival estimates of the general population.⁽²¹⁰⁾ The life tables (tables which show, for each age, the probability of death before the next birthday) are matched to the relevant context, most notably in terms of the geographical area, year, age and sex.⁽²⁰⁹⁾ Individuals surviving longer than the follow-up duration are censored, meaning that they contribute to the survival estimates as having survived for at least the duration of the follow-up.⁽²⁰⁹⁾

Survival following cancer diagnosis has generally improved in Ireland over the years.⁽²⁰⁴⁾ The age-standardised five-year net survival rate among CRC patients for the latest analysed period (2014–2018) stands at 66%, compared to 50% for the 1994–1998 period.⁽²⁰⁴⁾ An increase in the net survival estimate may reflect later deaths (for example, due to improved treatment), earlier detection (for example, due to a screening programme) and over-diagnosis (slow-growing cancers in

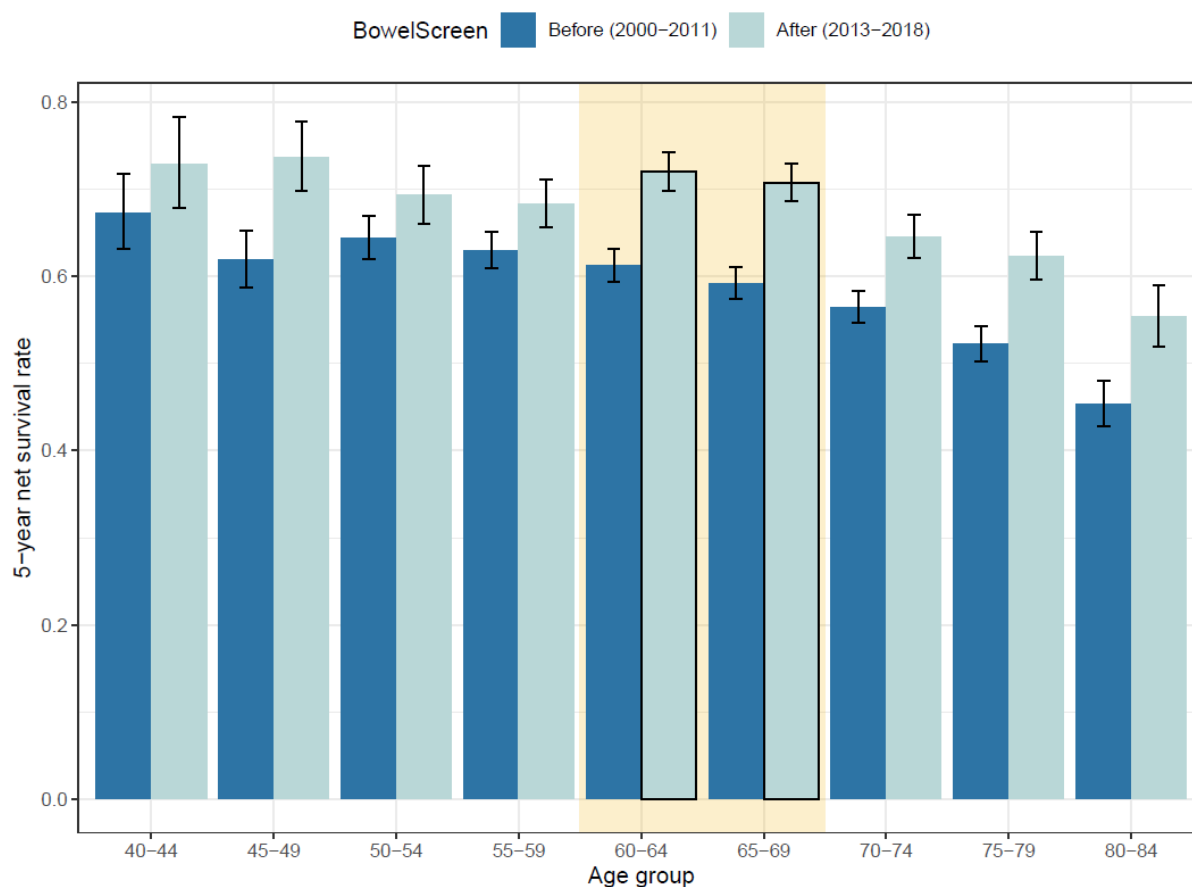
individuals who die of other causes).⁽²⁰⁹⁾ The apparent increase in survival time resulting from earlier diagnosis through screening – irrespective of whether the patient actually lives longer – is referred to as lead-time bias. Lead time is the interval between the early detection of cancer via screening and its typical clinical presentation and diagnosis. For CRC, this lead time is estimated to be at least two years.⁽²¹¹⁾

For the latest analysed period (2014–2018), female and male patients experienced comparable survival rates: 66% and 67% respectively.⁽²¹²⁾ Early detection is crucial, as the survival prospect declines at more advanced stages (five-year net survival: 97, 90, 73 and 14% for Stages I, II, III and IV, respectively).^(205, 212)

Age-specific colorectal cancer survival

Younger people diagnosed with CRC are likely to have a better survival outlook compared to their older counterparts, as demonstrated by the age-specific five-year net survival rates before the introduction of BowelScreen (Figure 3.9; Appendix A, section A.2), although the 45–49 age group does not conform to this pattern. Following the introduction of BowelScreen in 2012, five-year net survival rate estimates for CRC cases diagnosed between 2013 and 2018 for the screening eligible age groups (60–69; black outlines) were 71% (95% CI: 70 – 73) compared with 68% (95% CI: 66 – 71) in the adjacent age group below the population-based screening age (age 55–59), (log-rank type test for net survival;⁽²¹³⁾ p-value = 0.063). The improved survival in the screening eligible age group is consistent with the finding that screening leads to earlier detection (Figure 3.7), and the prospect of CRC survival is improved when cancer is detected and subsequently treated earlier. However, the extent of any survival gains as a result of screening will depend on the uptake rate.⁽²⁰⁵⁾

Figure 3.9 Estimated five-year net survival rate for colorectal cancer patients in Ireland before and after the introduction of BowelScreen across age groups



Source: NCRI and CSO (life tables). BowelScreen was introduced to people aged 60 to 69 years old in 2012 (yellow background). The periods "Before" and "After" BowelScreen refer to 2000 to 2011 and 2013 to 2018, respectively. The cohorts that were eligible for BowelScreen are emphasised by the black outline. The error bars represent the 95% confidence intervals. The net survival analysis was implemented using the relSurv package⁽²¹⁴⁾ in R 4.3. with the Pohar-Perme estimator.⁽²¹⁰⁾ The life tables used in the analyses were estimated by LSHTM⁽²¹⁵⁾ using the population and mortality data from CSO.⁽²⁰⁶⁾

Key: CSO – Central Statistics Office, LSHTM – London School of Hygiene and Tropical Medicine, NCRI – National Cancer Registry Ireland.

3.9.5 Adenoma prevalence

Adenomas are a precursor to CRC that frequently grow unnoticed due to a lack of obvious symptoms, and are detected and removed during colonoscopy. Consequently, the prevalence of adenomas in Ireland in the general population is unknown. International estimates of adenoma prevalence are briefly outlined in Section 3.10.2.

3.9.6 Future projection

A 2019 NCRI report provides cancer incidence projections for all cancers to the year 2045.⁽²¹⁶⁾ Due to the increasing and ageing population of Ireland, the number of CRC cases is projected to roughly double to 5,793 cases per year by 2045 (93–129% increase compared to 2015; including anal cancers, ICD-10 C21). However, the age-standardised incidence rate of colon and rectal cancers per capita is expected to remain stable (ranging from a 3% decrease to 2% increase) in the 30-year timeframe from 2015.⁽²¹⁶⁾ These projections do not account for future changes in screening programmes, treatments, or risk factors.⁽²¹⁶⁾

3.10 Burden of colorectal cancer in an international context

3.10.1 Colorectal cancer incidence and mortality

Worldwide, colorectal cancer incidence rates have increased over the last 30 years, while mortality has generally decreased. An analysis of data from the Global Burden of Disease Study 2017 reported an age-standardised CRC incidence rate of 23.2 per 100,000 person years, representing an increase of 9.5% between 1990 and 2017.⁽²¹⁷⁾ The age-standardised death rate in 2017 was 11.5 per 100,000 person-years,³ a decrease of 13.5% from 1990.⁽²¹⁷⁾ A 2021 analysis of GLOBOCAN data (combining colon, rectal and anal cancers; that is C18–21) suggested that CRC incidence rates were highest in Europe, Australia, New Zealand, Northern America and Eastern Asia,⁽⁵⁾ with incidence rates approximately four times higher in countries with a high High Development Index (HDI), compared with countries with a low or medium HDI.^(5, 218)

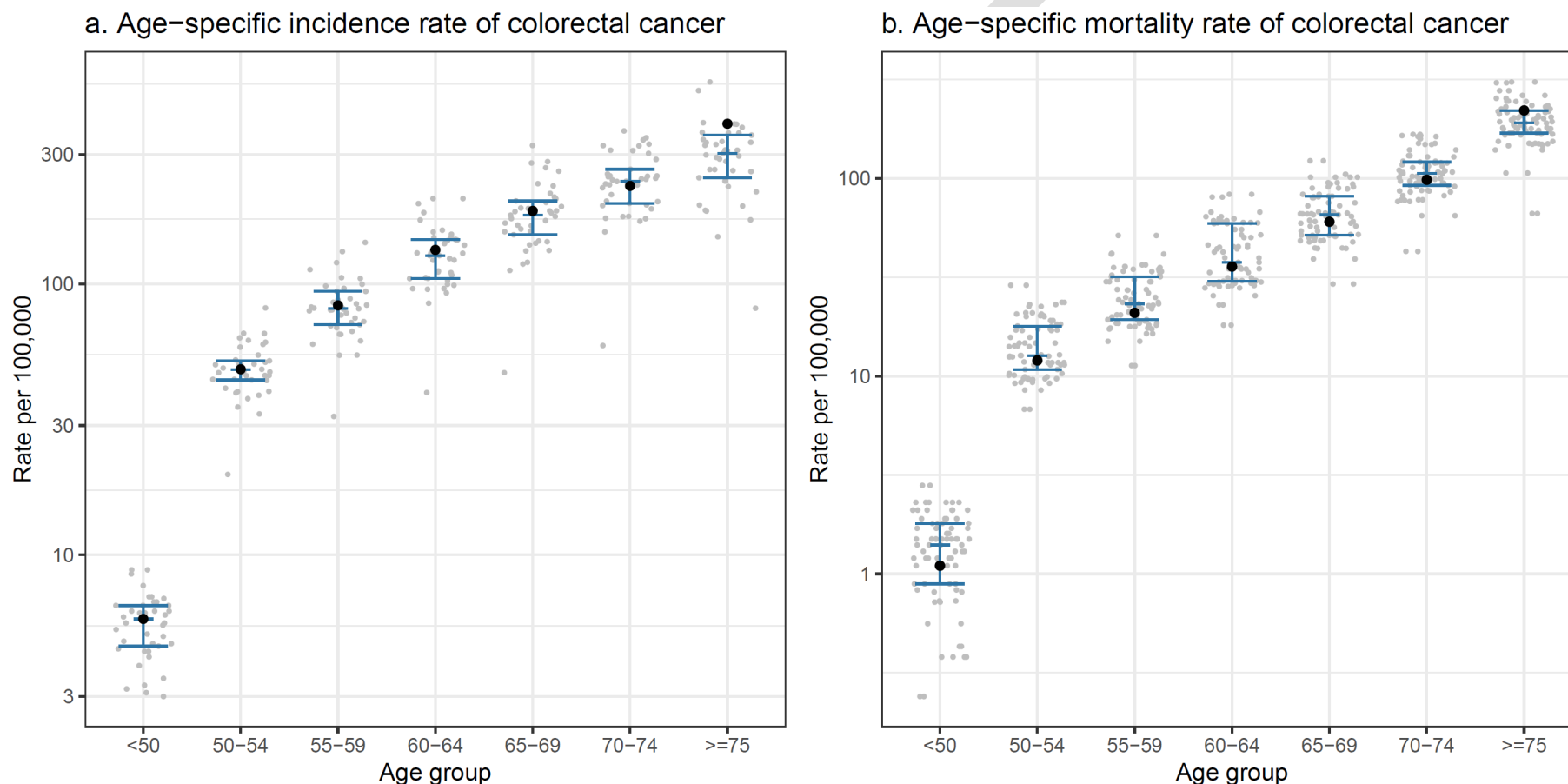
³ Note that mortality rates are commonly reported in the literature as either per persons or per person-years, which are not directly comparable. The former is the number of deaths in a scaled population (for example, 100,000 people) per unit of time, while the latter expresses the time-at-risk across patients.

In Europe, the number of new CRC cases increased by 70.2%, from 261,306 in 1990 to 444,872 in 2019, based on Global Burden of Disease data for 28 European Union countries.⁽²¹⁹⁾ The age-standardised incidence rate increased by 11.9% from 37.8 to 42.3 per 100,000 person-years between 1990 and 2019.⁽²¹⁹⁾ Age-standardised incidence rates in 2019 ranged from 29.2 per 100,000 person-years in Lithuania to 56.4 and 55.5 per 100,000 person-years in Slovakia and the Netherlands, respectively.⁽²¹⁹⁾ This compares with an age-standardised incidence rate of 46.0 per 100,000 person-years in Ireland in the same analysis. The age-standardised mortality rate also decreased in the EU by 16.9% from 22.4 to 18.6 per 100,000 person-years over the same time period.⁽²¹⁹⁾ Age-standardised mortality rates ranged from 12.3 per 100,000 person-years in Finland to 28.6 per 100,000 in Hungary. This compares with an age-standardised mortality rate of 18.0 per 100,000 person-years, in Ireland in the same analysis.

Age-specific colorectal cancer burden

The latest estimates of the age-specific CRC incidence and mortality rates per 100,000 people in Ireland are comparable to the European norm (that is, the middle 50% of values) in all but the oldest age group (over 75), for whom the rates are in the highest 25% of the European countries (Figure 3.10). Globally, both CRC incidence and mortality are higher in those aged over 50 years, compared to younger adults (86.3 vs. 2.9, 40.9 vs. 0.99 per 100,000 persons in 2020).⁽²¹⁸⁾ While the absolute number of CRC cases in people aged under 50 years is low compared to older age groups, some studies have noted an increase in CRC incidence rates in those under 50 years.⁽²²⁰⁾ A global analysis published in 2019 reported stable incidence rates in people under 50 in 14 of 36 countries, with declining incidence rates in this age group in three countries (Austria, Lithuania and Italy), and increasing incidence rates in the remaining 19 countries.⁽²²⁰⁾ In nine of the countries with increasing incidence rates in those aged under 50 (Australia, Canada, Denmark, Germany, New Zealand, Slovenia, Sweden, UK and US), the incidence rates in people aged 50 and older either decreased or remained stable over the same time period, highlighting the expanding risk of early-onset CRC.⁽²²⁰⁾ In Europe, CRC incidence increased from 0.8 to 2.3 cases per 100,000 persons in those aged 20–29 between 1990 and 2016.⁽²²¹⁾ In those aged 30–39, the incidence for men increased from 3.7 to 7.1 cases per 100,000 persons between 1990 and 2016, and from 2.8 to 6.4 cases per 100,000 persons in women between 2006 and 2016.⁽²²¹⁾ In those aged 40–49, the incidence increased from 15.5 to 19.2 cases per 100,000 persons between 2005 and 2016, following a period of relative stability between 1990 and 2004 (a decrease of 0.8%).⁽²²¹⁾

Figure 3.10 Age-specific incidence rate (a) and mortality rate (b) of colorectal cancer per 100,000 people in Ireland (black), other European countries (grey) and European quantiles (blue) in 2020



Source: GLOBOCAN.⁽⁵⁾ The upper and lower boundary of the error bars represent the first and third quantiles (25% and 75%) and the shorter bar in between represents the second quantile (50%, that is, the median). The y-axis is $\log_{10}$ transformed. Jurisdictions with fewer than 100,000 people were excluded. GLOBOCAN estimates are considered unaffected by the COVID-19 pandemic as they are based on data collected in years before the pandemic.⁽⁵⁾

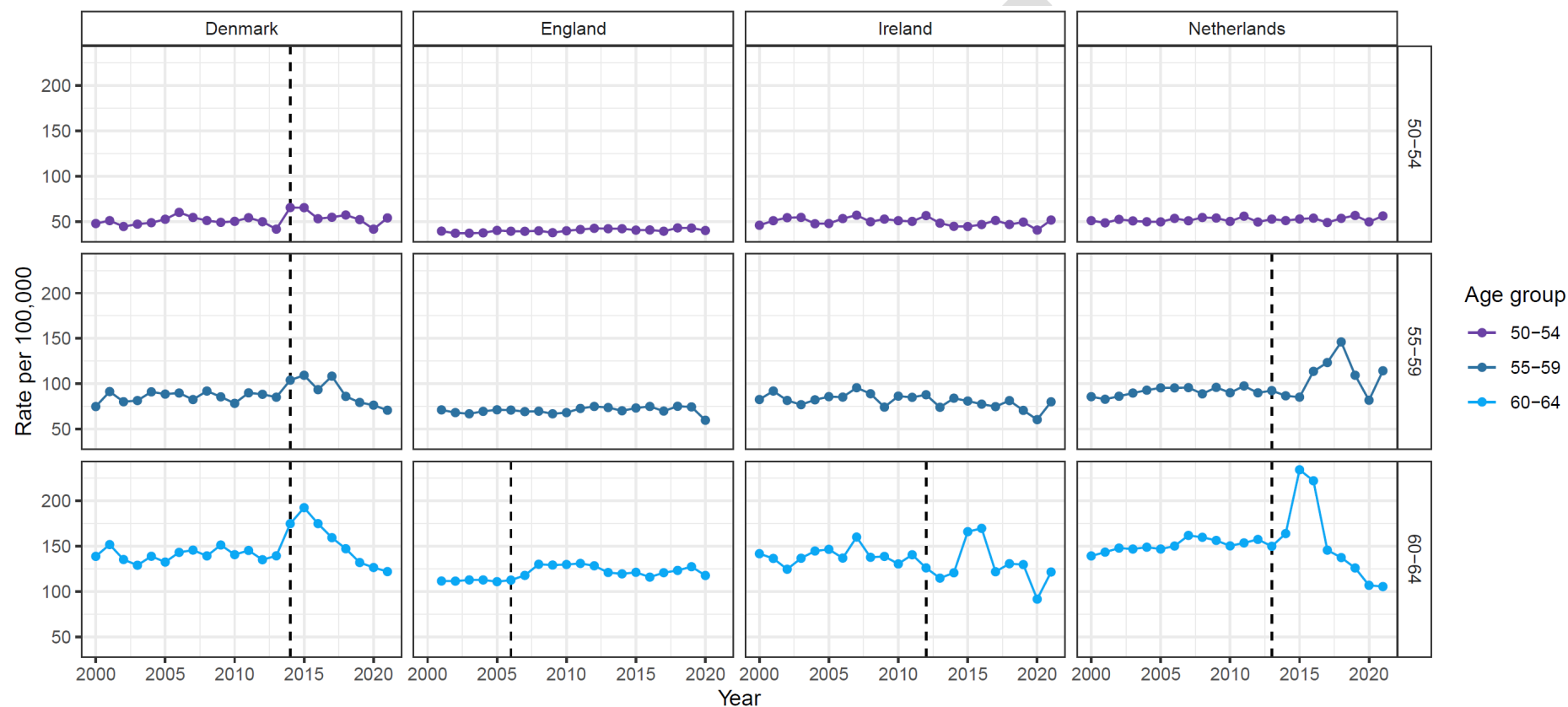
While early-onset CRC affecting those aged 50 or under has received ample attention in the international literature,^(220, 222-224) few analyses have focused on those aged 50–54, for whom an extension to the BowelScreen programme is under consideration. One study observed that the CRC incidence rate in those aged 50–54 is increasing in the US following a previous rise in early-onset CRC.⁽²²⁵⁾ A survey of northern European countries with various CRC screening programmes demonstrated that the CRC incidence rate in those aged 50–54 has remained stable since the early 2000s in Denmark and the Netherlands, with a modest 0.5% increase per year in England (Figure 3.11; Appendix A, section A.2). In these countries, the incidence rate in adjacent older cohorts (that is, 55–59 and 60–64) was greater than in those aged 50–54 (Figure 3.11). The incidence rate of CRC in Ireland in those aged 50–54 is equivalent to the European-wide incidence rate (48.4 per 100,000) according to the 2021 GLOBOCAN estimate.⁽⁵⁾

A statistically significant decline in the incidence rate following the introduction of a screening programme was observed in Denmark (among those aged 55–59 and 60–64). In England and the Netherlands, there was a statistically significant increase in the CRC incidence rate followed by a subsequent decline among those aged 60–64 following the introduction of a screening programme (Figure 3.11; Appendix A, section A.2).

3.10.2 Prevalence of colorectal adenomas

A 2020 meta-analysis of 70 population-based observational studies published between 1999 and 2018 reported a pooled prevalence of colorectal adenomas of 23.9% (95% CI 22.2% – 25.8%), with a prevalence of 4.6% (95% CI 3.8 – 5.5%) for advanced adenomas and 0.4% (95% CI, 0.3 – 0.5%) for CRC.⁽²²⁶⁾ The prevalence of adenomas, advanced adenomas and CRC was higher among males and people aged 50 years and older.⁽²²⁶⁾ A study of 296,170 screening colonoscopy patients in Austria between 2012 and 2018 reported a prevalence of adenomas of 16.3% in those aged 50–54, compared to 20.1% in those aged 55–59 and 23.6% in those aged 60–64.⁽²²⁷⁾ The prevalence of advanced adenomas was 4.7%, 6.1% and 7.5% in those aged 50–54, 55–59 and 60–64, respectively.

Figure 3.11 Colorectal cancer incidence rate per 100,000 people across age groups in Denmark, England, Ireland, and Netherlands



Source: ANCR (Denmark),⁽²²⁸⁾ NHS (England),⁽²²⁹⁾ NCRI (Ireland) and NCR (Netherlands).⁽²³⁰⁾

The dashed vertical lines represent the year of introduction of a colorectal cancer screening programme in the corresponding age group.

Key: ANCR – Association of Nordic Cancer Registries, NCR – Netherlands Cancer Registry, NCRI – National Cancer Registry Ireland, NHS – National Health Service.

3.11 Discussion

CRC is the third most commonly diagnosed cancer and the second leading cause of cancer death globally. The number of CRC cases in Ireland has risen over the past two decades, with the crude incidence rate peaking in 2015 and remaining stable since then. Worldwide, CRC incidence rates have increased over the last 30 years, while mortality has generally decreased. Consistent with global projections, the absolute burden of CRC is expected to continue to rise due to the projected increase in the population size and ageing population.^(144, 216, 231) Because early CRC development goes unnoticed in the absence of obvious symptoms, population-based screening programmes are a cornerstone of public health strategy against CRC.

Age is a key factor in shaping the risk of CRC, which is of particular relevance to the present assessment to evaluate evidence for extending BowelScreen to those aged 50–54. Treatment options, patient survival and quality of life generally worsen with increasing age.⁽¹⁷⁴⁾ Nonetheless, global and Irish data indicate that the burden of CRC has been increasing in younger people. As previously documented,⁽²³²⁾ the incidence rate of early-onset CRC, affecting people younger than 50, has been increasing in Ireland, despite the general decline in the CRC incidence rate among older age groups. This trend is generally replicated in other high-income countries.⁽²²²⁾

3.11.1 CRC incidence, mortality and stage distribution in those aged 50–54

Although analyses focusing specifically on those aged 50–54 are rare, the CRC incidence rate in this age group is rising in the US following a previous increase in early-onset CRC.⁽²²⁵⁾ In comparison, incidence among those aged 50–54 has remained stable since the early 2000s in Northern Europe, including Denmark, England, Ireland, and the Netherlands. In Ireland, the incidence rate for 50–54-year-olds averaged 47.3 per 100,000 between 2013 and 2021, mirroring the European average of 48.4 per 100,000 in this age group according to the 2021 GLOBOCAN estimate.⁽⁵⁾ Additionally, across the aforementioned Northern European countries, including Ireland, the incidence in those aged 50–54 has remained lower than the adjacent older cohorts (55–59 and 60–64).

Colorectal cancer mortality in those older than 60 in Ireland has declined over time. A European-wide study in 2017 found similar trends in other countries with an established screening programme (for example, Belgium, Denmark, Ireland, Lithuania, the Netherlands, and Slovenia), highlighting the plausible role of screening programmes in lowering mortality.⁽²³³⁾ Despite the general downward trend, the mortality rate in the US has increased by 0.5% to 3% each year in early-onset CRC patients between 2011 and 2020.⁽²³⁴⁾ Similarly, in Canada, the rectal cancer mortality rate of those aged 50 and under increased by 3.4–3.8% annually from

2000 to 2018.⁽²³⁵⁾ Nonetheless, the increasing trend in the CRC mortality rate among younger people is not universal in high-income settings: for example, Taiwan has seen a decline in mortality despite an increasing incidence.⁽²³⁶⁾ Some authors have suggested that the Western diet may have a role in elevating the mortality risk among younger CRC patients.⁽²³⁶⁾

Among adults aged between 40 and 84 in Ireland with symptomatically detected CRC, those aged 50–54 have the highest proportion of cancers detected at Stage III or Stage IV (67%, compared with 65% in those aged 55–59 and 63% in those aged 60–64). While the reason behind this observed peak at 50–54 is unclear, studies in several countries (Canada, Spain, Sweden, UK and US) have also reported a higher proportion of advanced stages among younger CRC patients.^(237–241) Some have speculated the role of physician bias, as younger patients may not be suspected of CRC upon symptomatic presentation.⁽²³⁸⁾ Among these countries – Canada, Spain, Sweden, UK and US – where advanced stages were more likely to be found in younger people, population-based CRC screening begins at the age of 50–60 (see Chapter 2, section 2.6). While some US guidelines recommend screening from the age of 45, uptake remains low.⁽²⁴²⁾ Low uptake of screening among younger people may delay the discovery of CRC in early stages.⁽²³⁸⁾ Furthermore, a survey study conducted in the UK concluded that public awareness of CRC symptoms was generally low among younger people (including those under 50).⁽²⁴³⁾ Since its introduction in 2012, the uptake rate of BowelScreen has been below 50%, ranging from 38.1% in those aged 60–64 to 49.9% in those aged 65–69. Screening uptake will be discussed further in Chapter 8 on Organisational considerations and Chapter 9 on Ethical, patient and social considerations.

3.11.2 Incidence, mortality, cancer stage distribution and adenoma prevalence in the current population eligible for screening

The Irish CRC screening programme, BowelScreen, was introduced in 2012 for people aged between 60 and 69. The majority of CRCs detected by BowelScreen during the first screening round was at Stage I, with males twice as likely to have CRC in every age group.⁽⁶¹⁾ Following its introduction, the proportion of CRC cases detected by screening increased over time, reaching the current level of roughly one fifth to a quarter by 2013–2014 and 2015–2016 among the older (65–69) and younger (60–64) cohorts, respectively. A population-based study of nine European countries found a wide range in the proportion of screen-detected cancers across countries, with many countries reporting screen detection in less than a third of colorectal cancers.⁽²⁴⁴⁾ The countries and regions with the highest proportions of screen-detected cancers (40–60%) were those with well-established FIT-based programmes with uptake rates over 50%.⁽²⁴⁴⁾

Net survival statistics were presented within this chapter for the period 2000–2011 and the five-year period 2013–2018 (post introduction of BowelScreen, 2012),

though comparisons between age groups were made only within the time period 2013–2018. Comparisons were not made between the two time periods given the likely impact of improvements in treatments over time on survival. Furthermore, while five-year survival is presented for 2013–2018, in terms of this representing the post-BowelScreen time period, it is important to note that screening was not rolled out to all those aged 60–69 immediately. While a five-year period from, for example, 2016–2021 might better reflect the full opportunity for screening for those aged 60–69, using this time period would be more limited with respect to survival analysis given the greater role of right censoring in those diagnosed in more recent years; that is, if death were to occur, this would be after the follow-up period had ended. Notwithstanding these caveats, among the age group that has been eligible for screening, the cohort aged 60–64 experienced higher five-year net survival (72%) compared to those aged 55–59 who remained ineligible (68%), based on five years of follow-up post diagnosis over the time period 2013–2018. This finding is despite the general negative impact of age on survival. Although other causes may contribute to the improved survival, screening leads to earlier detection, which can in turn improve the chance of CRC survival post-diagnosis. In Ireland, up to 38–41% of CRCs detected through screening have been found in the least advanced Stage I, while only 14–15% of symptomatically detected cases were found in Stage I.

Generally across Europe, a population-based study of nine countries corroborates that screen-detected cancers were more often at Stage I and less often at Stage IV compared to non-screen-detected cancers.⁽²⁴⁴⁾ It is worth noting, however, that early detection could also inflate net survival estimates with no influence on death if it leads to over-diagnosis of cancers that develop so slowly that the patient would eventually die of other causes.⁽²⁰⁹⁾ As such, mortality is considered a more appropriate statistic than survival for comparing across populations and time.⁽²⁰⁹⁾ Clinically, over-diagnosis and associated unnecessary patient harms have been a topic of much discussion in the context of breast cancer and prostate cancer.⁽²⁴⁵⁾ The possibility for CRC over-diagnosis was raised in a 2018 commentary,⁽²⁴⁶⁾ which speculates that the risk of over-diagnosis may be higher among older individuals with comorbidities.

An increase in the incidence following the introduction of a screening programme, and a subsequent decrease, has been documented in other countries and regions including the Netherlands, Denmark, Slovenia and Basque country.^(233, 247, 248) The initial increase in cases is attributed to the screening programme detecting cancer at earlier stages than it would be caught in routine clinical settings. Subsequently, the decrease in cases is attributed to the removal of cases by the screening programme that would have otherwise presented with symptoms, as well as adenomas that may have developed into CRC.⁽²⁴⁹⁾ While such a trend was absent in Ireland, it is possible

that a future expansion of BowelScreen may lead to a similar temporary pattern in the newly screening-eligible age group.

The estimated prevalence of adenomas in the population ranges from 22.2 to 25.8% in the international literature.⁽²²⁶⁾ In Ireland, only screening participants with a positive result on the faecal immunochemical test (FIT) are referred for colonoscopy. FIT detects blood in stool and has relatively low sensitivity for adenoma detection. The reported sensitivity of FIT for detecting advanced adenomas ranges from 18–31%,⁽⁴⁰⁾ and may be lower for detecting adenomas in general. Therefore, it is challenging to compare Irish adenoma data from BowelScreen to international estimates based on colonoscopy screening, which is the reference standard for adenoma and CRC detection. Age-specific estimates of adenoma prevalence are rare in the literature. However, an Austrian study from 2023 reported a prevalence of adenomas of 16.3% in those aged 50–54, compared to 20.1% in those aged 55–59 and 23.6% in those aged 60–64.⁽²²⁷⁾

3.11.3 Future projections

Due to the increasing and ageing population of Ireland, the overall number of CRC cases is projected to roughly double by 2045 (93–129% increase compared to 2015; including anal cancers, ICD-10 C21).⁽²¹⁶⁾ Specifically, the absolute burden of CRC in those aged 50–54 is expected to rise due to the projected increase in the population size: the CSO projected a 20.5% increase in the population size of this age group between 2024 and 2057.^(250, 251)

In addition to the increase in the absolute burden, the incidence rate for those aged 50–54 years may change over time. The expanding CRC burden in younger cohorts, including early-onset CRCs affecting those under 50, is of particular relevance to the proposed expansion of BowelScreen. Notably, it is plausible that the 50–54 age group in Ireland could experience an increased CRC incidence in the future, given that early-onset CRC incidence is already on the rise. Such a trend has been observed in the US, where the incidence rate among those aged 50–54 has risen following a previous increase in early-onset CRC.⁽²²⁵⁾ Mechanisms behind the increase in early-onset CRC remain an open question, as most young adults diagnosed with CRC lack known risk factors.⁽²⁵²⁾ Some authors allude to the role of early life exposure to risk factors, which may influence CRC development throughout the life course.⁽¹⁴⁵⁾

3.11.4 Conclusion

CRC often develops slowly with subtle symptoms in its early stages. This silent development highlights the importance of early detection and intervention. Cancers detected through the BowelScreen programme, which began in 2012, are largely detected at an early stage. As in several other high-income settings, the incidence of

CRC is increasing overall in Ireland, and particularly among people under 50. As the cohort matures, a similar increase is expected to be seen in older cohorts, for example in people aged 50–54, for whom the expansion of BowelScreen is proposed.

DRAFT

4 Test accuracy of FIT for the detection of colorectal cancer: consideration of differences by age

4.1 Key points

- This chapter reviewed the evidence on the clinical test accuracy of faecal immunochemical tests (FIT) for the detection of colorectal cancer (CRC) in asymptomatic, average-risk populations at thresholds similar to that used by the BowelScreen programme in Ireland (that is, 45µg of haemoglobin (Hb) per gram of faeces, µg/g). The review aimed to determine whether FIT test accuracy at a threshold of 45µg/g varies by age.
- A 2019 systematic review of the effect of age and positivity threshold on FIT test accuracy was used as a key source to identify relevant studies. An additional systematic search was performed to capture studies published since this review.
- Eleven studies, reported across 14 publications, met the inclusion criteria, with FIT thresholds ranging from 40 to 50µg/g. One study, reported across two publications, used thresholds of 40µg/g for women and 80µg/g for men.
- Six studies with a colonoscopy reference standard primarily focused on advanced neoplasia (AN) (a composite that includes both CRC and advanced adenoma (AA)) as the target condition. The reference standard for the remaining five studies was cancer or patient registry or medical record follow-up to identify interval cancers, and reported CRC as the target condition. Sample sizes, based on the number of participants with a valid FIT and colonoscopy or registry follow-up, ranged from 779 to over 2 million participants.
- Five studies, reported across six publications, included data stratified by age for FIT thresholds ranging from 40 to 80µg/g. Based on these limited data, no clear or consistent evidence was identified to suggest that FIT test accuracy for the detection of CRC at a threshold of 45µg/g varies significantly by age.
- The remaining seven studies reported data at FIT thresholds ranging from 40 to 45µg/g, without age stratification. Sensitivity and specificity of FIT for the detection of CRC varied considerably across all of these studies. With a colonoscopy reference standard, sensitivity of the OC-Sensor™ FIT device at a threshold of 40µg/g ranged from 60% (95% Confidence Interval [CI]: 26%, 88%), among participants aged 40–79 in the Oshima cohort study in

Japan, to 80% (95% CI 35%, 100%) in participants aged 50–69 in a colonoscopy screening trial in Spain, with a specificity of between 97% and 95%, respectively.

- Sensitivity for the detection of AN was similarly uncertain, with estimates ranging from 10% with the OC-Sensor™ FIT device in people aged 60 participating in a screening trial in Sweden, to 29% with FOB Gold® in colonoscopy screening participants aged 50–79 in Germany, both at a threshold of 40µg/g.
- One study with a registry reference standard, based on the Danish CRC screening programme, reported data for the FIT device, threshold, and target age range of the BowelScreen programme. Sensitivity of the OC-Sensor™ FIT device for the detection of CRC at a threshold of 45µg/g in participants aged 50–74 was 76% (95% CI: 74%, 77%), with a specificity of 96% (95% CI: 96%, 96%).
- FIT test accuracy for the detection of CRC may be impacted by a range of factors, including the FIT device and buffer solution used, as well as the presence of other health conditions and use of certain medications. Some of these may interact with age, limiting the comparisons that can be made across different settings and populations.

4.2 Introduction

Colonoscopy is considered the reference standard for the detection of colorectal cancer (CRC) and pre-cancerous lesions. However, it is an invasive procedure that is associated with risks of complications, including bleeding and perforation.^(49, 253)

Colonoscopy is also resource intensive, requiring access to specialist endoscopy facilities and trained endoscopists. When used as the primary screening modality, uptake rates tend to be low.^(254, 255) As a result, most population-based CRC screening programmes use a two-step strategy, in which non-invasive screening tests are used to identify individuals for further diagnostic testing. The most commonly used non-invasive CRC screening tests are faecal occult blood tests (FOBT), which aim to detect hidden (occult) blood in stool (see Chapter 2, section 2.3.1). FOBT-based CRC screening operates on the premise that blood vessels within larger colorectal polyps or cancers are fragile and easily damaged, resulting in bleeding.⁽²⁷⁾ As a result, blood in the stool is a potential indicator of pre-cancerous lesions or CRC.⁽²⁷⁾

Quantitative FIT are a type of FOBT that estimate the concentration of haemoglobin (Hb) in stool, measured in microgram (μg or mcg) of haemoglobin (Hb) per gram of faeces (or nanogram (ng) of Hb per ml of buffer solution). The concentration of Hb at or above which an individual is considered to have a positive screening test result is referred to as the FIT threshold, and determines whether or not they are referred for further investigation.^(25, 37) FIT thresholds are not fixed, and may be adjusted based on the positivity rate, sensitivity for CRC, or colonoscopy capacity.^(256, 257) In Ireland, the BowelScreen programme uses a quantitative FIT device (OC-Sensor™) as its primary screening tool, with a decision threshold of 45 μg Hb/g faeces (45 $\mu\text{g/g}$).

4.3 FIT test accuracy for the detection of colorectal cancer

The term 'test accuracy' can reflect either the analytical validity or laboratory accuracy of a test (that is, the closeness of measurements to the true value of the substance being measured), or its clinical performance characteristics as a diagnostic or screening test (that is, how well it discriminates between those who do and those who do not have a specific condition).⁽²⁵⁸⁾ In this HTA, the term 'test accuracy' is used to refer to the ability of FIT to detect colorectal cancer, rather than the extent to which the test accurately determines the level of Hb in stool. As the purpose of FIT is to detect Hb, some individuals who do not have colorectal cancer or pre-cancerous lesions will have a level of Hb above the screening threshold (for example, due to the presence of other medical conditions), and will be referred for colonoscopy. For screening purposes, this is referred to as a 'false positive' result, as the screening target condition has not been identified. Conversely, as CRC bleeds intermittently, some individuals who receive a 'negative' FIT result will in fact have colorectal cancer. In the context of CRC screening, this is considered a 'false negative' result.

To determine the accuracy of a screening test, its performance is compared with that of a 'reference standard'; that is, the best available method for determining the presence of the target condition. Sensitivity and specificity are common measures used to evaluate the performance of a screening or diagnostic test. An overview of these measures is provided in Box 4.1. Given the natural history of CRC, the target condition for screening is usually not limited to cancer, but also includes advanced pre-cancerous lesions (see Chapter 3, Section 3.3).

Box 4.1 Overview of measures used to determine test accuracy

Index test result (FIT)	Reference standard (Colonoscopy)	
	Condition present	Condition absent
Positive	True positive (a)	False positive (b)
Negative	False negative (c)	True negative (d)

- **Sensitivity** describes the proportion of those with the target condition that are correctly classified as positive by the index test:
 - Sensitivity = $a / (a + c)$
- **Specificity** describes the proportion of those without the target condition that are correctly classified as negative by the index test:
 - Specificity = $d / (b + d)$

Key: FIT – faecal immunochemical test.

The reported sensitivity and specificity of FIT for the detection of CRC and pre-cancerous lesions has varied widely, with differences varying according to the FIT device used and threshold applied to denote test positivity.^(40, 73, 259) A 2019 systematic review reported that for studies using OC-Sensor™ or OC-Micro FIT devices, sensitivity for CRC increased from 64% (95% Confidence Interval [CI]: 26%, 90%) at thresholds above 20µg/g to 74% (95% CI: 65%, 81%) at thresholds ≤10µg/g, while specificity correspondingly decreased from 96% (95% CI: 95%, 97%) to 90% (95% CI: 85%, 93%).⁽⁴⁰⁾ Sensitivity for advanced colorectal neoplasia ranged from 10% to 37% in a study comparing five different FIT devices, with specificity ranging from 86% to 97%.⁽³³⁾ FIT devices and systems vary in terms of sample collection techniques, buffer composition and volume, haemoglobin stability after sample collection and analytical technique.⁽³²⁾ Reporting of faecal haemoglobin concentration (f-Hb) is not standardised and a variety of units are used, with Hb concentration most commonly reported in µg Hb/g of faeces or ng Hb/ml of buffer. The latter reflects haemoglobin concentration in the sample buffer rather than the stool sample itself,⁽³²⁾ and is unique to each device or system. For OC-Sensor™ FIT devices, 100ng Hb/ml corresponds to 20µg Hb/g. However, there is no standard unit conversion that can be applied to all FIT devices, making it challenging to compare across studies and settings using different devices, thresholds or reporting units.

There is evidence to suggest that faecal haemoglobin levels increase with age.⁽²⁶⁰⁻²⁶³⁾ While CRC incidence also increases with age, elevated levels of f-Hb may be associated with other health conditions or the use of medications such as aspirin,^(264, 265) which are more common in older age groups. As CRC and pre-cancerous lesions

bleed intermittently, higher levels of background f-Hb among older screening participants could increase FIT sensitivity for the detection of these conditions. Conversely, in the absence of CRC or pre-cancerous lesions, higher levels of f-Hb (above the positivity threshold) among older age groups could result in lower specificity compared with younger participants. The extent to which test accuracy of FIT for the detection of CRC and pre-cancerous lesions at a threshold of 45µg/g may vary according to age is not clear. To inform decision-making by the National Screening Advisory Committee, this chapter aimed to assess whether the test accuracy of FIT for the detection of CRC at a threshold of 45µg/g (that is, the threshold currently used by the BowelScreen programme), varies by age.

4.4 Methods

This review is reported according to the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy studies (PRISMA-DTA) statement.⁽²⁶⁶⁾ A detailed background to the review and description of associated methods is provided in the accompanying [protocol](#). The protocol for this review was registered on the International Prospective Register of Systematic Reviews (PROSPERO, registration number: CRD42024532045).

4.4.1 Aim and review question

The aim of this review was to assess whether test accuracy of FIT for the detection of colorectal cancer varies by age. Specifically, the review sought to answer the following question:

- Does test accuracy of FIT for the detection of CRC at a threshold of 45µg/g vary by age?

Previous reviews of the sensitivity and specificity of FIT for the detection of advanced adenomas (AA) and CRC have generally considered lower FIT thresholds. Therefore, this review also considered the overall sensitivity and specificity of FIT for the detection of CRC at thresholds similar to that used by the BowelScreen programme in Ireland.

The review question was formulated according to the Population, Index test, Target condition (PIT) framework, presented in Table 4.1. Given the potential for screening to reduce CRC incidence through the detection and removal of pre-cancerous lesions, the following were included as target conditions in addition to CRC: adenomas; advanced adenomas; and advanced neoplasia (AN; consisting of CRC or AA).

Table 4.1. Research question for assessing FIT test accuracy

Population	Average-risk population, stratified by age where available.
Index test	Faecal immunochemical test (FIT) at a threshold of 45 ug/g. A range of thresholds may also be considered.
Target condition	Adenoma, advanced adenoma, advanced neoplasia, colorectal cancer.

4.4.2 Study eligibility

Table 4.2 outlines the inclusion and exclusion criteria. Eligible studies were required to include as reference standard either a direct visualisation test (preferably colonoscopy) for all participants, or follow-up of participants using medical records or a cancer or patient registry to identify interval cancers (that is, people who received a false negative FIT result). Studies of qualitative FITs (such as Hemoccult[®] ICT or Hemosure[®] iFOB), which require visual interpretation and cannot be subjected to automated analysis,^(32, 33) were excluded. Studies were not excluded on the basis of study design.

4.4.3 Identification of studies

Initial scoping identified a number of systematic reviews of FIT test accuracy, including a 2021 review by the United States Preventive Services Task Force (USPSTF)⁽⁷³⁾ and a 2019 review by Selby et al.,⁽⁴⁰⁾ the latter of which specifically explored FIT test accuracy at different thresholds and according to age. These reviews were chosen as a key source for identification of test accuracy studies for the present review. A de novo search strategy was developed by a librarian and peer reviewed by a second librarian. This search was designed to identify relevant studies published since the 2019 Selby et al. review. The complete reproducible search strategy for all databases searched is available on Zenodo[®].⁽²⁶⁷⁾ Forward citation searching of the Selby et al. review and of included studies was performed using the Citationchaser package.⁽²⁶⁸⁾

Table 4.2 Inclusion and exclusion criteria for assessing test accuracy

	Inclusion criteria	Exclusion criteria
Population	Average-risk asymptomatic population, stratified by age where available.	Symptomatic populations or those at high genetic risk of CRC, including Lynch syndrome or hereditary non-polyposis colorectal cancer and familial adenomatous polyposis.
Index test	Quantitative FIT	Qualitative FIT, guaiac-based faecal occult blood tests (gFOBT)
Reference standard	Colonoscopy (or other direct visualisation test) for all participants, or colonoscopy (direct visualisation) for FIT-positive participants in combination with at least one year of follow-up of FIT-negative participants using medical records or cancer registry.	Colonoscopy or other direct visualisation test for FIT-positive participants only with no follow-up of FIT-negative participants.

Key: CRC – colorectal cancer. FIT – faecal immunochemical tests. gFOBT – guaiac-based faecal occult blood test.

Study selection

Studies included in the Selby et al. and USPSTF reviews were examined for relevance to the present review according to the criteria outlined in Table 4.1 and Table 4.2. Two reviewers screened the titles and abstracts identified through the search for additional studies and independently assessed the full text of potentially eligible studies according to the criteria outlined in Table 4.2. Disagreements were resolved by discussion or a third reviewer. Screening was undertaken using Covidence software.

4.4.4 Data extraction and management

The following data were extracted for each study: publication year, first author, country or region and setting, sample size, details of the FIT and reference standard (FIT device and threshold, type and timing of reference standard), target conditions (CRC, AN, AA), and number of participants with each condition. True positives (TP), false positives (FP), true negatives (TN), false negatives (FN), sensitivity and specificity were extracted for each target condition (CRC, AN, AA) if reported by each study. Where sensitivity and specificity were not reported, estimates were calculated as detailed in Box 4.1. For studies that reported sensitivity and specificity

without the corresponding 2x2 tables, TP, FP, TN and or FN were derived from the available data (Box 4.2). Data were extracted by one reviewer using Microsoft Excel software and reviewed by a second reviewer, with disagreements resolved by discussion. Where data were presented graphically only, numeric estimates were extracted using WebPlotDigitizer. For publications with overlapping data, data from the most recent publication were extracted, supplemented with additional information from earlier publications where appropriate. Where studies reported data for multiple rounds of FIT screening, or for multiple FIT samples, data relating to the first screening round and first FIT sample were extracted to improve comparability across studies.

Box 4.2 Calculation of 2x2 tables based on sensitivity and specificity

Parameter	Formula
True positives (TP)	$(\text{Sensitivity}) \times (\text{Prevalence}) \times (\text{Total})$
False negatives (FN)	$(\text{Prevalence}) \times (\text{Total}) \times (1 - \text{Sensitivity})$
True negatives (TN)	$(\text{Specificity}) \times (\text{Total}) \times (1 - \text{Prevalence})$
False positives (FP)	$(\text{Total}) \times (1 - \text{Prevalence}) \times (1 - \text{Specificity})$

Risk of bias and applicability assessment

The risk of bias and applicability of each study was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2).⁽²⁶⁹⁾ QUADAS-2 consists of four domains: patient selection, index test, reference standard, and flow and timing. Risk of bias is assessed for each domain, while the applicability of the results of each study to the review question is assessed for the first three domains.⁽²⁷⁰⁾ Each study was assessed by one reviewer, with the assessment cross-checked by a second reviewer.

Data synthesis

Results were synthesised narratively according to target condition and reference standard. Due to variations in FIT devices, target conditions, reference standards and exclusion criteria, meta-analysis was not conducted.

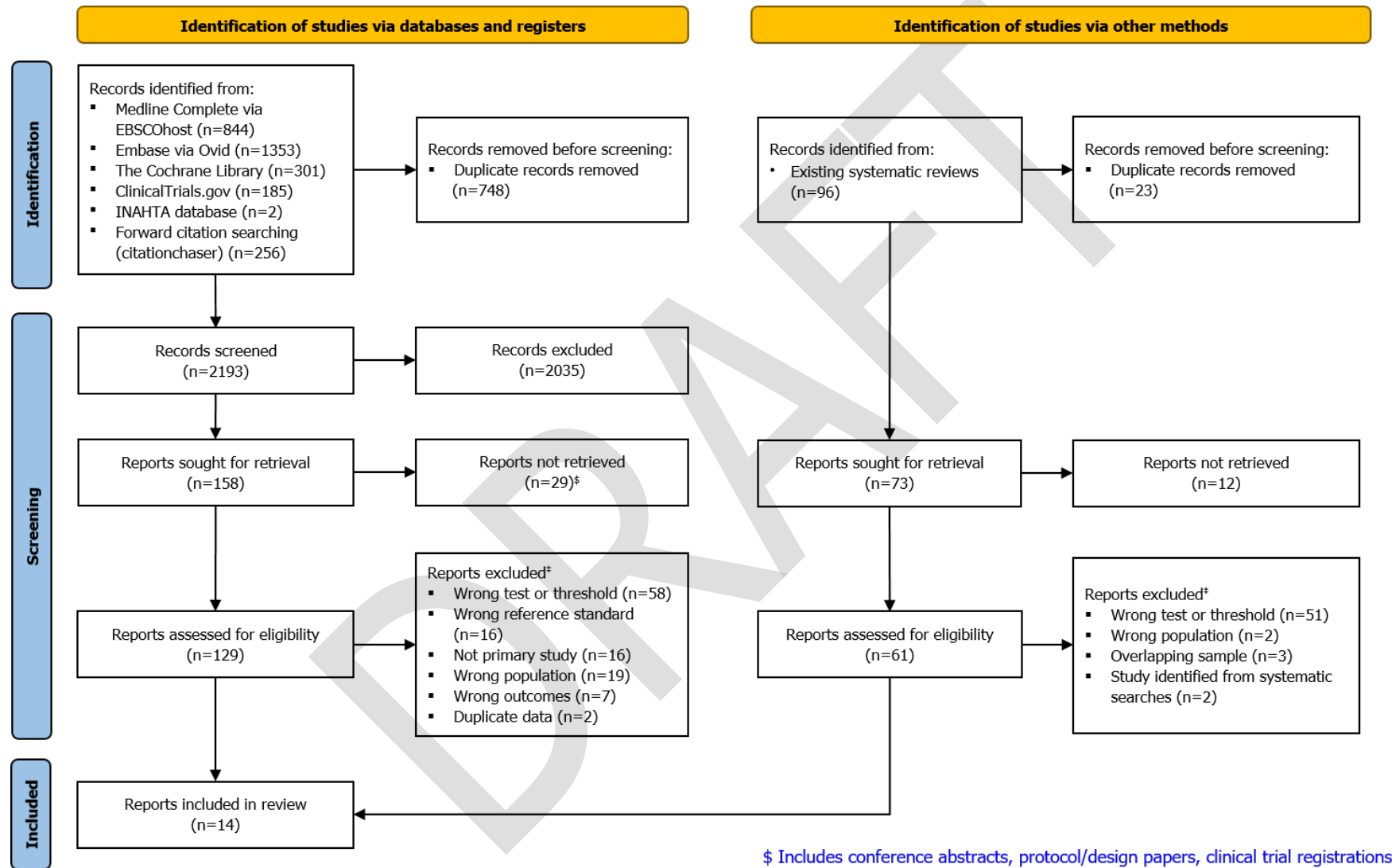
4.5 Results

An overview of the study selection process is presented in Figure 4.1. The de novo and forward citation searches (that is, updated searches) resulted in the identification of 2,941 records. After removal of duplicates, 2,193 titles and abstracts were assessed for eligibility. As initial scoping had identified limited studies that reported FIT test accuracy data for thresholds $\sim 45\mu\text{g/g}$, a two-step process was followed for title and abstract and full-text screening. Firstly, all studies reporting relevant data for FIT thresholds above $20\mu\text{g/g}$, and all studies with age-stratified data, regardless of threshold, were identified. A total of 29 records from the updated searches met these initial broad inclusion criteria. Ten studies that met these criteria were identified from the 2019 review by Selby et al., with one additional study identified from the 2021 USPSTF review.

Studies were excluded if they included health examination or hospital inpatient and outpatient populations (that is, not general screening populations), or calculated individualised FIT cut-offs based on age, sex or according to desired positivity thresholds or specificity (see Appendix B, Table B.1). Of the 29 records from the updated searches, 24 were carried forward based on these exclusions. Among the remaining 24 publications, eight studies reported across 11 publications included sufficient data for FIT thresholds between 40 and $50\mu\text{g/g}$ to enable calculation of sensitivity and specificity. Considering the 10 studies in the Selby et al. 2019 systematic review, three additional studies were identified to have reported data for FIT thresholds between 40 and $50\mu\text{g/g}$. No additional studies were identified from the 2021 USPSTF review.

As the main question of interest to this review was whether FIT test accuracy at a threshold of $45\mu\text{g/g}$ varies by age, and given that other systematic reviews have synthesised data on FIT test accuracy at lower thresholds,^(40, 73) the present review was limited to these 11 studies (three from the Selby et al. review, and eight from the updated searches), reported across 14 publications.^(89, 110, 256, 257, 271-280)

Figure 4.1 Flowchart of included studies



4.5.1 Characteristics of included studies

Table 4.3 details the characteristics of included studies. Of the 14 publications, two each reported on data from the Dutch CRC screening programme,^(110, 256) a colonoscopy screening study in Germany (Begleitende Evaluierung innovativer Testverfahren zur Darmkrebsfrüherkennung: BLITZ),^(271, 272) and a regional CRC screening programme in Stockholm-Gotland in Sweden.^(89, 274) One study each reported findings from a colonoscopy screening trial in Spain (COLONPREV)⁽²⁷⁹⁾ and the colonoscopy screening arm of a screening trial in Sweden (SCREENing of Swedish COLons: SCREESCO).⁽²⁷³⁾ The remaining studies reported data from the Danish CRC screening database,⁽²⁷⁵⁾ the Scottish Bowel Screening Programme,⁽²⁸⁰⁾ a multi-centre cohort study of regional CRC screening programmes in Spain (CRIBEA-CIN),⁽²⁷⁶⁾ the Oshima cohort study in Japan,⁽²⁷⁷⁾ a population-based screening pilot in the Netherlands,⁽²⁷⁸⁾ and a multi-centre health promotion programme in Thailand.⁽²⁵⁷⁾ Sample sizes, based on the number of participants with a valid FIT and colonoscopy or registry follow-up, ranged from 779 to 2,302,711. The age of participants ranged from 40 to 80 years, with eight studies including individuals from age 50.^(257, 271, 272, 275, 276, 278-280) Sample descriptions and demographic characteristics are included in Appendix B (Table B.2).

The majority of studies used OC-Sensor™ FIT devices,^(89, 257, 273-275, 277-279) with studies reporting data from the Dutch CRC screening programme and the German BLITZ study using FOB Gold®.^(110, 256, 271, 272) The CRIBEA-CIN study involved the use of various FIT devices during the study period.⁽²⁷⁶⁾ The FIT device used in the Scottish Bowel Screening Programme was not specified.⁽²⁸⁰⁾ Seven publications included colonoscopy for all participants as reference standard and predominantly reported AN as the target condition.^(257, 271-273, 277-279) The remaining seven publications included two-year cancer registry or medical record follow-up of all participants to identify interval cancers as reference standard, and reported CRC as the target condition.^(89, 110, 256, 274-276, 280) Studies with a colonoscopy reference standard reported data for a variety of thresholds, ranging from <1.7 to 50µg/g for FOB Gold®, and from 5 to 200µg/g for OC-Sensor™ (corresponding to 25 to 1000ng/ml).^(257, 271-273, 277-279) The Stockholm-Gotland screening programme used a threshold of 40µg/g for women and 80µg/g for men.^(89, 274) Two studies reported FIT sensitivity for the detection of advanced adenomas.^(271, 277)

Table 4.3 Characteristics of included studies

Author, year	Country	Design and setting	Age range	Age-stratified results	Target conditions	FIT device, thresholds	Reference standard
Aniwan 2017 ⁽²⁵⁷⁾	Thailand	Multi-centre health promotion study	50–75	NR	AN	OC-Sensor™ 25 to 200ng/ml	Colonoscopy
Breekveldt 2023 ⁽²⁵⁶⁾	Netherlands	National CRC screening cohort	55–75	55–59, 60–64, 65–69, 70–74, 75+	CRC	FOB Gold® 47µg/g	2yr registry follow-up
Brenner 2018 ^{¥(271)}	Germany	Screening cohort (BLITZ study)	50–79	50–64, 65–79	CRC, AN, AA	FOB Gold® 10 to 50µg/g	Colonoscopy
Digby 2023 ⁽²⁸⁰⁾	Scotland	National CRC screening cohort	50–74	50–54, 55–59, 60–64, 65–69, 70–74 ^Ω	CRC	Not reported 40µg/g, 80µg/g	2yr registry follow-up
Grobbee 2017 ⁽²⁷⁸⁾	Netherlands	Population-based screening pilot	50–75	NR	CRC, AA, AN	OC-Sensor™ 10 to 40µg/g	Colonoscopy
Hernandez 2014 ⁽²⁷⁹⁾	Spain	COLONPREV screening trial	50–69	NR	CRC, AN	OC-Sensor™ 50 to 200ng/mL	Colonoscopy
Niedermaier 2023 ⁽²⁷²⁾	Germany	Screening cohort (BLITZ study)	50–80	50–59, 60–79	AN	FOB Gold® <1.7 to 50µg/g	Colonoscopy
Njor 2021 ⁽²⁷⁵⁾	Denmark	Register-based prospective cohort	50–74	NR	CRC	OC-Sensor™ 35 to 1000ng/ml	2yr registry follow-up
RibbingWilén 2019 ⁽²⁷³⁾	Sweden	SCREESCO screening trial (colonoscopy arm)	60	NR	CRC, AA, AN, non-AA	OC-Sensor™ 10 to 80µg/g	Colonoscopy
RibbingWilén 2022 ^{±(274)}	Sweden	Population-based screening cohort	60–69	60–64, 65–69	CRC	OC-Sensor™ 40µg/g (women), 80µg/g (men)	2yr registry follow-up
RibbingWilén 2024 ⁽⁸⁹⁾	Sweden	Population-based screening cohort	60–69	60–64, 65–69 (by sex only)	CRC	OC-Sensor™ 40µg/g (women), 80µg/g (men)	2yr registry follow-up
Sekiguchi 2021 ⁽²⁷⁷⁾	Japan	Oshima cohort	40–79	NR	AN	OC-Sensor™ 50 to 200ng/mL	Colonoscopy
Toes-Zoutendijk 2020 ^{\$(110)}	Netherlands	National CRC screening cohort	60–76	60, 63, 65, 67, 75, 76	CRC	FOB Gold® 15, 47µg/g	2yr registry follow-up
Vanaclocha-Espi 2021 ⁽²⁷⁶⁾	Spain	CRIBEA-CIN multi-centre cohort	50–69	50–59, 60–69	CRC	Various 20 to 40µg/g	2yr registry follow-up

¥ Study sample overlaps with Niedermaier 2023. ± Study sample overlaps with RibbingWilén 2024. \$ Study sample overlaps with Breekveldt 2023.

Ω Age-stratified results for FIT threshold 80µg/g only.

Key: AA – Advanced adenoma. AN – Advanced neoplasia. BLITZ – Begleitende Evaluierung innovativer Testverfahren zur Darmkrebsfrüherkennung.

CRC – colorectal cancer. NR – not reported. SCREESCO – SCREening of Swedish COLons.

4.5.2 Sensitivity and specificity of FIT for the detection of CRC or AN by age

Five studies, reported across six publications, either reported age-stratified results for FIT sensitivity and specificity at thresholds between 40 and 80µg/g, or included sufficient data to facilitate the calculation of these estimates.^(89, 256, 271, 272, 274, 276) Of these, two studies presented age-stratified results by sex only.^(89, 276) One additional study reported age-stratified results at a FIT threshold of 80µg/g only.⁽²⁸⁰⁾

Detection of CRC: studies with a registry follow-up reference standard

Table 4.4 displays estimates of sensitivity and specificity for the detection of CRC by age based on three studies, reported across four publications, with a medical record or registry reference standard.^(89, 256, 274, 276) Based on data from the Dutch CRC screening programme with FOB Gold® at a threshold of 47µg/g, sensitivity for CRC appeared to decrease with age, ranging from 88.1% (95% CI: 86.1%, 90.0%) in those aged 55–59 to 82.7% (95% CI: 81.3%, 84.0%) in those aged 75 and over.⁽²⁵⁶⁾ Specificity ranged from 95.6% in those aged 55–59 to 91.6% in those aged 75 and over (95% CI not reported).

Sensitivity for the detection of CRC at a threshold of 40µg/g in the CRIBEA-CIN study was 79.7% among women aged 50–59, compared to 76.4% in women aged 60–69. Among men, sensitivity for CRC was 77.8% in those aged 50–59 and 81.8% in those aged 60–69.⁽²⁷⁶⁾ In a study reporting data from a regional CRC screening programme in Sweden, which uses different positivity thresholds for men and women, sensitivity for the detection of CRC in men aged 60–64 and 65–69 at a threshold of 80µg/g was 69.2% and 59.4%, with a specificity of 97.7% and 97.2%, respectively.⁽⁸⁹⁾ In women, sensitivity at a threshold of 40µg/g was similar in both age groups (75.6% in those aged 60–64 and 75.9% in those aged 65–69), with a specificity of 97.5% in the younger and 97.0% in the older age group. While these estimates are based on the first FIT screening round, FIT screening was preceded by a gFOBT programme in the Stockholm-Gotland region, which may partially explain the lower sensitivity among men aged 65–69, who would have been eligible for a greater number of previous screening rounds compared to those aged 60–64. The preceding gFOBT screening was noted by the authors to have been less effective in women, leading to increased CRC detection in women after switching to FIT.⁽⁸⁹⁾ The pooled sensitivity for men and women, reported in an earlier publication, was 69.7% in those aged 60–64 and 65.3% in those aged 65–69.⁽²⁷⁴⁾ Specificity, derived from the available data, was 97.6% and 97.1% in those aged 60–64 and 65–69, respectively.

Table 4.4 Sensitivity and specificity of FIT for the detection of CRC by age and sex (registry reference standard)

Author, year	FIT device, threshold ^{\$}	Age	Sex	FIT participants <i>n</i>	Positivity rate	Cases (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity
Breekveldt 2023 ⁽²⁵⁶⁾	FOB Gold® 47µg/g	55–59	NA	353,178	4.6%	899/1,021	88.1 (86.1, 90.0)	95.6 ^Ω
		60–64	NA	813,106	5.6%	3,248/3,842	84.5 (83.4, 85.7)	94.8 ^Ω
		65–69	NA	673,110	6.9%	3,985/4,714	84.5 (83.5, 85.6)	93.6 ^Ω
		70–74	NA	187,583	8.3%	1,511/1,790	84.4 (82.7, 86.1)	92.4 ^Ω
		75+	NA	275,734	9.2%	2,540/3,072	82.7 (81.3, 84.0)	91.6 ^Ω
Vanaclocha-Espi 2021 ^{&(276)}	Various 40µg/g	50–59	Male	NR	NR	NR	77.8	95.5
		60–69	Male	NR	NR	NR	81.8	94.0
		50–59	Female	NR	NR	NR	79.7	97.4
		60–69	Female	NR	NR	NR	76.4	96.6
Ribbing Wilén 2024 ⁽⁸⁹⁾	OC-Sensor™ 80µg/g	60–64	Male	42,159	2.5%	72/104	69.2 ^Ω (60, 78)	97.7 ^Ω
		65–69	Male	26,679	3.0%	63/106	59.4 ^Ω (50, 69)	97.2 ^Ω
	OC-Sensor™ 40µg/g	60–64	Female	46,460	2.6%	59/78	75.6 ^Ω (66, 85)	97.5 ^Ω
		65–69	Female	31,680	3.2%	63/83	75.9 ^Ω (67, 85)	97.0 ^Ω
Ribbing Wilén 2022 ⁽²⁷⁴⁾	OC-Sensor™ 40–80µg/g [¥]	60–64	Both	88,619	2.0%	131/188	69.7	97.6 ^Ω
		65–69	Both	58,359	2.4%	126/193	65.3	97.1 ^Ω

Note: Unadjusted 95% CI as reported by the included studies. \$ converted from ng/ml for OC-Sensor™ if appropriate. & Sensitivity and specificity extracted from a figure using WebPlotDigitizer. ¥ FIT threshold 40µg/g for women, 80µg/g for men. Ω Estimates derived from available data.

Key: FIT – Faecal immunochemical test. NA – not applicable. NR – Not reported. SD – screen detected.

Detection of AN: studies with a colonoscopy reference standard

Two publications with overlapping data from the BLITZ colonoscopy screening study reported – or included sufficient information to facilitate the calculation of – sensitivity and specificity for advanced neoplasia by age.^(271, 272) Niedermaier et al. reported data for a FIT threshold of 45µg/g, with results stratified by age 50–59 and 60–79 (Table 4.5).⁽²⁷²⁾ The sensitivity of FIT for the detection of AN in those aged 50–59 years was 22.9%, compared to 29.9% in those aged 60–79 (95% CIs not reported). Specificity in those aged 50–59 and 60–79 was 97.4% and 96.9%, respectively. As neither tests for difference nor 95% confidence intervals for the point estimates were reported, it is not clear to what extent these estimates represent true differences between the age groups.

Table 4.5 Sensitivity and specificity of FIT for the detection of AN by age (colonoscopy reference standard)

Author, year	Age	FIT participants <i>n</i>	Positivity rate	AN cases SD/all <i>n</i>	Sensitivity	Specificity
Niedermaier 2023 ⁽²⁷²⁾	50–59	3,605	4.2%	67/293	22.9 ^Ω	97.4 ^Ω
	60–79	3,793	6.2%	130/435	29.9 ^Ω	96.9 ^Ω

^Ω Estimates derived from available data. 95% confidence intervals for sensitivity and specificity not reported.

FIT device: FOB Gold® with a threshold of 45µg/g.

4.5.3 Sensitivity and specificity of FIT for the detection of CRC and AN at a threshold of 45µg/g: all ages

This section considers the sensitivity and specificity of FIT at thresholds similar to that used by the BowelScreen programme in Ireland (that is, close to the 45µg/g threshold). Study data that were presented for these thresholds were not broken down by age group; therefore, this section considers overall sensitivity and specificity.

Studies with a colonoscopy reference standard

Estimates of sensitivity and specificity of FIT for the detection of CRC varied considerably across studies (Table 4.6). With a colonoscopy reference standard, the reported sensitivity for the detection of CRC of OC-Sensor™ at a threshold of 40µg/g ranged from 60.0% (95% CI: 26.2%, 87.8%) in a study of 1,191 participants aged 40–79 in the Oshima CRC screening cohort study in Japan, to 80.0% (95% CI: 35.0%, 100.0%) in the COLONPREV colonoscopy screening trial in Spain, with specificity ranging from 94.7% (95% CI: 93.0%, 96.0%) to 96.6% (95% CI not

reported). Figure 4.2 displays a forest plot of FIT sensitivity and specificity for the detection of CRC for studies with a colonoscopy reference standard, calculated using extracted or derived 2x2 tables (see Appendix B Table B.3 for 2x2 tables).

The number of CRC cases in studies with a colonoscopy reference standard were low, ranging from a single cancer case in a sample of participants from the SCREESCO trial and five cases in the COLONPREV trial to 54 in the German BLITZ study. As a result, these studies focused mainly on advanced neoplasia (AN), a composite target condition that includes both CRC and advanced adenoma (AA). Sensitivity for AN ranged from 9.9% (95% CI: 4.4%, 18.5%) with OC-Sensor™ at a threshold of 40µg/g in the SCREESCO trial, to 28.6% (95% CI: 23.7%, 34.0%) with FOB Gold® at a threshold of 40µg/g in the BLITZ study (Table 4.6). The single case of CRC detected in the SCREESCO trial may have contributed to the lower FIT positivity rate (2.4%) and sensitivity in this study; sensitivity for the detection of AN in all other studies was above 16%. Specificity ranged from 96.3% to 98.6% (95% CIs not reported). Figure 4.3 displays a forest plot of FIT sensitivity and specificity for the detection of AN for studies with a colonoscopy reference standard, calculated using extracted or derived 2x2 tables.

Two studies with colonoscopy as reference standard reported FIT sensitivity for advanced adenomas, with sensitivity ranging from 13.7% (95% CI: 7.7%, 22.0%) to 24.1% (95% CI: 19.3%, 29.5%) (Table 4.6).^(271, 277)

Table 4.6 Sensitivity and specificity of FIT for the detection of CRC and AN (colonoscopy reference standard)

Author, year	FIT device, threshold ^{\$}	FIT participants <i>n</i>	Positivity rate	Colorectal cancer			Advanced neoplasia			Advanced adenomas	
				CRC (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity (95% CI)	AN (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity (95% CI)	AA (SD/all) <i>n</i>	Sensitivity (95% CI)
Aniwan 2017 ⁽²⁵⁷⁾	OC-Sensor™ 40µg/g	1,479	4.9%	9/14	64.3 (38.4, 88.2)	95.6 (94.5, 96.7)	23/137	16.8 (11.5, 23.9)	96.3 (95.1, 97.1)	<i>NR/123</i>	<i>NR</i>
Brenner 2018 ^{*(271)}	FOB Gold® 40µg/g	3,211	5.2%	20/25	80.0 (59.3, 93.2)	95.4 ^Ω	89/311	28.6 (23.7, 34.0)	97.3 (96.7, 97.9)	69/286	24.1 (19.3, 29.5)
	FOB Gold® 50µg/g	3,211	4.5%	18/25	72.0 (50.6, 87.9)	96.0 ^Ω	77/311	24.8 (20.1, 29.9)	97.7 (97.0, 98.2)	59/286	20.6 (16.1, 25.8)
Grobbee 2017 ⁽²⁷⁸⁾	OC-Sensor™ 40µg/g	1,256	3.5%	<i>NR/8</i>	<i>NR</i>	<i>NR</i>	28/119	23.5 ^Ω	98.6 ^Ω	<i>NR/111</i>	<i>NR</i>
Hernandez 2014 ⁽²⁷⁹⁾	OC-Sensor™ 40µg/g	779	5.8%	4/5	80.0 (35.0, 100.0)	94.7 ^Ω (93.0, 96.0)	27/97	27.8 ^Ω (18.0, 37.0)	97.4 ^Ω (96.0, 99.0)	<i>NR/92</i>	<i>NR</i>
Niedermaier 2023 ^{*(272)}	FOB Gold® 45µg/g	7,398	5.2%	43/54	79.6 ^Ω	95.3 ^Ω	197/728	27.1 ^Ω	97.1 ^Ω	<i>NR/674</i>	<i>NR</i>
RibbingWilén 2019 ⁽²⁷³⁾	OC-Sensor™ 40µg/g	806	2.4%	<i>NR/1</i>	<i>NR</i>	<i>NR</i>	8/81 [¥]	9.9 (4.4, 18.5)	98.5 (97.3, 99.2)	<i>NR/80</i>	<i>NR</i>
Sekiguchi 2021 ⁽²⁷⁷⁾	OC-Sensor™ 40µg/g	1,191	3.9%	6/10	60.0 (26.2, 87.8)	96.6 ^Ω	20/112	17.9 (11.3, 26.2)	97.6 (96.5, 98.4)	14/102	13.7 (7.7, 22.0)

Note: Unadjusted 95% CI as reported by studies.

* Overlapping study samples.

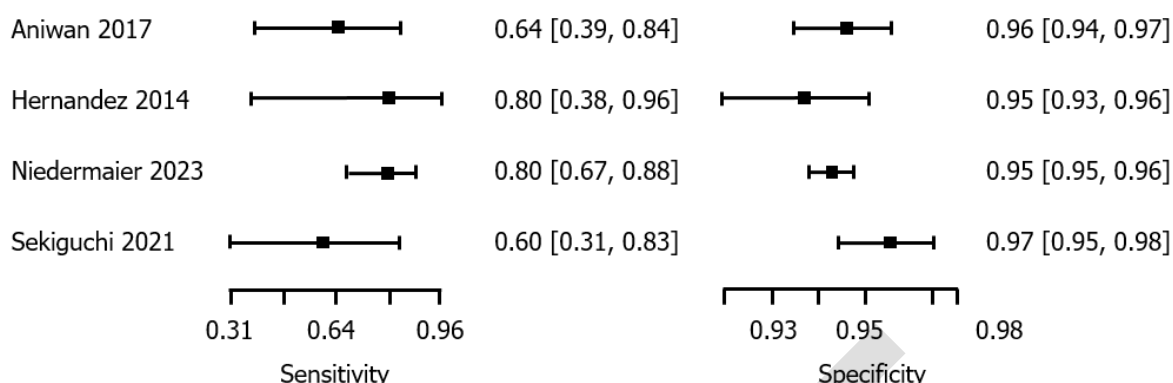
\$ converted from ng/ml for OC-Sensor™ if appropriate.

¥ 81 AN: 80 AA, 1 CRC.

Ω Estimates derived from available data.

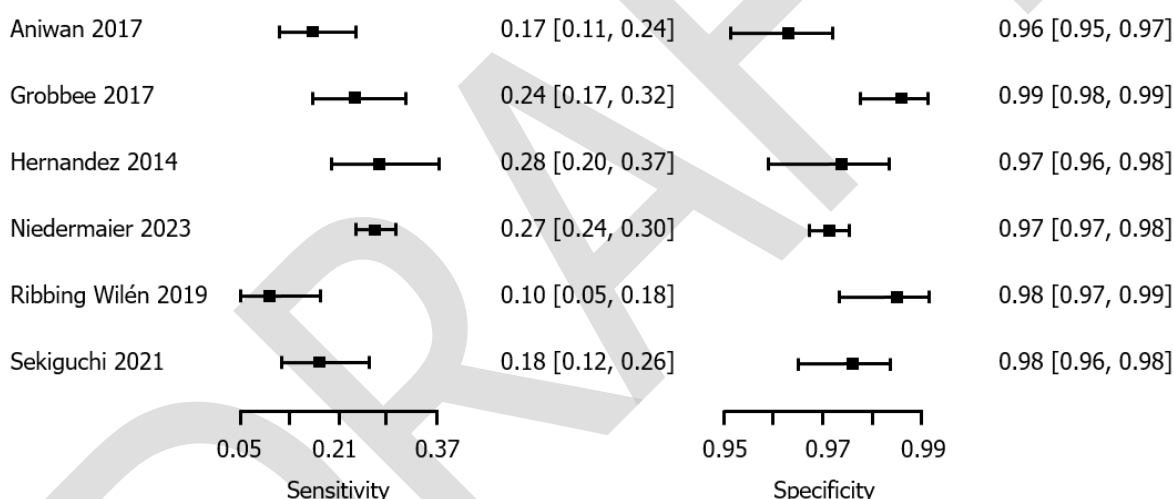
Key: AA – advanced adenoma. CI – confidence interval. FIT – Faecal immunochemical test. NR – Not reported. SD – screen detected.

Figure 4.2 Sensitivity and specificity of FIT for the detection of CRC



Note: Colonoscopy reference standard. FIT device: FOB Gold® with a threshold of 45µg/g (Niedermaier 2023), OC-Sensor™ with a threshold of 40µg/g (all other studies).
Key: CRC – colorectal cancer. FIT – faecal immunochemical test.

Figure 4.3 Sensitivity and specificity of FIT for the detection of AN



Note: Colonoscopy reference standard. FIT device: FOB Gold® with a threshold of 45µg/g (Niedermaier 2023), OC-Sensor™ with a threshold of 40µg/g (all other studies).
Key: AN – advanced neoplasia. FIT – faecal immunochemical test.

Studies with a registry follow up reference standard

For studies that used medical records or a cancer registry to identify interval cancers, FIT sensitivity for the detection of CRC ranged from 72.4% (95% CI not reported) using an unspecified FIT device in the Scottish Bowel Screening Programme to 84.4% (95% CI: 83.8%, 85.0%) with FOB Gold® at a threshold of 47µg/g in the Dutch CRC screening programme. Specificity ranged from 94.0% (95% CI not reported) to 96.2% (95% CI: 96.2%, 96.3%) (Table 4.7). Sensitivity of OC-Sensor™ at a threshold of 45µg/g in the Danish CRC screening programme was

75.5% (95% CI: 74.2%, 76.8%). Figure 4.4 displays FIT sensitivity and specificity for the detection of CRC for studies with registry follow-up as reference standard, calculated using extracted or derived 2x2 tables. (see Appendix B Table B.4 for 2x2 tables).

Table 4.7 Sensitivity and specificity of FIT for the detection of CRC (registry reference standard)

Author, year	FIT device, threshold ^{\$}	FIT participants <i>n</i>	Positivity rate	CRC cases (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity (95% CI)
Breekveldt 2023 ⁽²⁵⁶⁾	FOB Gold®, 47µg/g	2,302,711	6.5%	12,183/14,439	84.4 (83.8, 85.0)	94.0 ^Ω
Digby 2023 ⁽²⁸⁰⁾	NR, 40µg/g	232,076	5.3%	309/427	72.4 ^Ω	94.8 ^Ω
Njor 2021 ⁽²⁷⁵⁾	OC-Sensor™, 45µg/g	531,828	4.1%	1,923/2,547	75.5 (74.2, 76.8)	96.2 (96.2, 96.3)
Vanaclocha-Espi 2021 ⁽²⁷⁶⁾	Various, 40µg/g	545,505	4.3%	1,737/2,185	79.5 (77.8, 81.8)	96.0 (96.0, 96.1)

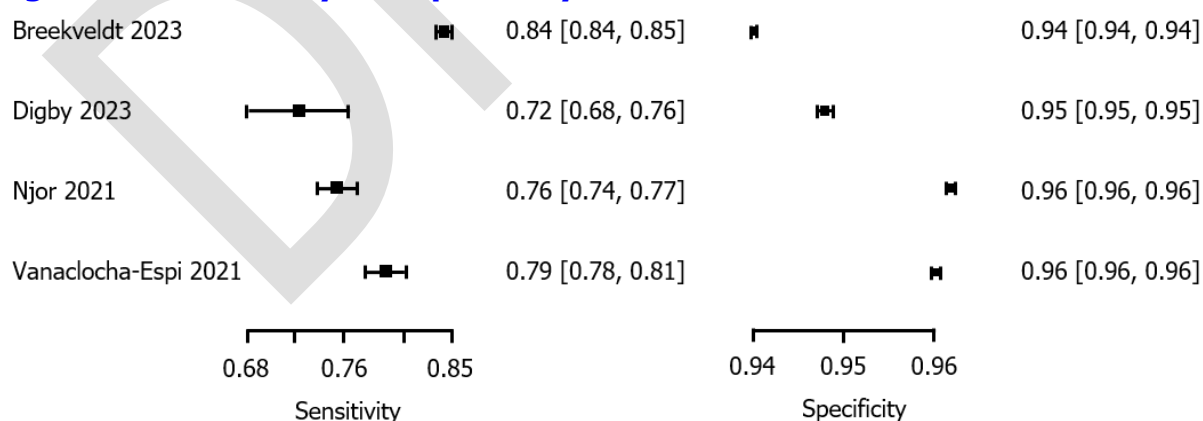
Note: Unadjusted 95% CI as reported by studies.

^{\$} converted from ng/ml for OC-Sensor™ if appropriate.

^Ω Estimates derived from available data.

Key: CI – confidence interval. FIT – Faecal immunochemical test. NR – Not reported. SD – screen detected.

Figure 4.4 Sensitivity and specificity for the detection of CRC



Note: Registry reference standard. FIT devices: FOB Gold®, 47µg/g (Breekveldt 2023); OC-Sensor™, 45µg/g (Njor 2021); various, 40µg/g (Vanaclocha-Espi 2021); unspecified, 40µg/g (Digby 2023).

4.5.4 Risk of bias and applicability assessment

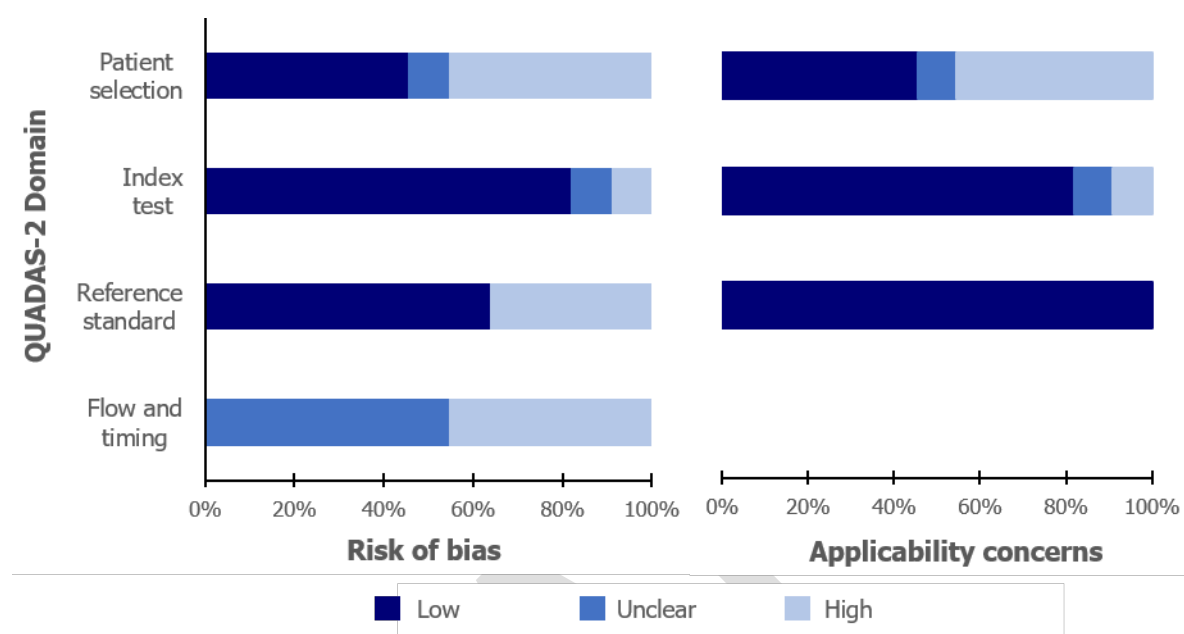
Risk of bias and applicability were assessed using QUADAS-2.⁽²⁶⁹⁾ The overall ratings for each of the four domains are shown in Figure 4.5. Studies were generally deemed at low risk of bias with low applicability concerns for the index test, as only studies that used a quantitative FIT and reported data for thresholds between 40 and 50µg/g were included. The majority of studies used OC-Sensor™ FIT devices, which are used by BowelScreen. One study each included various FIT devices⁽²⁷⁶⁾ or did not specify the FIT device,⁽²⁸⁰⁾ while the Stockholm-Gotland screening programme in Sweden used a higher threshold of 80µg/g for men, with a threshold of 40µg/g for women.⁽⁸⁹⁾ Studies with a colonoscopy reference standard were considered at low risk of bias for the reference standard domain. Conversely, studies that utilised registry follow-up to detect interval cancers as reference standard were considered at high risk of bias in this domain. Use of registry follow-up could result in overestimation of FIT sensitivity, as early-stage CRC, or asymptomatic CRC at any stage, may not have been detected as interval cancer within the follow-up period. Similarly, FIT sensitivity may be underestimated if interval cancers detected within the follow-up timeframe were present as advanced adenomas at the time of FIT testing.⁽²⁵⁶⁾ While the target conditions considered by the included studies varied depending on the reference standard, both CRC and AN were relevant to the review question. As such, there were no applicability concerns for the reference standard domain.

Studies reporting data from population-based screening programmes were generally considered to be at low risk of bias for patient selection. Studies with colonoscopy reference standard were rated at high or unclear risk of bias, with additional applicability concerns in this domain. This was due to the exclusion of participants with conditions such as inflammatory bowel disease (IBD), or those who had previously undergone a faecal occult blood test or colonoscopy. The exclusion of individuals who may be more likely to have a false positive or false negative test result could lead to inflated estimates of test accuracy.⁽²⁷⁰⁾ As BowelScreen invites all eligible persons for screening on the basis of age, exclusion of individuals for other reasons may limit the applicability of data from these studies.

In terms of flow and timing, the included studies were considered to be at uncertain or high risk of bias, due to limited information or the exclusion of participants with incomplete colonoscopy or unanalysable stool samples, as well as those who did not complete FIT or colonoscopy. The exclusion of individuals who may be more difficult to diagnose could inflate estimates of test accuracy.⁽²⁷⁰⁾ Partial verification of true negatives, and differential verification for 'FIT positive' and 'FIT negative' participants, was an additional concern for studies that used registry follow-up to identify interval cancers. This is reflected in the high risk of bias of these studies in

the reference standard domain. QUADAS-2 summary ratings for each study are included in Appendix B (Figure B.1).

Figure 4.5 Risk of bias and applicability concerns of included studies



Note: Proportion of studies rated at low, unclear and high risk of bias; and proportion of studies rated as having low, unclear and high applicability concerns using QUADAS-2.

4.6 Discussion

The aim of this chapter was to review the test accuracy of FIT at a threshold of 45µg/g, and to assess whether sensitivity and specificity of FIT for the detection of CRC varies by age. Eleven studies, reported across 14 publications, were included. The extent to which FIT test accuracy was found to vary by age, as well as the overall findings on sensitivity and specificity of FIT at a threshold of 45µg/g, are discussed below. Other factors that may impact estimates of FIT sensitivity and specificity are also considered.

4.6.1 Does sensitivity and specificity of FIT for the detection of CRC at a threshold of 45µg/g vary by age?

This review aimed to determine if FIT test accuracy at a threshold of 45µg/g varies by age. While there was some variation in sensitivity and specificity estimates across age groups in the four studies that reported age-stratified data at thresholds between 40 and 50µg/g, there was insufficient evidence of a strong or consistent trend. A previous meta-analysis of three studies of OC-Sensor™ at a threshold of

20µg/g with both colonoscopy and registry reference standards found no differences according to age.⁽⁴⁰⁾ While the pooling of studies with different reference standards may not be appropriate, the 2021 USPSTF review similarly found no evidence of a consistent pattern or difference in the sensitivity and specificity of FIT for the detection of CRC across different age groups.⁽⁷³⁾

Data from two studies with a colonoscopy reference standard published since the 2019 Selby et al. and 2021 USPSTF reviews did not indicate a significant pattern in FIT sensitivity or specificity by age at lower FIT thresholds.^(47, 281) One study based on data from the Dutch CRC screening programme, using FOB Gold® with a threshold of 47µg/g, suggested a potential trend for both increased sensitivity and specificity in the younger age groups.⁽²⁵⁶⁾ However, given the potential misclassification of 'FIT negative' participants in studies with a registry reference standard and lack of a consistent trend across studies, these findings should be interpreted with caution. Based on the limited available data, there was insufficient evidence to suggest that FIT test accuracy at a threshold of 45µg/g varies significantly by age.

4.6.2 Sensitivity and specificity of FIT for the detection of CRC or AN at a threshold of 45µg/g

Sensitivity of FIT for the detection of CRC at thresholds between 40 and 50µg/g varied considerably across the included studies, ranging from 60.0% (95% CI: 26.2%, 87.8%) in participants aged 40–79 in a screening cohort in Japan to 80.0% (95% CI 35.0%, 100.0%) in participants aged 50–69 in the COLONPREV screening trial in Spain, both using OC-Sensor™ at a threshold of 40µg/g and with a colonoscopy reference standard.^(277, 279) Specificity ranged from 94.7% to 96.6% in the four studies with a colonoscopy reference standard. The sensitivity of FIT for the detection of AN (a composite consisting of CRC and AA) was similarly uncertain, with estimates ranging from 9.9% with OC-Sensor™ at a threshold of 40µg/g in the SCREESCO trial to 28.6% with FOB Gold® at a threshold of 40µg/g in the BLITZ study.^(271, 273)

Given the heterogeneity in FIT device, target condition, reference standard and exclusion criteria across the included studies, meta-analysis was not conducted. Previous meta-analyses have considered FIT test accuracy at lower thresholds. Based on studies with colonoscopy follow-up and various FIT devices at all thresholds above 30µg/g, Selby et al. reported a pooled sensitivity for the detection of CRC of 66% (95% CI: 55%, 75%), with a pooled specificity of 96% (95% CI: 94%, 97%).⁽⁴⁰⁾ The 2021 USPSTF review pooled nine studies that used OC-Sensor™ with a colonoscopy reference standard at a threshold of 20µg/g, reporting a pooled sensitivity for the detection of CRC of 74% (95% CI: 64%, 83%), with a pooled specificity of 94% (95% CI: 93%, 96%).⁽⁷³⁾ Both reviews found that sensitivity

increased and specificity decreased at lower FIT thresholds, although neither pooled studies at thresholds $\geq 40\mu\text{g/g}$.

At a threshold of $45\mu\text{g/g}$, sensitivity of OC-Sensor™ for the detection of CRC in participants aged 50–74 in the Danish colorectal cancer screening programme was 75.5% (95% CI: 74.2%, 76.8%).⁽²⁷⁵⁾ While this is within the range of estimates provided by studies with a colonoscopy reference standard, it is higher than expected based on the pooled estimates for lower thresholds reported by the two index reviews. Notwithstanding the limitations of the registry reference standard (as described in section 4.5.4), the setting, age range, FIT device and threshold of this study may be most likely to reflect the Irish context.

Previous reviews demonstrating the superior performance of FIT in CRC screening compared with gFOBT have largely considered lower FIT thresholds than those referred to thus far in this section. A 2022 Cochrane review reported a summary estimate of the sensitivity of gFOBT for the detection of CRC of 39% (95% CI: 25%, 55%), compared to a sensitivity of 76% (95% CI: 57%, 88%) for FIT with a threshold of $10\mu\text{g/g}$, and 65% (95% CI: 46%, 80%) for FIT with a threshold of $20\mu\text{g/g}$, based on studies with a colonoscopy reference standard.⁽³¹⁾ Similarly, the summary estimate of the sensitivity of gFOBT for the detection of AN was 15% (95% CI: 12%, 20%), compared to 33% (95% CI: 27%, 40%) and 26% (95% CI: 21% to 31%) for FIT thresholds of $10\mu\text{g/g}$ and $20\mu\text{g/g}$, respectively.⁽³¹⁾ The USPSTF review included two studies of 'high sensitivity' gFOBT with a colonoscopy reference standard, with sensitivity for CRC ranging from 50% to 75% (95% CI range: 9% to 100%) and specificity ranging from 96% to 98% (95% CI range: 95% to 99%).⁽⁷³⁾ At thresholds of 40 to $50\mu\text{g/g}$, all of the studies included in the present review demonstrated higher levels of sensitivity for CRC compared with gFOBT.

4.6.3 Factors that can affect FIT test accuracy

Several factors may impact FIT test accuracy, for example, by influencing the quantity of analyte (faecal haemoglobin, f-Hb) present. Factors influencing the quantity of f-Hb may include the health characteristics of screening participants, characteristics of the target condition and demographics. Some of these, such as the presence of other conditions and use of medications, may interact with age. The characteristics of the screening programme, FIT device and sample also affect estimates of FIT sensitivity and specificity for the detection of CRC, and may account for some of the variation in estimates reported across studies and settings.

Other conditions and use of medications

Faecal haemoglobin concentration may indicate the presence of several non-CRC diseases, including inflammatory bowel disease (IBD), haemorrhoids, and anal fissures, which could affect estimates of FIT test accuracy. In Denmark, CRC

screening participants with IBD, fissures or haemorrhoids, and those with a history of CRC, were significantly more likely to receive a false positive FIT result.^(282, 283) Data from the German BLITZ study indicated an increased risk of false positive FIT associated with male sex, age ≥ 65 years, obesity, smoking, aspirin use, IBD and other non-neoplastic findings.⁽²⁸⁴⁾ A systematic review of risk factors for false positive and false negative FIT results in CRC screening found that the use of non-steroidal anti-inflammatory drugs or proton pump inhibitors, as well as the presence of peptic ulcer or anal fissure, were associated with an increased risk of false positive FIT results.⁽²⁸⁵⁾ Neither the use of antithrombotic or anticoagulant medications, nor the presence of haemorrhoids increased the risk of false positive FIT. Conversely, a higher risk of false negative results was observed in males, those with a family history of CRC, current or former smokers, and those with elevated blood glucose or hypertension.⁽²⁸⁵⁾

In addition to links with CRC mortality, elevated levels of f-Hb appear to be associated with increased risk of all-cause mortality, mortality from non-colorectal cancers, cardiovascular disease and respiratory disease.⁽²⁸⁶⁻²⁸⁸⁾ Associations have also been reported between faecal haemoglobin and other inflammatory conditions, including psoriasis and rheumatoid arthritis.^(289, 290) While the reasons for these associations are not fully understood, one potential explanation is that systemic inflammation could manifest as subclinical inflammation in the colon, leading to elevated f-Hb in the absence of CRC or pre-cancerous lesions.⁽²⁸⁸⁾ It has been suggested, therefore, that f-Hb may be a marker of systemic inflammation, and could indicate the presence or risk of several chronic conditions.⁽²⁸⁸⁾ Differences in the prevalence of health conditions may therefore limit comparability of FIT test accuracy estimates for the detection of CRC across studies.

Characteristics of the target condition

While screening for CRC has the potential to reduce incidence through the detection and removal of pre-cancerous lesions, advanced adenomas may bleed sporadically, and are therefore less likely to be detected by FIT. As a result, the sensitivity of FIT for the detection of AA is low, ranging from 13.7% to 24.1% at a threshold of 40 μ g/g in two studies.^(271, 277) Selby et al. reported a pooled estimate of sensitivity for AA at thresholds above 30 μ g/g of 19% (95% CI: 14%, 25%), with a specificity of 97% (95% CI: 96%, 98%).⁽⁴⁰⁾ Pooled sensitivity of OC-Sensor™ for the detection of AA at a threshold of 20 μ g/g, based on 10 studies with a colonoscopy reference standard included in the USPSTF review, was 23% (95% CI: 20%, 25%), with a specificity of 96% (95% CI: 95%, 97%).⁽⁷³⁾

Some studies have suggested that FIT sensitivity may be higher for distal compared with proximal lesions.^(33, 291) It has been hypothesised that this may be due to an increased likelihood of Hb degradation from right-sided lesions as a result of longer

colonic transit times,⁽²⁹²⁾ or characteristics of proximal lesions, which may be more likely to be flat or sessile.⁽²⁹³⁾ Sessile serrated lesions (SSLs) are more likely to be located in the proximal colon and may be less likely to bleed,⁽²⁹⁴⁾ with lower levels of f-Hb reported in individuals with serrated lesions compared to those with advanced adenomas.⁽²⁹⁵⁾ Data from the Dutch CRC screening programme indicated that interval cancers diagnosed following a negative FIT were more often right sided, suggesting that FIT sensitivity could be higher for left-sided cancers.^(110, 256) Two studies included in the present review reported sensitivity of FIT for the detection of proximal or right-sided and distal or left-sided AN at thresholds of $\sim 45\mu\text{g/g}$, with the point estimates of both studies suggesting that sensitivity may be higher for left-sided (distal) AN (see Table B.7, Appendix B).^(257, 277) However, the estimates were imprecise, with overlapping confidence intervals. Based on a sample of participants from the SCREESCO trial, Ribbing Wilén et al. found no evidence of an independent association between adenoma location and FIT positivity.⁽²⁷³⁾ Three studies with colonoscopy and registry reference standards included in the USPSTF review considered test accuracy of OC-Sensor™ for the detection of CRC by location, with inconsistent findings.⁽⁷³⁾

None of the studies included in the present review explicitly considered sessile serrated lesions. Based on four studies included in the USPSTF review, sensitivity of FIT for the detection of SSLs at a threshold of $20\mu\text{g/g}$ was reported to range from 2% to 7% (95% CI range, 0% to 15%).⁽⁷³⁾

Sex

While faecal haemoglobin concentration (f-Hb) and FIT positivity rates are consistently higher in men than women, relatively few studies have explored differences in FIT test accuracy according to sex. Based on three studies with either colonoscopy or registry reference standards, Selby et al. reported a pooled estimate of sensitivity for the detection of CRC of 77% in men (95% CI: 75%, 79%) and 81% in women (95% CI: 60%, 100%), with a pooled specificity of 92% (95% CI: 89%, 95%) and 94% (95% CI: 91%, 97%), respectively.⁽⁴⁰⁾ The 2021 USPSTF review highlighted inconsistent findings on sex differences in test accuracy of OC-Sensor™ from three studies with either colonoscopy or registry reference standard, with some evidence to suggest that sensitivity to detect CRC might be higher, and specificity lower, in men compared to women.⁽⁷³⁾ Five studies included in this review included sex-stratified data for FIT thresholds of $40\text{--}50\mu\text{g/g}$, of which two reported results stratified by both age and sex (see Table B.5 and Table B.6, Appendix B). In all studies, there appeared to be a trend towards lower sensitivity and higher specificity in females compared to males.

A number of authors have highlighted disparities affecting women in FIT-based CRC screening programmes, including lower FIT positivity rates, increased risk of false

positive FIT results and higher interval cancer rates, as well as a lower reduction in CRC incidence and mortality in women compared to men.^(296, 297) In both Sweden and Finland, higher FIT thresholds have been introduced or piloted for men, decreasing the difference in positivity rates between men and women.^(89, 298) However, it has been suggested that the use of sex-specific thresholds could introduce sex differences in positive and negative predictive values,^(271, 278) and may disadvantage men.⁽²⁹⁶⁾ A 2018 meta-analysis suggested that men were at lower risk of false positive and higher risk of false negative FIT results, with the authors suggesting that lower FIT thresholds could be considered for men to reduce the number of missed neoplasia.⁽²⁸⁵⁾ Any consideration of risk-based screening strategies, including the use of sex-specific thresholds, warrants careful deliberation to avoid unintended consequences.

Characteristics of the screening programme and FIT device

FIT sensitivity is expected to decline across multiple screening rounds, as existing or prevalent cancers are detected in the initial 'prevalence' round of a population-based screening programme. In the Dutch programme, the sensitivity of FIT for the detection of CRC decreased from 84.4% (95% CI: 83.8%, 85.0%) in the first screening round to 73.5% (95% CI: 71.8%, 75.2%) in the second round.⁽²⁵⁶⁾ In this review, to increase comparability with studies that excluded individuals with a previous colonoscopy or FOBT, data pertaining to the first round of CRC screening programmes were extracted where available. However, some studies included individuals who had participated in gFOBT screening prior to the introduction of FIT, and therefore did not represent true screening naïve populations.⁽⁸⁹⁾ The inclusion or exclusion of previously screened participants may account for some of the heterogeneity of test accuracy estimates across studies.

The included studies mainly used FOB Gold® or OC-Sensor™ FIT devices. While the accuracy of FOB Gold® and OC-Sensor™ for the detection of AN and CRC has been reported to be similar at a threshold of 15µg/g,⁽²⁹⁹⁾ positivity rates at thresholds of 25–150µg/g may be higher for FOB Gold® than OC-Sensor™.⁽³⁰⁰⁾ Given that test performance varies according to the specific FIT used, it has been suggested that FIT devices should not be considered to be interchangeable.⁽³³⁾ Therefore, estimates of test accuracy for the two devices at similar thresholds may not be directly comparable, and it may be more appropriate to compare FIT devices at the same positivity rates, rather than at the same threshold.⁽²⁹⁷⁾ In the first BowelScreen screening round, the positivity rate with OC-Sensor™ at a threshold of 45µg/g was 4.5% (95% CI: 4.4%, 4.6%).⁽⁶¹⁾ Based on data from the German BLITZ study, FOB Gold® at a threshold of 50µg/g yielded an equivalent 4.5% positivity rate, with a sensitivity for the detection of CRC of 72.0% (95% CI: 50.6%, 87.9%) and a specificity of 96.0%.⁽²⁷¹⁾

FIT test accuracy may also be impacted by environmental factors such as temperature, which can affect haemoglobin concentration in FIT samples.^(301, 302) In recognition of Hb degradation at higher ambient temperatures, FIT manufacturers have reformulated sample buffers to improve Hb stability.^(303, 304) As a result, the performance of FIT with a new buffer at a higher threshold may be comparable to the performance of FIT with an old buffer at a lower threshold.⁽¹¹⁰⁾ One study comparing the original and reformulated OC-Sensor™ buffer found that Hb was maintained above 80% for 20 days at room temperature in the new buffer, compared to six days with the original. At 35°C, Hb in the new buffer was maintained above 80% for eight days.⁽³⁰⁴⁾ The BowelScreen *Standards for Quality Assurance in Colorectal Screening* include a quality assurance requirement that the 'FIT kit device must maintain the stability of the sample for up to 10 days at 35°C'.⁽³⁰⁵⁾ In practice, given average temperatures in Ireland, the potential impact of temperature on haemoglobin concentration in BowelScreen FIT samples is expected to be minimal.

4.6.4 Positive and negative predictive values

This chapter examined the sensitivity and specificity of FIT for the detection of CRC and AN. These measures of test accuracy are intrinsic characteristics of the screening test and are independent of the prevalence of the condition in the population being tested. However, the underlying prevalence of the condition is important when considering the clinical relevance of a test result. The positive predictive value (PPV) measures the probability that a positive test result identifies a person with the target condition. It takes into account the test accuracy as well as the underlying prevalence of the condition. Among the studies that reported the positive predictive value for a FIT threshold of 40µg/g (that is, a threshold close to that used within BowelScreen), the PPV for AN ranged from 32% (95% CI 22, 43)⁽²⁵⁷⁾ to 60% (95% CI 44, 75).⁽²⁷⁹⁾ As the prevalence of CRC and advanced neoplasia is lower in those aged 50–54 compared to older age cohorts, the PPV of FIT testing in those aged 50–54 will also be lower. This means that the proportion of colonoscopies in which no lesions will be detected may be higher among those aged 50–54 compared to older age groups. Among the included studies, age-stratified PPV was reported by Brenner et al.⁽²⁷¹⁾ At a threshold of 40µg/g, the PPV for AN was 50.6% in those aged 50–64, and 57.0% in those aged 65–79, although 95% confidence intervals were not reported.

The negative predictive value (NPV) measures the probability that a negative result identifies people who do not have the target condition. As the prevalence is lower in those aged 50 to 54 years than in older cohorts, the NPV will be higher in the younger group. This means that the ratio of true negatives to undetected CRC or AN cases will also be higher in this group. Among the included studies that reported

negative predictive values for a FIT threshold of 40µg/g, NPV for AN ranged from 90% (95% CI 88, 93)⁽²⁷⁹⁾ to 92% (95% CI 90, 94).⁽²⁷⁷⁾ The study by Brenner et al. reported a NPV for AN of 92.8% and 92.5% in those aged 50–64 and 65–79, respectively.⁽²⁷¹⁾

It is important to note that while there was no consistent evidence that test accuracy differs by age, the differences in PPV and NPV across age groups mean that the benefit-harm balance in those aged 50–54 may be different compared to that in older age groups. However, this does not account for other confounding factors associated with age and test accuracy described above, such as co-morbid conditions. As the prevalence of CRC and adenoma are expected to be different across countries and according to the screening history of the population, the PPV or NPV from the studies included in this chapter would not be transferable to the Irish setting.

4.6.5 Limitations

As the main question of interest to this review was whether FIT test accuracy for the detection of CRC at a threshold of 45µg/g varies by age, studies of lower thresholds were excluded, limiting the available data. Several of the included studies were not designed specifically to assess the clinical performance of FIT, but reported sufficient data to facilitate the calculation of sensitivity and specificity, or of the corresponding 2x2 tables. Given differences in FIT devices and thresholds, reference standards, target conditions and exclusion criteria across the included studies, meta-analysis was not conducted.

All studies were considered to be at high risk of bias within at least one QUADAS-2 domain. While studies that included colonoscopy for all participants were at low risk of bias for the reference standard, this was coupled with a high risk of bias with high applicability concerns for patient selection. The sample sizes of colonoscopy screening studies were relatively small, resulting in a lack of precision. Estimates of sensitivity and specificity from these studies may not reflect the test accuracy of FIT in a population-based screening programme such as BowelScreen, due to the exclusion of participants with incomplete colonoscopies or those who had undergone previous faecal occult blood testing or colonoscopy, as well as those with certain health conditions.

Studies of population-based screening programmes with registry follow up to identify interval cancers following a negative FIT included considerably larger samples (ranging from 232,076 to 2,302,711), with less restrictive inclusion criteria and uptake rates of up to 72%. Sensitivity and specificity estimates for the detection of CRC based on these studies were less variable and more precise. While studies with a registry reference standard may be more likely to reflect a general screening

population, they were at higher risk of bias due to the imperfect reference standard and risk of misclassification of participants who did not undergo colonoscopy.

As noted above, while blood in stool is a potential indicator of CRC and pre-cancerous lesions, f-Hb can also be affected by the presence of other health conditions and use of certain medications. As a result, FIT test accuracy may be impacted by a range of factors, limiting the comparisons that can be made across different settings and populations. Given the limited data at thresholds $\sim 45\mu\text{g/g}$, the available evidence should be interpreted with caution.

4.6.6 Conclusion

While a wide range of FIT thresholds has been applied internationally, the majority of FIT test accuracy studies have focused on manufacturer-recommended thresholds, with less evidence on test accuracy at higher cut-offs. As a result, the sensitivity and specificity of FIT for the detection of CRC at a threshold of $45\mu\text{g/g}$ is uncertain, with estimates of sensitivity ranging from 60% to 80%, and specificity ranging from 95% to 97%. Few studies have reported age-stratified results for FIT thresholds between 40 and $50\mu\text{g/g}$. Based on the limited available data, no clear or consistent evidence was identified to suggest that FIT test accuracy for the detection of CRC at a threshold of $45\mu\text{g/g}$ varies significantly by age.

5 Review of the clinical effectiveness of colorectal cancer screening in those aged 50 to 54 years

5.1 Key points

- This chapter reviewed the evidence on the clinical effectiveness and safety of colorectal cancer (CRC) screening with a starting age of 50 compared to a starting age of 55. Given a relative lack of evidence specific to screening with faecal immunochemical tests (FIT), evidence for a broad range of screening modalities was considered.
- A 2021 systematic review from the United States Preventive Services Task Force (USPSTF) and a 2023 review from the European Commission Initiative on Colorectal Cancer (ECICC) Working Group were used as key sources to identify relevant studies of clinical effectiveness and safety. An additional de novo systematic search was performed to identify relevant studies published since these systematic reviews.
- Ten studies, reported across 12 publications, were identified that met the inclusion criteria for the review and included participants from the age of 45 (n=3), 50 (n=6) or 52 (n=1). These included: four randomised controlled trials (RCTs) of CRC screening with guaiac-based faecal occult blood tests (gFOBT), one RCT of screening with flexible sigmoidoscopy (FSIG) with or without FIT, and five observational studies of screening with FIT. All studies assessed the effectiveness of screening (or invitation to screening) compared to no screening. No study directly compared the clinical effectiveness of CRC screening with a starting age of 50 to a starting age of 55.
- There was consistent evidence from nine of the ten included studies that screening reduces CRC mortality. Based on four RCTs, gFOBT screening was associated with a reduction in CRC mortality of between 6% and 22% compared to no screening at 30 years of follow-up, in participants ranging in age from 45–80. The included observational FIT studies generally reported larger reductions in CRC mortality, although estimates varied widely: reductions ranged from 10% with six years of follow-up to 65% with 11 years of follow-up in participants ranging in age from 50–69.
- All five RCTs reported CRC incidence outcomes. Significant relative reductions in CRC incidence with screening, compared with no screening, were reported by two of the five RCTs. These ranged from a reduction of 15% at 18 years of follow-up in those screened with gFOBT, to a

reduction of 22% at 15 years in those screened with FSIG with or without FIT. Effects on incidence were reported by three of the five observational studies of FIT screening; these suggested reductions in CRC incidence ranging from 31% with 11 years of follow-up to 33% with five years of follow-up.

- Evidence on screening specifically for those aged 50–54 was limited to one observational FIT study and one RCT that reported data for this age group. Based on data from the RCT, which examined screening with FSIG with or without FIT, screening was associated with a 35% reduction in CRC incidence in males aged 50–54 at 14.8 years of follow-up, with no reduction among females. However, this trial was not powered to detect an effect in this age group. The observational study found that, compared to no screening, screening with FIT in those aged 50–54 was associated with a CRC mortality reduction of 64% in females and 71% in males, and a CRC incidence reduction of 25% in females and 30% in males at 11 years of follow-up.
- Observational studies represent a weaker form of evidence than RCTs and are subject to important limitations, which may artificially inflate the effect estimates observed. These include, for example, selection bias due to a lack of randomisation (that is, the 'healthy screenee effect'). For this reason, the estimates of reductions in CRC incidence and mortality from observational studies within this review are likely to overestimate the added value of screening.
- Three studies reported on the physical harms of colonoscopy (for example, pain, bleeding, or perforation risk) following a positive FIT. In two studies, harms, which were of low risk overall, were lower in younger age groups. Three studies reported on the impact of FIT-based screening on psychosocial outcomes, one of which considered age. While age was not associated with experiencing general psychological consequences following colonoscopy after a positive FIT, worry about developing cancer appeared to increase slightly with decreasing age. Overall, participants in this study did not regret their decision to participate in screening.
- Notwithstanding the limitations of the evidence identified, there is consistent evidence that screening from age 50 reduces CRC mortality compared to no screening. While some evidence suggests that FIT screening may reduce CRC incidence, this was based mainly on observational studies, with a higher risk of bias.

5.2 Introduction

In line with the agreed scope of this health technology assessment (HTA), this chapter examined the evidence of effectiveness and safety of colorectal cancer (CRC) screening in those aged 50 to 54.

Studies examining the clinical effectiveness of CRC screening have considered a variety of screening modalities such as colonoscopy, flexible sigmoidoscopy and faecal occult blood tests, including guaiac-based faecal occult blood tests (gFOBT) and faecal immunochemical tests (FIT). These studies have either compared CRC screening to no screening, or have explored the comparative effectiveness of different screening modalities. Randomised controlled trial (RCT) evidence of the effectiveness of stool-based CRC screening is based on older, guaiac-based faecal occult blood tests (gFOBT); however, these have largely been replaced with newer, more sensitive FIT tests in screening programmes (see Chapter 2, section 2.3.1).

This chapter presents a review of clinical effectiveness and safety of CRC screening, updating previous recent systematic reviews. As per the [protocol](#), this review focused on identification of high-quality studies that evaluated the clinical effectiveness of extending CRC screening to people aged 50 to 54 to reduce CRC mortality, CRC incidence, or all-cause mortality. The review of safety evidence (section 0) focused on studies that evaluated the risk of serious adverse events associated with colonoscopy following a positive FIT result, and also included studies reporting psychosocial effects associated with participation in FIT screening. The Discussion section of the chapter (section 5.5) interprets the findings of the review of clinical effectiveness and safety, along with a discussion of the use of modelling studies to support evaluation of clinical effectiveness.

5.3 Methods

The review described within this chapter is reported according to the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.⁽³⁰⁶⁾ A detailed background to the review and description of associated methods is provided in the accompanying HTA [protocol](#). The protocol for this review was registered on the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42024579663).

5.3.1 Review question

Initial scoping indicated limited evidence comparing the effectiveness of FIT-based CRC screening at younger starting ages to older starting ages. Given the variety of screening modalities considered and the dearth of studies specifically addressing the strategy of interest to this HTA, a broad Population, Intervention, Comparator, Outcome, Study design (PICOS) framework was applied to ensure a sufficient

breadth of evidence was captured. The review question was formulated according to the PICOS framework presented in Table 5.1. The review sought to answer the following question:

- What is the clinical effectiveness of colorectal cancer screening with a starting age of 50 compared to a starting age of 55?

Table 5.1 Review question for assessing clinical effectiveness

Population	Average-risk, asymptomatic populations
Intervention	<i>Ideal intervention and comparator for HTA research question:</i> <i>Colorectal cancer screening using FIT-based strategies at a starting age of 50 years (with screening age up to 74), compared to a starting age of 55.</i> Range of evidence that will be considered: Colorectal cancer screening using a range of modalities (colonoscopy, flexible sigmoidoscopy, guaiac-based faecal occult blood test, faecal immunochemical test, CT colonography), where the intervention eligibility age incorporates people aged between 50 and 54 years. All screening intervals (annual, every two years or longer) will be considered.
Comparator	Later starting age of screening, or no screening.
Outcomes	Colorectal cancer mortality and incidence, all-cause mortality, screening-related adverse events (for example, perforation, bleeding, death).
Study design	RCTs, non-randomised control trials, cohort studies, population-based case control studies.

Key: CT – computed tomography. FIT – faecal immunochemical tests.
RCT – randomised control trial.

5.3.2 Study eligibility

The inclusion criteria for this review were based on age and screening modality. Only studies that included participants in the 50 to 54 age range were included. A preliminary review of evidence indicated a lack of RCTs of FIT-based screening; therefore, cohort and case-control studies of FIT screening were considered eligible for inclusion. For other screening modalities, such as gFOBT or colonoscopy, only RCTs were included. Studies of the harms of screening were included if they

involved consideration of the effects of age and examined adverse events related to physical harms of colonoscopy as a follow-up to a FIT positive result. Psychosocial harms associated with participation in FIT testing were also included.

5.3.3 Identification of studies

Preliminary scoping identified a 2021 systematic review from the US Preventive Services Task Force (USPSTF) and a 2024 review by the European Commission Initiative on Colorectal Cancer (ECICC) Working Group.^(73, 80) These reviews were chosen as key sources for identification of clinical effectiveness studies. A de novo electronic search for clinical effectiveness studies was performed on 12 July 2024 in Medline via EBSCOhost, Embase via Ovid, the Cochrane Library CENTRAL database and ClinicalTrials.gov to identify cohort and case-control studies published since the last search of the USPSTF review (from 1 December 2019 to 12 July 2024), and RCTs and non-randomised trials published since the last search of the ECICC review (from 1 December 2022 to 12 July 2024). The electronic search strategy was developed by a librarian and peer reviewed by a second librarian using the PRESS tool,⁽³⁰⁷⁾ and is available on Zenodo®.⁽³⁰⁸⁾

Forward citation searching of the USPSTF systematic review was carried out using CitationChaser software on the PubMed, PubMed Central, CrossRef, Microsoft Academic Graph and CORE databases.⁽²⁶⁸⁾

Study selection

With respect to the de novo electronic search, the titles and abstracts of identified records were screened by one reviewer using Covidence software. Titles and abstracts of studies included in the USPSTF and ECICC systematic reviews were examined for relevance according to the criteria outlined in Table 5.1 by one reviewer. The full texts of potentially eligible studies were retrieved and independently assessed for eligibility by two reviewers according to the criteria outlined in Table 5.1, with any disagreements resolved by discussion if required.

5.3.4 Data extraction and management

Data extraction was performed by one reviewer using a standardised data extraction template developed in Covidence, and subsequently downloaded and refined using Microsoft Excel. The following information was extracted for each study: publication year, authors, country or region, study design, details of the screening strategy (screening start and stop ages, screening modalities and intervals used, FIT thresholds), comparators, colorectal cancer mortality and incidence outcomes, all-cause mortality, and harms of screening. All data extracted were quality assessed by a second reviewer, with disagreements resolved by discussion. Where data were reported or stratified by individual rounds of screening, the results for all rounds

(one or more rounds) of screening are reported. Some studies did not specify what the upper limit was for the number of rounds reported. Outcomes for CRC incidence, CRC mortality and all-cause mortality were extracted as reported from publications noting any adjustments.

Quality assessment

The quality of observational studies was assessed with the Newcastle Ottawa Scale (NOS).⁽³⁰⁹⁾ This scale assesses quality for cohort studies across three domains of 'selection', 'comparability', and 'outcomes', while case-control studies are assessed on 'selection', 'comparability' and 'exposure'. Within each domain, individual items are assessed as adequate or inadequate based on a star rating system, where allocation of a star indicates an adequate rating for that individual scoring item.

Interpretation of study quality as 'poor', 'fair' or 'good' was based on the following scheme, which provides for an overall rating based on the need to demonstrate quality across all three domains:⁽³¹⁰⁾

- Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome or exposure domain
- Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome or exposure domain
- Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome or exposure domain.

A quality assessment template based on the NOS domain criteria was developed in Covidence. Each study was quality assessed by one reviewer, with the assessment cross-checked by a second reviewer. The quality assessments for studies included in the USPSTF review were extracted as reported in the review based on its published criteria for RCTs and cohort studies, which grade quality as 'poor', 'fair' or 'good'.⁽³¹⁰⁾ Studies relating to harms and safety were not quality assessed.

Data synthesis

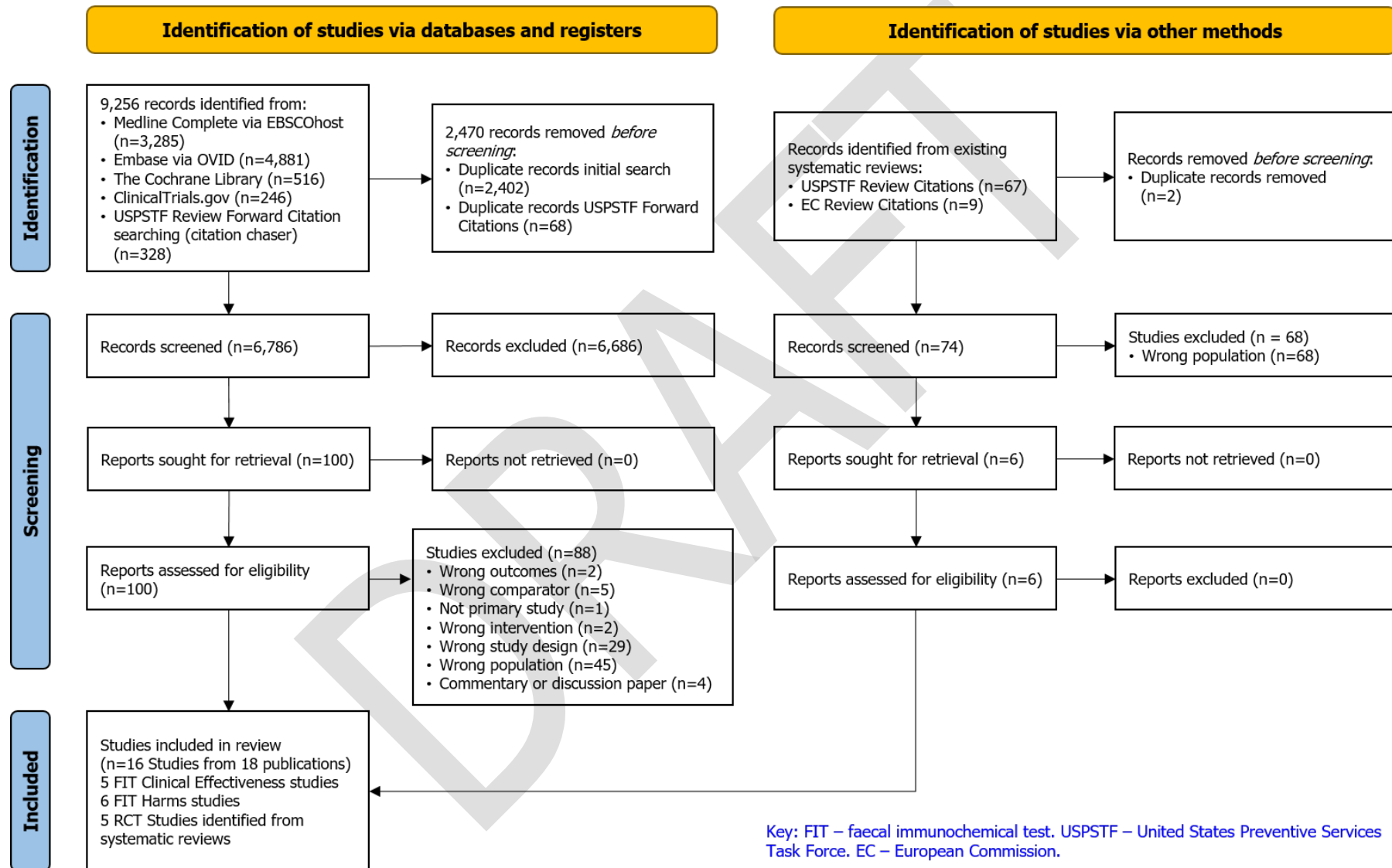
Given the range of screening strategies, modalities, length of follow-up and age ranges, results were synthesised narratively.

5.3.5 Protocol deviations

Titles and abstracts of identified records were screened by one reviewer rather than two due to the volume of returned records. Reference lists of studies included from the USPSTF review were not searched for potentially relevant citations.

5.4 Results

An overview of the study selection process is provided in Figure 5.1. After removal of duplicates, 6,786 titles and abstracts were assessed for eligibility. Five observational studies of FIT screening were identified from the de novo search strategy, of which four were rated as poor-to-fair quality and one as good quality.⁽³¹¹⁻³¹⁶⁾ Five fair-to-good quality RCTs of gFOBT or flexible sigmoidoscopy screening, reported across six publications,^(84, 85, 317-320) were identified from the USPSTF and ECICC reviews, as was one fair quality FIT-based cohort publication, which reported older results from a study also identified through the de novo search strategy.⁽³¹²⁾ These ten studies, reported across twelve publications, assessed the clinical effectiveness of CRC screening and included participants aged between 50 and 54 years (Table 5.3 and Table 5.4).^(84, 85, 311, 312, 314-320) Six additional studies that assessed the safety of FIT-based screening programmes, including assessment of physical or psychosocial harms, were identified from the updated search.⁽³²¹⁻³²⁶⁾

Figure 5.1 PRISMA flow diagram of study selection process

5.4.1 Characteristics of included studies

All ten included studies reported CRC mortality outcomes.^(84, 85, 311-320) CRC incidence outcomes were reported in three of the FIT-based observational studies^(311, 314, 316) and all five RCTs.^(84, 85, 317, 319, 320) All-cause mortality outcomes were reported in one cohort study⁽³¹⁴⁾ and four RCTs.^(84, 85, 317, 320) Two studies (one RCT of FSIG with or without FIT, and one observational FIT study) provided age-stratified data for the 50–54 age group.^(314, 317) In the other eight studies the reported age strata and subgroup analyses varied.

Table 5.2 summarises the number of studies identified for each screening modality by study type, intervention, clinical effectiveness outcome and whether or not a 50 to 54 age group stratification was available; this highlights a lack of high-quality evidence for FIT screening with age-stratified data for the 50 to 54 age group.

Table 5.2 Number of publications* contributing evidence for clinical effectiveness of screening in people aged 50 to 54

Intervention		Outcomes					
		CRC mortality		All-cause mortality		CRC incidence	
		RCT	Observ	RCT	Observ	RCT	Observ
FIT	Stratified age 50–54		n=1				n=1
	Not stratified		n=4		n=1		n=2
gFOBT	Stratified age 50–54						
	Not stratified	n=5		n=4		n=4	
FSIG	Stratified age 50–54	n=1		n=1		n=1	
	Not stratified						

Key: CRC – colorectal cancer; FIT – faecal immunochemical test; FSIG – flexible sigmoidoscopy; gFOBT – guaiac-based faecal occult blood test; Observ – observational study; RCT – randomised controlled trial.

* Some studies were reported across multiple publications.

FIT-based CRC screening studies

Two FIT-based prospective cohort studies reported across three publications,^(311, 312, 316) two retrospective cohort studies,^(314, 315) and one case-control study⁽³¹³⁾ were included. Three of the FIT-based publications reported on overlapping cohorts from a Taiwanese screening programme;^(311, 312, 316) one of these was reported across two publications.^(311, 312) The remaining three studies were based in Denmark, Italy and

the US.⁽³¹³⁻³¹⁵⁾ The characteristics of these studies are shown in Table 5.3, with additional details presented in Appendix C, Table C.1. All five studies compared CRC mortality, CRC incidence or all-cause mortality rates in screened and unscreened participants and one study also compared invited and not-yet-invited individuals. Follow-up times ranged from 3.8 to 11 years, with the number of participants ranging from 10,711 to 5,418,651. Across the studies, the earliest year of screening invitation was 2004,^(311, 312) while the latest year of invitation was 2017.⁽³¹⁵⁾ The threshold for interpreting a positive FIT result was 20µg/g for all studies. Frequency of screening was biennial, with one or more rounds of screening included; one of the four studies reported data for one round of screening only, while studies with multiple screening rounds did not clearly specify the upper limit. Study quality was rated 'good' for one study,⁽³¹³⁾ 'fair' for two studies^(311, 314) and 'poor' for the remaining two,^(315, 316) with follow-up times under 10 years considered inadequate in terms of time for CRC outcomes to develop.

RCTs of CRC screening using gFOBT or flexible sigmoidoscopy

Five fair to good-quality RCTs that recruited eligible participants including those aged 50–54 were identified from the USPSTF systematic review.^(84, 85, 317, 319, 320) One additional report published in 2021, which included 30 year follow-up data from one of the trials included in the USPSTF review (the Funen trial, previously reported by Kronborg et al. in 2004) was also included.⁽³¹⁸⁾ Four of these reported on the effectiveness of gFOBT screening, with one reporting on flexible sigmoidoscopy with or without FIT testing.^(84, 85, 317, 319, 320) Follow-up times ranged from 11 to 30 years. The characteristics of these studies are described in Table 5.4, with additional details presented in Appendix C, Table C.2.

Table 5.3 Study and population characteristics of included FIT observational studies

Author, year, years of invitation	Country	Screening frequency, (No of rounds)	N Participants (screened/ unscreened)	Maximum follow-up (years)	Age range	Stratified data for age 50–54	Outcomes assessed	NOS quality rating
Baldacchini 2022 ⁽³¹⁴⁾ (2005–2016)	Italy	Biennial (1 or more)	380,651/327,100	11 (Median 9.5)	50–69	Yes	CRC incidence CRC mortality All-cause mortality	Fair
Chiu 2015 ^{*(312)} (2004–2009)	Taiwan	Biennial (1–3)	1,160,895/4,257,756	6 (Mean 3.09)	50–69	No	CRC mortality	USPSTF rated – Fair
Chiu 2021 ^{*(311)} (2004–2009)	Taiwan	Biennial (1 or more)	3,067,853/2,349,846	10	50–69	No	CRC incidence CRC mortality	Fair
Doubeni 2024 ⁽³¹³⁾ (2007–2013)	USA	(1 or more)	1,103 cases/ 9,608 controls	NA	52–85	No	CRC mortality	Good
Hsiao 2024 ^{*(316)} (2010–2013)	Taiwan	Biennial (1 or more)	719,073/877,922	5 for incidence 7 for mortality	50–69	No	CRC incidence CRC mortality	Poor
Njor 2022 ⁽³¹⁵⁾ (2014–2017)	Denmark	Biennial (1 round)	175,480/634,919	3.8 (Median 3.3)	50–71	No	CRC mortality	Poor

* Overlapping Taiwan screening cohorts.

Key: CRC – colorectal cancer. FIT – faecal immunochemical test. NA – not applicable; case control study design. NOS – Newcastle Ottawa Score.

Table 5.4 Study and population characteristics of included randomised controlled trials

Trial, author years of invitation	Country	Screening frequency, (No of rounds)	N Participants (screened/ unscreened)	Screening modality	Maximum follow-up (years)	Age range	Stratified data for age 50– 54	Outcomes assessed	USPSTF quality rating
Burgundy Trial Faivre 2004 ⁽³¹⁹⁾ (1988–1998)	France	Biennial (6)	45,642/45,557	gFOBT	11	45–74	No	CRC incidence CRC mortality	Fair to Good
Funen Trial Kronborg 2004 ⁽³²⁰⁾ (1985–1994)	Denmark	Biennial (9)	30,967/30,966	gFOBT	17	45–75	No	CRC incidence CRC mortality All-cause mortality	Fair to Good
Funen Trial Shaukat 2021 ^{*(318)} (1985–1994)	Denmark	Biennial (9)	30,966/30,964	gFOBT	30	45–75	No	CRC mortality All-cause mortality	Fair to Good
Minnesota Colon Cancer Control Study Shaukat 2013 ⁽⁸⁴⁾ (1976–1992)	USA	Annual (11)	15,587/15,394	gFOBT	30 (mortality) 18 (incidence)	50–80	No	CRC incidence CRC mortality All-cause mortality	Fair to Good
		Biennial (6)	15,570/15,394						
NORCCAP Trial Holme 2018 ⁽³¹⁷⁾ (1999–2000)	Norway	once only	20,552/78,126	FSIG with or without FIT	14.8	50–64	Yes	CRC incidence CRC mortality All-cause mortality	Fair to Good
Nottingham Trial Scholefield 2012 ⁽⁸⁵⁾ (1981–1991)	England	Biennial (3–5)	76,056/75,919	gFOBT	28	45–74	No	CRC incidence CRC mortality All-cause mortality	Fair to Good

Key: CRC – colorectal cancer. FIT – faecal immunochemical test. FSIG – flexible sigmoidoscopy. gFOBT – guaiac-based faecal occult blood test. NORCCAP – Norwegian colorectal cancer prevention. USPSTF – United States Preventive Services Task Force.

* Updated data from the Funen trial, quality assessment as per Kronborg et al.

5.4.2 FIT-based screening study findings

A summary of FIT studies with reported CRC clinical effectiveness outcomes is provided in Table 5.5 (screened versus unscreened). None of the included studies were designed to assess the clinical effectiveness of screening with a starting age of 50 compared to screening with a later starting age of 55. One study, by Baldacchini et al., reported on the clinical effectiveness of FIT-based screening with a specific subgroup analysis for the 50–54 age group, which allowed comparison with older age groups.⁽³¹⁴⁾ One study from Denmark,⁽³¹⁵⁾ two from Taiwan^(311, 316) and one from the USA⁽³¹³⁾ reported clinical effectiveness outcomes for FIT-based screening in broader age groups with participants aged 50 up to age 85.

CRC mortality and all-cause mortality findings in FIT-based screening studies

One fair-quality cohort study was set in a regional CRC screening programme in northern Italy and used biennial FIT screening with a positivity threshold of $\geq 20\mu\text{g/g}$.⁽³¹⁴⁾ This study by Baldacchini et al. compared, as a primary objective, age-specific CRC incidence rates (as well as incidence rates according to sex, tumour stage and tumour site) between attenders (those who responded to both of the first two screening invitations) and non-attenders (those who did not respond to the first two invitations). The secondary objective was to compare incidence-based CRC mortality rates and all-cause, non-CRC-related mortality. Participants were invited for screening between 2005 and 2016 and the study had a follow-up time of 11 years (median 9.5 years), with a total of 707,751 individuals followed. Reported risk ratios were based on age-standardised rates controlling for age at first invitation to screening. Of those aged 50 to 54 who were invited, 89,166 (48.7%) attended screening. Considerable CRC mortality reductions in the 50 to 54 age group were reported in both sexes, with a reduction of 71% in males (adjusted RR 0.29 [95% CI, 0.20 to 0.42]) and a reduction of 64% in females (adjusted RR 0.36 [95% CI, 0.24 to 0.54]). An overall reduction in CRC mortality of 65% was reported in the FIT-screened group compared to the unscreened group for all participants aged 50–69 with 11 years of follow-up (adjusted RR 0.35 [95% CI, 0.31 to 0.39]).

Considering all-cause, non-CRC-related mortality, this was calculated by Baldacchini et al. according to the following criteria: (1) deaths from CRC were excluded by censoring follow-up at the date of CRC diagnosis; (2) subjects with CRC, diagnosed on any date, who died from causes other than CRC were included; and (3) deaths from chronic diseases other than CRC were included irrespective of the date of diagnosis. Based on this definition, significant reductions in non-CRC all-cause mortality with screening were reported, based on data from 380,651 FIT-screened and 327,100 unscreened participants aged 50–69 with 11 years of follow-up. Age-adjusted estimates were reported for both male and female participants, with

apparent reductions of 54% (adjusted RR 0.46 [95% CI, 0.45 to 0.48]) and 56% (adjusted RR 0.44 [95% CI, 0.42 to 0.45]), respectively. In discussing the considerable difference in all-cause, non-CRC mortality, the authors noted expected differences in behaviours and epidemiological factors in screening attendees versus non-attendees, otherwise known as the 'healthy screenee' effect. This likely serves to explain much of the difference observed, and may also partly explain the large reductions observed in CRC mortality. This, and other biases, are explored further in the Discussion (see section 5.5.3).

A 2024 study by Doubeni et al. reported a nested case-control study that aimed to estimate associations of FIT screening with CRC mortality.⁽³¹³⁾ This study was based on 10,711 participants who completed FIT screening in community settings (two Kaiser Permanente healthcare systems) in the US. The study included participants aged 52 to 85 years. Individuals who died of CRC between 2011 and 2017 (n=1,103) were each matched using an incidence density approach to eight randomly selected people who were alive and not known to have CRC at the index date; matching was based on birth year, sex, health plan membership duration and locality. The date of colorectal cancer diagnosis was set as the reference date for each participant and if unknown, the death date was used. Exposure to FIT was defined as completing one or more FITs with a valid laboratory result for screening up to ten years prior to the reference date. In addition to matching, the analysis attempted to account for potential confounders by exclusion (of those who had undergone screening colonoscopy) and additional model-based adjustment, beyond matching variables, for race and ethnicity, socioeconomic status, and healthcare utilisation history. Age-stratified results were not reported. CRC mortality outcomes were assessed based on comparison of those exposed to one or more FIT screenings compared to those without history of FIT screening during a five-year period from 2007 to 2013. The primary finding from this study was that FIT screening with one or more rounds was associated with a 33% lower likelihood of death from CRC (adjusted Odds Ratio 0.67 [95% CI 0.59 to 0.76]).⁽³¹³⁾ The authors reported that study results were broadly similar to those obtained in randomised and non-randomised studies of the association of gFOBT screening with mortality from CRC, and were consistent with observed reductions in CRC mortality rates following the initiation of organised screening, also within Kaiser Permanente health systems.⁽³¹³⁾

A 2024 study from a Taiwanese national CRC screening programme (Hsiao et al.) compared CRC outcomes for participants aged 50–69 and screened from 2010 to 2013 (one or more rounds of screening) with unscreened participants followed up for five years.⁽³¹⁶⁾ This study was based on an eligible screening cohort of 1,596,995 people, of whom 797,880 (50%) were aged 50–54. A total of 719,073 (45%) of the eligible screening cohort participated in at least one screening round during the

study period. CRC mortality hazard ratios were reported for the 50–69 age group based on Cox regression analysis adjusted for entry age, sex, and urbanisation levels. The reported hazard ratio suggested a 47% reduction in CRC mortality between the screened and unscreened groups (HR 0.53, [95% CI 0.50 to 0.57]) $p < 0.0001$).

Two publications, based on the same prospective cohort from the Taiwanese screening programme, evaluated CRC mortality outcomes for ages 50–69 (Chiu et al. 2015 and 2021).^(311, 312) The 2021 study reported on the Taiwan national CRC screening programme with 5,417,699 eligible participants aged 50–69 screened between 2004 through 2009 and followed up to 2014. The biennial FIT-screened group comprised 3,067,853 participants (57%) who had participated in at least one round of FIT screening, with 2,349,846 individuals in the unscreened group, followed up for a period of five to ten years. Screened participants were tested with one of two FIT devices using a positivity threshold of $\geq 20\mu\text{g/g}$. The 2015 publication compared CRC mortality rates in 1,160,895 participants attending one or more rounds of FIT screening from 2004 to 2009, with 4,257,756 unscreened individuals. Considering the 2015 study, the age-adjusted reduction in CRC mortality was 10% (adjusted RR 0.90 [95% CI, 0.84 to 0.95]), with a mean follow-up time of three years.⁽³¹²⁾ The subsequent study in 2021 showed a larger reduction in CRC mortality of 40% (adjusted RR 0.60 [95% CI, 0.57 to 0.64]), with a longer follow-up of 5 to 10 years, when adjusted for age, gender, attendee self-selection bias, colonoscopy uptake rate, selection of diagnostic examination modality and completeness of colonoscopy. Adjustments for self-selection bias were based on a method developed by Duffy et al., whereby an RCT intention-to-treat analysis was applied using the pre-screening group and natural incidence rate of CRC as a proxy to model the CRC mortality risk in an uninvited group.⁽³²⁷⁾ The reported reductions in mortality varied by CRC location and were greater for those with distal CRC (44%; adjusted RR 0.56 [95% CI, 0.53 to 0.59]) compared to those with proximal CRC (21%; adjusted RR 0.79 [95% CI, 0.72 to 0.87]).

A study by Njor et al. compared CRC mortality rates in 175,480 participants in a screening programme in Denmark with 634,919 eligible individuals who were awaiting invitation to screening. The median follow-up time was 3.3 years, the shortest among the studies discussed in this section.⁽³¹⁵⁾ Those aged 50–71 on 1 January 2014 were eligible for screening and were followed from March 2014 to December 2017. CRC mortality was not found to have been significantly reduced when adjusted for self-selection bias for the entire screened group (adjusted RR 0.71 [95% CI, 0.46 to 1.08]). Similarly, no statistically significant reduction in CRC mortality rate was reported in screened males or females from the younger 50–59 age group. However, when the data were broken out by sex, a reduction in CRC mortality was observed in males aged 50–71 (adjusted RR 0.49 [95% CI, 0.33 to

0.97]). Examining age groups, no statistically significant reduction was observed in males aged 50–59 (adjusted RR 0.88 [95% CI, 0.19 to 4.09]), though a reduction was observed in those aged 60–71 (adjusted RR 0.49 [95% CI, 0.27 to 0.89]). No significant reductions were found in the adjusted rates for any of the female age groups (age 50–71 adjusted RR 0.93 [95% CI 0.47 to 1.83], age 50–59 adjusted RR 0.87 [95% CI 0.22 to 3.40], age 60–71 adjusted RR 0.93 [95% CI 0.43 to 2.02]). Adjustments for self-selection bias were based on a method developed by Duffy et al. that was also applied in the studies by Chiu et al.⁽³²⁷⁾ However, this study was limited by a short median follow-up time of 3.3 years and a single round of screening; the authors acknowledged that demonstrating long-term effectiveness for CRC mortality reductions would require multiple rounds of screening.⁽³¹⁵⁾

CRC incidence findings in FIT-based screening studies

The study by Baldacchini et al. reported an age-adjusted reduction in CRC incidence of 31% in the FIT-screened group compared to the unscreened group for all participants aged 50–69 with 11 years of follow-up (adjusted RR 0.69 [95% CI, 0.66 to 0.72]).⁽³¹⁴⁾ Among people aged 50–54, the reduction in CRC incidence was 30% in FIT-screened males (adjusted RR 0.70 [95% CI, 0.61 to 0.80]) and 25% in females (adjusted RR 0.75 [95% CI, 0.65 to 0.86]) when compared to the unscreened group, with 11 years of follow-up. The reduction in CRC incidence was 35% for males aged 50–69 (adjusted RR 0.65 [95% CI, 0.61 to 0.69]) and 25% (adjusted RR 0.75 [95% CI, 0.70 to 0.80]) for females. When additionally adjusted for self-selection bias using a method proposed by Puliti et al.,⁽³²⁸⁾ the reported CRC incidence reduction was 33% for males (self-selection adjusted RR 0.67 [95% CI, 0.62 to 0.72]) and 21% for females (self-selection adjusted RR 0.79 [95% CI, 0.62 to 0.72]).⁽³¹⁴⁾

The study by Hsiao et al. reported a reduction in CRC incidence of 33% between FIT-screened participants (one or more rounds of screening) and unscreened participants aged 50–69 with five years follow-up (Cox regression age and sex-adjusted HR 0.67, [95% CI, 0.65 to 0.69]).⁽³¹⁶⁾ No specific sub-group analysis for CRC incidence was provided for the 50–54 age group.

The 2021 study by Chiu et al. reported a decrease in the incidence of advanced stage CRC (stage II+) of 34% (RR 0.66 [95% CI, 0.63 to 0.70]) between screened (one or more rounds) and unscreened participants.⁽³¹¹⁾ This rate was adjusted for age, sex, attendee self-selection bias, colonoscopy uptake rate, selection of diagnostic examination modality and completeness of colonoscopy. Adjustments for self-selection bias were based on a method described by Duffy et al., whereby an RCT intention-to-treat analysis was applied using the pre-screening group and natural incidence rate of CRC as a proxy to model the CRC mortality risk in an uninvited group.⁽³²⁷⁾ A larger decrease of 39% in adjusted incidence of advanced stage distal cancers (adjusted RR 0.61 [95% CI, 0.58 to 0.64]) was observed relative

to a decrease of 16% for advanced stage proximal cancers (adjusted RR 0.84 [95% CI, 0.77 to 0.92]).⁽³¹¹⁾

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Table 5.5 Clinical effectiveness of screening with FIT (screened vs unscreened)

Author, year (length of follow-up)	Sex	Age	No. participants exposed/unexposed	CRC Mortality (95% CI) Relative rate	Non-CRC all-cause Mortality (95% CI) Relative rate	CRC Incidence (95% CI) Relative rate
Baldacchini 2022 ⁽³¹⁴⁾ (11 years)	Both	50-69	380,651/327,100	0.35 (0.31, 0.39) [†]	<i>NR</i>	0.69 (0.66, 0.72) [†]
		50-69	176,130/166,151	0.32 (0.28, 0.37) [†]	0.46 (0.45, 0.48) [‡]	0.65 (0.61, 0.69) [†]
	Male	50-54	89,166/93,922	0.29 (0.20, 0.42) [†]	<i>NR</i>	0.70 (0.61, 0.80) [†]
		55-59	30,453/26,141	0.31 (0.22, 0.44) [†]	<i>NR</i>	0.66 (0.58, 0.75) [†]
		60-64	27,694/21,680	0.29 (0.21, 0.39) [†]	<i>NR</i>	0.60 (0.53, 0.67) [†]
		65-69	28,817/24,408	0.35 (0.28, 0.44) [†]	<i>NR</i>	0.67 (0.60, 0.74) [†]
	Female	50-69	204,521/160,949	0.40 (0.34, 0.47) [†]	0.44 (0.42, 0.45) [‡]	0.75 (0.70, 0.80) [†]
		50-54	103,310/86,849	0.36 (0.24, 0.54) [†]	<i>NR</i>	0.75 (0.65, 0.86) [†]
		55-59	37,300/25,237	0.30 (0.20, 0.44) [†]	<i>NR</i>	0.69 (0.60, 0.81) [†]
		60-64	31,644/22,085	0.34 (0.23, 0.49) [†]	<i>NR</i>	0.76 (0.66, 0.88) [†]
		65-69	32,267/26,778	0.52 (0.40, 0.67) [†]	<i>NR</i>	0.79 (0.70, 0.88) [†]
Chiu 2015 ⁽³¹²⁾ (6 years)	Both	50-69	1,160,895/4,257,756	0.90 (0.84, 0.95) ^{‡‡}	<i>NR</i>	<i>NR</i>
Chiu 2021 ⁽³¹¹⁾ (10 years)	Both	50-69	3,067,853/2,349,846	0.60 (0.57, 0.64) [§]	<i>NR</i>	0.66 (0.63, 0.70) ^{§††}
				Relative risk	Relative risk	Relative risk
Njor 2022 ⁽³¹⁵⁾ (3.8 years, median 3.3) (Participated vs Not yet invited)	Both	50-71	175,480/634,919	0.71 (0.46, 1.08) ^{§§}	<i>NR</i>	<i>NR</i>
		50-71	81,821/314,778	0.49 (0.33, 0.997) ^{§§}	<i>NR</i>	<i>NR</i>
	Male	60-71	48,477/172,054	0.49 (0.27, 0.89) ^{§§}	<i>NR</i>	<i>NR</i>
		50-59	33,344/142,724	0.88 (0.19, 4.09) ^{§§}	<i>NR</i>	<i>NR</i>
	Female	50-71	93,659/320,141	0.93 (0.47, 1.83) ^{§§}	<i>NR</i>	<i>NR</i>
		60-71	53,756/178,061	0.93 (0.43, 2.02) ^{§§}	<i>NR</i>	<i>NR</i>
		50-59	39,903/142,080	0.87 (0.22, 3.40) ^{§§}	<i>NR</i>	<i>NR</i>

Author, year (length of follow-up)	Sex	Age	No. participants exposed/unexposed	CRC Mortality (95% CI)	Non-CRC all-cause Mortality (95% CI)	CRC Incidence (95% CI)
				Relative risk	Relative risk	Relative risk
Njor 2022 ⁽³¹⁵⁾ (3.8 years, median 3.3) (Invited vs Not yet invited)	Both	50-71	262,893/634,919	0.83 (0.66, 1.03) ^{†††}	<i>NR</i>	<i>NR</i>
		50-71	130,160/314,778	0.74 (0.56, 0.98) ^{†††}	<i>NR</i>	<i>NR</i>
	Male	60-71	72,250/172,054	0.68 (0.49, 0.94) ^{†††}	<i>NR</i>	<i>NR</i>
		50-59	57,910/142,724	0.94 (0.54, 1.65) ^{†††}	<i>NR</i>	<i>NR</i>
	Female	50-71	132,733/320,141	0.96 (0.68, 1.35) ^{†††}	<i>NR</i>	<i>NR</i>
		60-71	74,746/178,061	0.95 (0.64, 1.43) ^{†††}	<i>NR</i>	<i>NR</i>
		50-59	57,987/142,080	0.93 (0.47, 1.81) ^{†††}	<i>NR</i>	<i>NR</i>
				Odds ratio	Odds ratio	Odds ratio
Doubeni 2024 ⁽³¹³⁾	Both	52-85	1,103 cases/9,608 controls	OR 0.67 (0.59, 0.76) ^{§§§}	<i>NR</i>	<i>NR</i>
				Hazard ratio	Hazard ratio	Hazard ratio
Hsiao 2024 ⁽³¹⁶⁾ (5 years incidence, 7 years mortality)	Both	50-69	719,073/877,922	HR 0.53 (0.50, 0.57) ^{†††}	<i>NR</i>	HR 0.67 (0.65, 0.69) [^]

Key: CI – confidence interval. CRC – colorectal cancer. FIT – faecal immunochemical test. HR – Hazard Ratio. NR – not reported.

† Age standardised rate ratios, controlling for age at first invitation.

‡ Controlling for 5-year age group and excluding those subjects who died within 90 days since the date of the first.

§ Adjusted for age, gender, attendance, referral, selection of diagnostic examination modality and completeness for colonoscopy.

†† Rate ratio for stage II+ advanced cancer.

†† Adjusted for self-selection bias.

§§ Kaplan Meier survival analysis – Relative risk at end of follow-up adjusted for self-selection bias.

††† Kaplan Meier survival analysis – Relative risk at end of follow-up.

††† Cox Regression Hazard Ratio Adjusted for entry age, sex, urbanisation levels

§§§ Unconditional logistic regression odds ratios adjusted for matching variables: age, sex, health plan membership duration, geographic region), race and ethnicity, socioeconomic status, comorbidity score, and wellness visits

5.4.3 gFOBT or FSIG screening study findings

Five RCTs of CRC screening using gFOBT or FSIG with or without FIT, and which included participants aged 50 to 54, were included in this review. All RCTs provided intention-to-screen analyses. The main clinical effectiveness outcomes are summarised in Table 5.6.

CRC mortality and all-cause mortality findings in studies of gFOBT and FSIG screening

One study by Holme et al., based on the NORCCAP RCT from Norway, reported subgroup analyses for participants aged 50–54.⁽³¹⁷⁾ The study compared CRC outcomes in 20,552 screened participants and 78,126 participants in a non-screened control group. Screened participants were randomised to one of two intervention groups: flexible sigmoidoscopy (FSIG) (n=10,271) or FSIG with a single round of FIT (FlexSure OBT, Beckman-Coulter; n=10,281). The median follow-up was 14.8 years. Initial study recruitment focused on participants aged 55–64 who were screened from 1999 to 2000, with screening expanded to include those aged 50–54 during 2001. The study reported outcomes for CRC mortality based on one round of screening with FSIG (with or without FIT). The study was powered to identify CRC incidence reductions of 30% over five years in those aged 55–64; it was not powered to detect reductions in the 50–54 age group. Study outcomes were reported for the entire 50–64 age group, as well as for the 55–64 age group. The overall age-standardised reduction in CRC mortality was 21% for the 50–64 age group (HR 0.79 [95% CI, 0.65 to 0.96]) and 18% in those aged 55–64 (HR 0.82 [95% CI, 0.66 to 1.02]). A reduction of 34% was reported in males aged 55–64 (HR 0.66 [95% CI, 0.48 to 0.90]), with no significant effect in females (HR 1.05 [95% CI, 0.77 to 1.42]). The point estimate for an age-standardised subgroup analysis of those aged 50–54 suggested a 33% reduction in CRC mortality rates for screening versus no screening, although this was not statistically significant (HR 0.67 [95% CI, 0.42 to 1.07]).⁽³¹⁷⁾ However, as mentioned, the study was not specifically powered to detect significant reductions in the 50–54 age group.

Four RCTs from Denmark, France, the UK and the US reported CRC outcomes for screened versus unscreened participants that included a broad age range including people aged 50–54.^(84, 85, 319, 320) Reductions in CRC mortality for biennial screening with gFOBT for all participants ranged from 9% to 22%. The Nottingham trial conducted three to five rounds of screening with participants followed up for 28 years (RR 0.91 [95% CI, 0.84 to 0.98]),⁽⁸⁵⁾ and the Minnesota Colon Cancer Control Study conducted six to eleven rounds of screening with participants followed up for 30 years (RR 0.78 [95% CI, 0.65 to 0.93]).⁽⁸⁴⁾ The Nottingham trial reported a reduction of 13% (RR 0.87 [95% CI 0.79, 0.97]) for the older 60–74 age group, compared to no significant effect in the younger 45–59 age group (RR 0.96 [95% CI

0.84, 1.10]). The Minnesota Colon Cancer Control Study reported no statistically significant CRC mortality reductions for biennial screening in the younger 50–59 age group in either males or females. The only age subgroup to show a significant reduction of 58% was males aged 60–69 (RR 0.42 [95% CI, 0.27 to 0.66]).

The study by Faivre et al., based on the Burgundy trial, showed a significant reduction in CRC mortality of 16% for screening over six rounds in participants aged 45–74 followed up for 11 years (RR 0.84 [95% CI, 0.71 to 0.99]).⁽³¹⁹⁾ This was consistent with the Funen trial from Denmark reported by Kronborg et al., which showed a 16% reduction in CRC mortality with nine rounds of screening for participants aged 45–75 followed up for 17 years (RR 0.84 [95% CI, 0.73 to 0.96]).⁽³²⁰⁾ A 2021 study by Shaukat et al. included 30-year follow-up data from the Funen trial previously reported by Kronborg et al. in 2004.^(318, 320) The authors reported a small difference in 30-year mortality between the screened and unscreened groups (RR 0.94, 95% CI 0.85, 1.04), although this was not statistically significant. No differences between the screening and control groups were reported by age or sex, although the trial was not powered to detect significant differences between these sub-groups.⁽³¹⁸⁾

Four RCTs included all-cause mortality outcomes, with no reductions in all-cause mortality reported (Table 5.6).^(84, 85, 317, 318, 320)

CRC incidence findings in studies of gFOBT and FSIG screening

Four RCTs of screening with gFOBT included participants aged 50–54 as part of a broader age range with 11 to 28 years of follow-up and three to 11 rounds of screening. Three studies from England, Denmark and France reported that biennial screening using gFOBT resulted in no significant reduction in CRC incidence (RR range from 0.97 to 1.02).^(85, 319, 320) The Minnesota Colon Cancer Control study reported a statistically significant reduction in CRC incidence of 15% for six rounds of biennial screening using gFOBT (RR 0.85 [95% CI, 0.74 to 0.96]) among people aged 50–80 with 18 years of follow-up.

Based on data from the NORCCAP trial in Norway, FSIG screening with or without FIT in the entire cohort aged 50–64 resulted in a 22% reduction in CRC incidence compared to no screening (age-adjusted HR 0.78 [95% CI, 0.70 to 0.87]).⁽³¹⁷⁾ This was comparable with a reduction of 21% in the older 55–64 age group (HR 0.79 [95% CI, 0.70 to 0.80]). The reduction in CRC incidence for both sexes aged 50–54 was not found to be statistically significant (HR 0.67 (95% CI, 0.42 to 1.07), although the study was not specifically powered to detect significant reductions in the 50–54 age group. Screening was associated with a statistically significant reduction in CRC incidence of 35% in male participants aged 50–54 compared to no screening (HR 0.65 [95% CI, 0.46 to 0.91]), in contrast to no statistically significant

reduction among female participants aged 50–54 (HR 0.86 [95% CI, 0.61 to 1.21]). Similarly, CRC incidence was reduced by 33% among older males in the 55–64 screening group (HR 0.67 [95% CI, 0.56 to 0.80]), in contrast to no significant reduction in females aged 55–64 (HR 0.93 [95% CI, 0.78 to 1.11]).⁽³¹⁷⁾

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Table 5.6 Clinical effectiveness of screening with gFOBT or FSIG (screened vs unscreened)

Trial, author, length of follow-up	Modality	Sex	Age	No. Participants intervention / control	CRC Mortality (95% CI)	All-cause Mortality (95% CI)	CRC Incidence (95% CI)
					Relative risk	Relative risk	Relative risk
Burgundy Trial Faivre 2004 ⁽³¹⁹⁾ 11 Years	gFOBT	Both	45-74	45,642/45,557	0.84 (0.71, 0.99)	<i>NR</i>	1.01 (0.91, 1.12)
Funen Trial Kronborg 2004 ⁽³²⁰⁾ 17 years	gFOBT	Both	45-75	30,967/30,966	0.84 (0.73, 0.96)	0.99 (0.97, 1.02)	1.02 (0.93, 1.12)
Funen Trial [†] Shaukat 2021 ⁽³¹⁸⁾ 30 years	gFOBT	Both	45-75	30,966/30,964	0.94 (0.85, 1.04)	1.00 (0.99, 1.01)	<i>NR</i>
			50-59	10,794/10,737	0.93 (0.78, 1.09)	<i>NR</i>	<i>NR</i>
			60-69	10,264/10,266	0.87 (0.73, 1.05)	<i>NR</i>	<i>NR</i>
			70+	4,836/4,893	0.86 (0.60, 1.23)	<i>NR</i>	<i>NR</i>
		Male	45-75	14,863/14,842	0.92 (0.80, 1.07)	<i>NR</i>	<i>NR</i>
			50-59	5,335/5,282	0.82 (0.65, 1.03)	<i>NR</i>	<i>NR</i>
			60-69	4,824/4,803	0.93 (0.69, 1.25)	<i>NR</i>	<i>NR</i>
			70+	2,161/2,186	1.18 (0.74, 1.88)	<i>NR</i>	<i>NR</i>
		Female	45-75	16,103/16,111	0.96 (0.83, 1.11)	<i>NR</i>	<i>NR</i>
			50-59	5,459/5,453	1.05 (0.83, 1.33)	<i>NR</i>	<i>NR</i>
			60-69	5,440/5,457	0.81 (0.63, 1.05)	<i>NR</i>	<i>NR</i>
			70+	2,675/2,706	0.80 (0.52, 1.25)	<i>NR</i>	<i>NR</i>

Trial, author, length of follow-up	Modality	Sex	Age	No. Participants intervention / control	CRC Mortality (95% CI)	All-cause Mortality (95% CI)	CRC Incidence (95% CI)
					Relative risk	Relative risk	Relative risk
Minnesota Colon Cancer Control Study ^{††} Shaukat 2013 ⁽⁸⁴⁾ Mortality: 30 years Incidence: 18 years	gFOBT	Both	50-80	15,587/15,394	0.78 (0.65, 0.93)	0.99 (0.98, 1.01)	0.85 (0.74, 0.96)
			50-59	6,403/6,367	0.90 (0.65, 1.24)	<i>NR</i>	<i>NR</i>
			60-69	6,485/6,446	0.67 (0.51, 0.89)	<i>NR</i>	<i>NR</i>
			70-80	2,699/2,581	0.66 (0.35, 1.26)	<i>NR</i>	<i>NR</i>
		Male	50-80	7,444/7,434	0.63 (0.48, 0.82)	<i>NR</i>	<i>NR</i>
			50-59	3,171/3,211	0.75 (0.48, 1.15)	<i>NR</i>	<i>NR</i>
			60-69	3,051/3,027	0.42 (0.27, 0.66)	<i>NR</i>	<i>NR</i>
			70-80	1,222/1,196	0.82 (0.40, 1.64)	<i>NR</i>	<i>NR</i>
		Female	50-80	8,143/7,960	0.92 (0.72, 1.18)	<i>NR</i>	<i>NR</i>
			50-59	3,232/3,156	1.14 (0.70, 1.84)	<i>NR</i>	<i>NR</i>
			60-69	3,434/3,419	0.90 (0.62, 1.30)	<i>NR</i>	<i>NR</i>
			70-80	1,477/1,385	0.63 (0.30, 1.35)	<i>NR</i>	<i>NR</i>
Nottingham Trial Scholefield 2012 ⁽⁸⁵⁾ 28 years	gFOBT	Both	45-74	76,056/75,919	0.91 (0.84, 0.98)	1.00 (0.99, 1.02)	0.97 (0.91, 1.03)
			45-59	<i>NR</i>	0.96 (0.85, 1.10)	<i>NR</i>	<i>NR</i>
			60-74	<i>NR</i>	0.87 (0.79, 0.97)	<i>NR</i>	<i>NR</i>
		Male	60-74	<i>NR</i>	0.91 (0.82 to 1.02)	<i>NR</i>	<i>NR</i>
		Female	60-74	<i>NR</i>	0.90 (0.80 to 1.01)	<i>NR</i>	<i>NR</i>

Trial, author, length of follow-up	Modality	Sex	Age	No. Participants intervention / control	CRC Mortality (95% CI)	All-cause Mortality (95% CI)	CRC Incidence (95% CI)
					Hazard ratio	Hazard ratio	Hazard ratio
Holme 2018 ^{§(317)} NORCCAP Trial (14.8 years)	FSIG with or without FIT [†]	Both	50-64	20,552/78,126	HR 0.79 (0.65, 0.96)	HR 0.98 (0.95, 1.02)	HR 0.78 (0.70, 0.87)
			55-64	<i>NR</i>	HR 0.82 (0.66, 1.02)	HR 1.02 (0.95, 1.08)	HR 0.79 (0.70, 0.89)
			50-54	<i>NR</i>	HR 0.67 (0.42, 1.07)	HR 1.02 (0.95, 1.08)	HR 0.67 (0.42, 1.07)
		Male	50-64	10,255/38,872	HR 0.63 (0.47, 0.83)	HR 0.96 (0.91, 1.00)	HR 0.66 (0.57, 0.78)
			55-64	<i>NR</i>	HR 0.66 (0.48, 0.90)	HR 0.94 (0.89, 1.00)	HR 0.67 (0.56, 0.80)
			50-54	<i>NR</i>	HR 0.49 (0.24, 1.02)	HR 0.99 (0.90, 1.10)	HR 0.65 (0.46, 0.91)
		Female	50-64	10,297/39,254	HR 1.01 (0.77, 1.33)	HR 1.02 (0.96, 1.07)	HR 0.92 (0.79, 1.07)
			55-64	<i>NR</i>	HR 1.05 (0.77, 1.42)	HR 1.02 (0.95, 1.08)	HR 0.93 (0.78, 1.11)
			50-54	<i>NR</i>	HR 0.90 (0.49, 1.65)	HR 1.00 (0.88, 1.13)	HR 0.86 (0.61, 1.21)

Key: CI – confidence interval. CRC – colorectal cancer. FIT – faecal immunochemical test. FSIG – flexible sigmoidoscopy. gFOBT – guaiac-based faecal occult blood test. HR – Hazard Ratio. NORCCAP – Norwegian colorectal cancer prevention. NR – not reported.

[†] Intervention group was made up of two randomised screening subgroups; one with FSIG only, and one with FSIG and FIT.

[‡] Funen trial – based on original study population from Kronborg 2004.

[§] Age standardised cox regression hazard ratios – rates include both screening groups.

^{††} Biennial screening.

5.4.4 Ongoing research trials

One relevant ongoing RCT was identified as part of this review. The CONFIRM trial, based in the US, is a pragmatic, multicentre, randomised, parallel group trial comparing screening with colonoscopy versus annual FIT in participants aged 50 to 75.⁽³²⁹⁾ The estimated study completion date is 2028.

5.4.5 Quality assessments of included studies

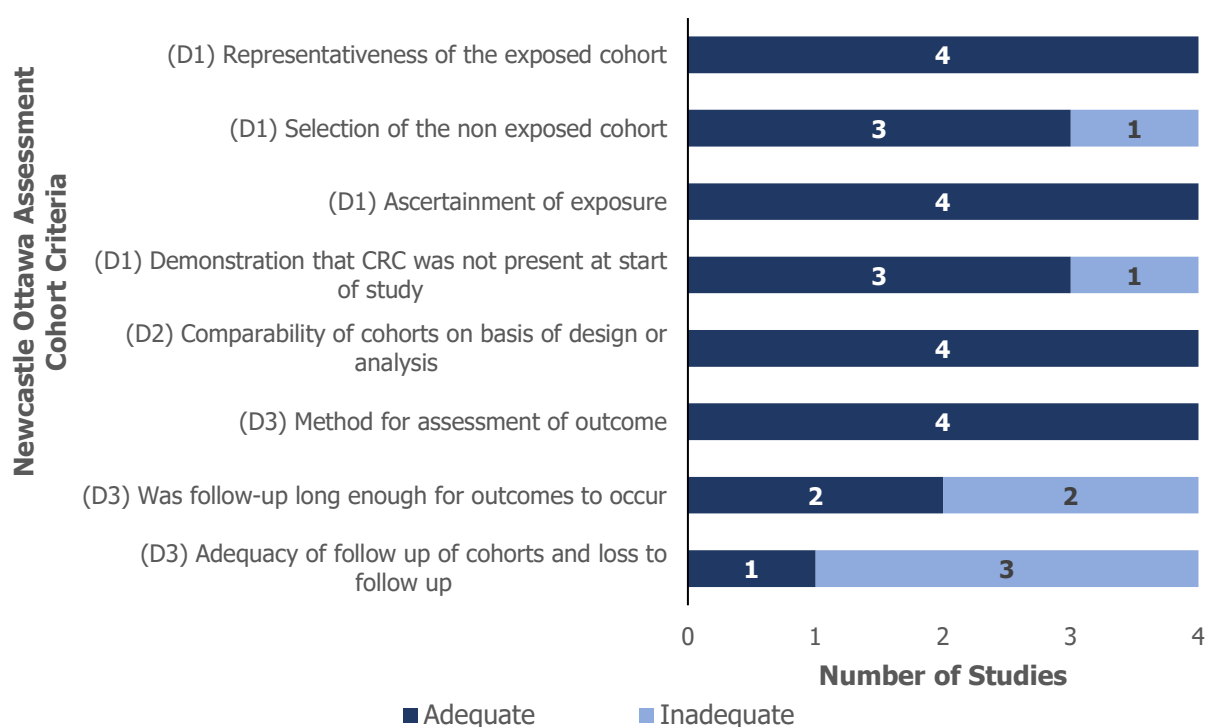
The USPSTF review rated study quality according to the criteria defined in the USPSTF procedure manual supplemented with assessment of cohort studies using the Newcastle Ottawa Scale (NOS).^(309, 310) The five RCTs included in this review were rated as 'fair to good' by the USPSTF,^(84, 85, 317, 319, 320) while the one cohort study was rated as 'fair'.⁽³¹²⁾

Of the five FIT studies identified through the de novo search, four were cohort studies and one was a case-control study. The quality and associated risk of bias of the five observational FIT studies was assessed with the NOS.⁽³⁰⁹⁾ The scale assesses cohort studies in three primary domains: (D1) selection of the cohort and or case-controls, (D2) comparability of the cohort and or case-controls, and (D3) assessment of clinical outcomes from the cohort and or case-controls. The quality assessments are shown in Figure 5.2 (cohort studies) and Table 5.7 (case-control studies).

Studies were generally of good quality in relation to selection of exposed and unexposed groups. Analyses were adjusted for appropriate factors such as self-selection bias, age and sex to allow for appropriate comparability of outcomes between screened and unscreened participants. The weakest domain related to assessment of the clinical outcomes and specifically the length of follow-up of cohorts and explicit statements accounting for loss to follow-up of participants in the cohort. The older RCTs included in this review had follow-up times of between 11 to 30 years. As a newer screening modality, the FIT cohort studies had much shorter follow-up times of between 3.8 to 11 years. For the purposes of this quality assessment, follow-up times under 10 years were considered inadequate in terms of time for CRC outcomes to develop. Only two studies reached that minimum threshold,^(311, 313, 314) of which only the Baldacchini study had an explicit statement describing the proportion and reasons for loss of participants to follow-up.⁽³¹⁴⁾ The nested case-control study by Doubeni et al. included a 10-year study period.⁽³¹³⁾ On that basis, one study was rated as 'good', two studies were rated as 'fair' and the other two as 'poor', primarily due to concerns about follow-up.

In addition to the above quality assessment, further discussion of biases likely to affect the observational FIT studies is provided in the Discussion of this chapter (see section 5.5.3).

Figure 5.2 Newcastle Ottawa quality assessments for FIT cohort studies



Key: CRC – colorectal cancer. D1 – selection of the cohort domain. D2 – comparability of the cohort domain. D3 – assessment of clinical outcomes from the cohort domain. FIT – faecal immunochemical test.

Table 5.7 Newcastle Ottawa quality assessment for Doubeni et al. case-control study

Criteria	Assessment
(D1) Is the case definition adequate?	Adequate
(D1) Representativeness of the cases	Inadequate
(D1) Selection of controls	Adequate
(D1) Definition of controls	Adequate
(D2) Comparability of cases and controls on the basis of the design or analysis	Adequate
(D3) Ascertainment of exposure	Adequate
(D3) Same method of ascertainment for cases and controls	Adequate
(D3) Non-response rate	Inadequate

Key: D1 – Selection. D2 – Comparability. D3 – Exposure.

5.4.6 Harms of colorectal cancer screening

The relevant results from the 2021 USPSTF review on harms of colonoscopy following a positive result on a stool-based test are summarised below. The de novo search detailed in Section 5.3.3 yielded six additional relevant studies;⁽³²¹⁻³²⁶⁾ three relating to the physical harms of screening,^(323, 325, 326) and three relating to psychosocial harms.^(321, 322, 324) Of the studies outlined, three considered physical harms of screening by age; two of these were identified from the USPSTF review and one as part of the de novo search. One study reporting on psychological harms considered age and was identified in the de novo search.

Physical harms of screening by age

Serious adverse events (SAEs) were defined in the USPSTF review as 'events requiring unexpected or unwanted medical attention and/or resulting in death', and included perforation, major bleeding, severe abdominal symptoms, and cardiovascular events.⁽⁷³⁾ Two studies included in the USPSTF review reported age-stratified data for SAEs of colonoscopy following stool-based tests (Table 5.8).^(330, 331) One of these studies, which reported on SAEs in those aged 59 years or younger and 60 years or older, found an increased rate of SAEs among the older age group.⁽³³⁰⁾ In those aged 59 years or younger (n=3,541), seven SAEs were reported, resulting in an SAE rate of 198 per 100,000 colonoscopies in this age group.⁽³³⁰⁾ In those aged 60 years or older (n=5,290), 16 SAEs were reported, resulting in a rate of 302 per 100,000 colonoscopies.⁽³³⁰⁾ The other study reported that perforation rates increased with age (p for trend: <0.001 in males and 0.037 in females);⁽³³¹⁾ however, it was not possible to calculate SAEs rates based on the data reported in this study.

One retrospective French cohort study identified from the de novo search reported adverse events (AEs) and severity for diagnostic and therapeutic colonoscopies following FIT testing as part of a screening programme from 2015 to 2018 (Table 5.8).⁽³²⁵⁾ Diagnostic colonoscopy in this study referred to colonoscopy to identify the presence of adenomas or CRCs, while therapeutic colonoscopy related to treatment, management, or biopsy of adenomas or tumours. AEs were defined and severity graded based on American Society for Gastrointestinal Endoscopy (AGSE) definitions.⁽³³²⁾ The mean age of participants was 63 years. A total of 180 AEs (1.88%) were reported from 9,576 colonoscopies in 9,061 participants. The severity was graded as mild in 123 AEs (1.28%), moderate in 40 (0.42%) and severe in 17 AEs (0.18%). Rates of AEs increased with age, from 1.34% among those aged 50–59 to 2.06% and 2.35% among those aged 60–69 and 70–75, respectively ($p=0.02$).⁽³²⁵⁾ A total of 18 (0.19%) perforations (three for diagnostic colonoscopies, 15 for therapeutic colonoscopies) and 43 (0.45%) bleeding events associated with therapeutic colonoscopies were reported.

Table 5.8 Summary of harms studies included in USPSTF review with age-stratified results

Study, Follow-up	Sex	Age	N colonoscopies	AE rate	N with serious bleeding	N with perforation	N with infectious event	N with other SAEs
Ibanez 2018 ⁽³³⁰⁾ 30 days	All	≤59	3,541	NR	NR	NR	NR	Any SAE: 7
		≥60	5,290	NR	NR	NR	NR	Any SAE: 16
	Male	All	5,126	NR	NR	NR	NR	Any SAE: 15
	Female	All	3,705	NR	NR	NR	NR	Any SAE: 8
Rim 2017 ⁽³³¹⁾ 3 months	Male	50–59	NR	NR	107	68	27	Other SAE: 5
		60–69	NR	NR	97	86	13	Other SAE: 7
		≥70	NR	NR	67	59	11	Other SAE: 3
	Female	50–59	NR	NR	47	30	13	Other SAE: 4
		60–69	NR	NR	54	32	8	Other SAE: 2
		≥70	NR	NR	21	19	4	Other SAE: 1
	All	50–59	NR	NR	154	98	40	Other SAE: 9
		60–69	NR	NR	151	118	21	Other SAE: 9
		≥70	NR	NR	88	78	15	Other SAE: 4
Denis 2021 ⁽³²⁵⁾ 30 days	All	All	9,576	1.88% (Overall) 1.28% (Mild) [†] 0.42% (Moderate) [†] 0.18% (Severe) [†]	43	18	NR	NR
	All	50–59	NR	1.34%	NR	NR	NR	NR
		60–69	NR	2.06%	NR	NR	NR	NR
		70–75	NR	2.35%	NR	NR	NR	NR

Key: AE – adverse events. NR – not reported. SAEs – serious adverse events. USPSTF – United States Preventive Services Task Force.

[†] According to the American Society for Gastrointestinal Endoscopy (ASGE) lexicon.

Psychological harms of screening by age

Three studies that reported psychological harms of FIT-based CRC screening were identified from the de novo search.^(321, 322, 324) Of these, a 2020 study of participants aged 55 to 75 referred for colonoscopy following a positive FIT (n=1,066) in the Netherlands considered differences by age. The study examined the psychological impact of the screening process itself, as measured by the 12-item Psychological Consequences Questionnaire (PCQ), and the associated fears of developing cancer, as measured by the Cancer Worry Scale (CWS).^(324, 333, 334) Age did not appear to be significantly associated with psychological consequences following colonoscopy after a positive FIT result (adjusted OR 0.97 per year, 95% CI 0.94 to 1.00, $p=0.075$). Worry about developing cancer, however, appeared to decrease with increasing age (adjusted OR 0.97 per year, 95% CI 0.95 to 1.00, $p=0.037$).

The other two studies on psychosocial outcomes of screening identified from the de novo search reported results without consideration of age.^(321, 322) A longitudinal study of people aged 50 to 74 from the Danish CRC screening programme investigated the psychosocial consequences of screening results, and found that individuals identified as having medium-risk and high-risk polyps experienced more negative psychosocial consequences compared to individuals with no abnormalities or low-risk polyps.⁽³²¹⁾ The second study examined the association between anxiety levels and the decision to participate in the Screening of Swedish Colons (SCREESCO) trial among people aged 60 to 62.⁽³²²⁾ Mean anxiety scores did not differ significantly between those participating in screening and those who made the decision not to participate.⁽³²²⁾ Overall, 21% of those surveyed experienced anxiety relating to their screening decision, regardless of whether they had decided to participate in screening or not.⁽³²²⁾

Harms reported by the BowelScreen programme

Rates of colonic perforation, post-polypectomy perforation, and post-polypectomy bleeding requiring transfusion following BowelScreen colonoscopies are rare, affecting fewer than 0.1% of index colonoscopies (Table 5.9). Rates of colonic perforation and post-polypectomy perforation between 2012 and 2023 were highest among older females (0.88 and 0.88 per 1,000 colonoscopies, respectively) and younger males (0.65 and 0.39 per 1,000 colonoscopies, respectively). Among colonoscopy procedures with polypectomy, the highest rate of procedures with post-polypectomy bleeding requiring transfusion was among males aged 60 to 64 years (1.5 per 1,000 procedures where the number of polyps excised was ≥ 1).

Table 5.9 BowelScreen colonoscopy harms (2012–2023)

Colonoscopy harms	Male		Female	
	60–64	65–69	60–64	65–69
Reported colonic perforation rate (per 1,000 colonoscopies)	0.65	0.10	0.18	0.88
Reported post-polypectomy perforation rate (per 1,000 colonoscopies)	0.39	0.10	0.18	0.88
Post-polypectomy bleeding requiring transfusion (per 1,000)*	1.50	0.60	0.30	0.50

Source: BowelScreen.

* Per 1,000 colonoscopy procedures where the number of polyps excised was ≥ 1 .

The BowelScreen Patient Reported Experience Measures programme, published in 2023, surveyed individuals who had undergone a colonoscopy following a positive FIT result.⁽³³⁵⁾ Of those surveyed, 10.7% (n=174 of n=1,633) reported developing symptoms related to their colonoscopy following discharge from hospital.⁽³³⁵⁾ These symptoms included stomach pain (40.4%, n=67) and bleeding (19.9%, n=33), while a further 33.7% (n=56) were listed as 'other'.⁽³³⁵⁾

In relation to non-physical harms of screening relating to the BowelScreen programme, a 2021 publication examining the characteristics and attitudes of 1,545 first round invitees to BowelScreen (aged 60 to 70+ years) found that 22% (n=249) of study participants found the programme to be stressful.⁽³³⁶⁾ Participants noted sources of stress associated with screening included: waiting for results; feelings of embarrassment; completing the stool test itself; and the concern of a cancer diagnosis.⁽³³⁶⁾ Those receiving positive FIT results were significantly more likely to express stress surrounding the programme than those who received a negative FIT result (OR 7.7, 95% CI 5.3 to 11.3).⁽³³⁶⁾ Age did not appear to be associated with the likelihood of experiencing stress; there was no statistical difference in participants aged over 68 in terms of stress levels when compared to younger participants (age >68 years versus ≤ 67 : OR 1.0, 95% CI 0.7 to 1.5).⁽³³⁶⁾

5.5 Discussion

The aim of this chapter was to assess the clinical effectiveness and safety of colorectal cancer screening in average risk, asymptomatic people aged 50 to 54, and to examine the effectiveness of screening with a starting age of 50, compared to a

starting age of 55. A review of trial and observational study evidence was performed. No studies were identified that directly compared screening from age 50 with screening from age 55. Five observational studies of FIT-based screening, reported across six publications, and five RCTs of gFOBT or FSIG with or without FIT, reported across six publications, were identified that included participants falling within the 50 to 54 age group. Six studies on harms associated with FIT screening were also identified. The following discusses the findings of existing reviews (section 5.5.1), followed by findings from the included studies on the effectiveness of screening with a starting age of 50 in terms of reductions in CRC mortality and CRC incidence (section 5.5.2), and findings on potential harms (section 5.5.5). This discussion also considers factors likely to influence effectiveness estimates (section 5.5.3), the appropriateness of all-cause mortality as an outcome measure (section 5.5.4), and the use of decision modelling to inform evaluations of screening effectiveness, with a case study examination of the USPSTF recommendations (section 5.5.6).

5.5.1 Findings of existing reviews

The review presented in this chapter updated two existing evidence reviews, both of which informed recommendations on colorectal cancer screening.^(73, 80) The USPSTF-commissioned review evaluated the clinical effectiveness of screening, in terms of reduction in mortality and incidence, and considered effects by age, sex, and race and ethnicity. Studies within the review included both RCT and observational evidence, and examined a range of screening modalities, including colonoscopy, CT colonography, FSIG, gFOBT and FIT. The European Commission Initiative on Colorectal Cancer (ECICC) Working Group review assessed whether screening for CRC should be used in adults aged 50 to 69 with an average risk of colorectal cancer, and considered diagnosis of CRC, death from CRC, stage of CRC, and harms. Only RCT evidence was included, and such studies included assessments of gFOBT, colonoscopy and FSIG.⁽⁸⁰⁾ The RCTs included in the USPSTF and ECICC reviews, and which examined mortality or incidence, varied in terms of the included age ranges; for example, five of the ten RCTs included in the USPSTF review, and four of the ten RCTs included in the ECICC review included participants falling within the 50–54 age group. Based on the USPSTF evidence review, which included studies published through December 2019, it was concluded with ‘high certainty’ that there is substantial net benefit for screening versus no screening of CRC in those aged 50 to 75, as previously concluded in 2016.⁽³³⁷⁾ The strength of evidence was rated as ‘high’, and considered to be ‘consistent and precise’ in showing reductions in CRC mortality through screening with gFOBT specifically. However, the evidence review also highlighted a lack of evidence for FIT-based screening.⁽⁷³⁾ The ECICC Working Group concluded that there was ‘moderate’ desirable effects and ‘moderate’ strength of evidence for screening, across modalities, in those aged 50 to 69.

The following section summarises the findings of the present review in relation to the outcomes of CRC mortality and CRC incidence, followed by consideration of the clinical effectiveness of screening specifically in those aged 50 to 54.

5.5.2 Reductions in CRC mortality and CRC incidence

Ten studies that reported on the clinical effectiveness of CRC screening and included participants falling within the 50 to 54 age group were included in this review. There was consistent evidence from nine of the ten studies that screening reduces CRC mortality.^(84, 85, 311-317, 319, 320) Based on four RCTs, gFOBT screening was associated with a reduction in CRC mortality of between 6% and 22% compared to no screening at 30 years, in participants ranging in age from 45 to 80.^(84, 85, 318-320) A 2021 individual participant data (IPD) meta-analysis, which included 30-year follow-up data from both the Minnesota and Funen trials, reported that screening with biennial gFOBT reduced CRC deaths by 10% (RR 0.90, 95% CI: 0.82, 0.98).⁽³¹⁸⁾ The included FIT cohort studies generally reported larger reductions in CRC mortality, although estimates varied widely: these ranged from 10% with six years of follow-up to 65% with 11 years of follow-up in participants ranging in age from 50 to 74.^(314, 316)

All five RCTs and three of the included observational studies reported CRC incidence outcomes. Three of the five RCTs found no effect of screening on CRC incidence, with 11 to 28 years of follow-up.^(85, 319, 320) Two RCTs reported reductions in CRC incidence, ranging from a reduction of 15% at 18 years of follow-up in those screened with gFOBT, to a reduction of 22% at 15 years in those screened with FSIG with or without FIT.^(84, 317) Three of the five FIT studies reported reductions in CRC incidence, ranging from 31% with 11 years of follow-up to 33% with 5 years of follow-up.^(311, 314, 316)

A number of important differences between the gFOBT and or FSIG RCTs and the observational FIT studies included in this review should be noted, which may explain differences in the magnitude of reported effect estimates. These are discussed below (see section 5.5.3).

Clinical effectiveness of screening in those aged 50 to 54

Evidence on screening specifically for those aged 50 to 54 was limited to one large observational FIT study (Baldacchini et al.) and one RCT of FSIG with or without FIT (NORCCAP) that reported data specifically for this age group. The observational study, which was rated as fair quality, suggested that one or more rounds of FIT screening was effective in reducing both CRC mortality and CRC incidence specifically in the 50–54 age group. Compared to no screening, FIT screening was associated with a 62% reduction in CRC mortality in females and a 71% reduction in males at five to 11 years of follow-up.⁽³¹⁴⁾ FIT screening was associated with a reduction in CRC incidence of 25% in females and 30% in males for those aged 50–54 with 11

years of follow-up.⁽³¹⁴⁾ Importantly, however, this study did not use an intention-to-screen approach and may be subject to healthy screenee bias.

There was no evidence of a reduction in CRC mortality in people aged 50–54 based on data from the NORCCAP RCT of screening with FSIG with or without FIT at 14.8 years of follow-up.⁽³¹⁴⁾ Screening was associated with a 35% reduction in CRC incidence in males aged 50–54, with no reduction among females. However, it is important to note that the trial was not powered to detect an effect in this age group. The IPD meta-analysis of 30-year follow-up data from the Minnesota and Funen trials reported a 19% reduction in CRC mortality for those aged 60–69 (RR 0.81, 95% CI 0.69, 0.94), compared with no significant reduction in those aged 50–59 (RR 0.93, 95% CI 0.80, 1.08).⁽³¹⁸⁾

The NORDICC study, reported in 2022 by Bretthauer et al., included participants aged 55 to 64 in a colonoscopy screening trial and was therefore not included in the present review.⁽³³⁸⁾ The results suggested some effectiveness of colonoscopy screening in reducing CRC incidence, but no significant reduction in CRC mortality. The short follow-up time of 10 years, the low uptake rate of 42%, and low adenoma detection rates (under 25%) for 29% of endoscopists, were commented on as possible reasons for the results.⁽³³⁹⁾

5.5.3 gFOBT RCTs and observational FIT studies: comparability, bias, and other factors that affect estimates of clinical effectiveness

This review included both RCTs of screening with gFOBT and FSIG, as well as observational FIT studies. In addition to differences in screening modalities, length of follow-up and developments in CRC diagnosis and treatment since the commencement of the RCTs, differences in study designs and risk of bias are likely to contribute to differences in the effect estimates reported by the included studies. Given that the outcomes of CRC mortality and CRC incidence are affected by study design bias in different ways, consideration of both outcomes is important when assessing the effectiveness of CRC screening.

Risk of bias in observational studies of CRC screening

Observational studies are subject to several limitations, including lead-time and length biases, lack of randomisation of participants leading to selection bias, and the potential for residual confounding despite adjustment methods applied to counteract these biases.

Lead-time bias occurs when a disease is detected by a screening test earlier than it would have been if it had been diagnosed symptomatically.⁽³⁴⁰⁾ If survival time is measured from the time of cancer diagnosis (rather than from the time of randomisation or invitation to screening), the apparent increased survival time in the

screened group compared with the control group will reflect the asymptomatic 'lead time' of the disease, rather than improved survival in the screening group.⁽³⁴⁰⁾ Similarly, slowly growing cancers, which may be less likely to become fatal, may have a longer pre-symptomatic screen-detectable phase. These cancers will therefore be more likely to be detected through screening, resulting in length bias.⁽³⁴¹⁾ These biases are avoided in analyses of RCTs, as 1) the time origin is taken as the point of randomisation, and 2) CRC mortality rates among participants randomised to screening are compared with mortality rates among those randomised to no screening, rather than comparing survival rates of CRC cases.⁽³⁴¹⁾

In the observational FIT studies, the presence of both biases is likely to contribute to an overestimation of the effectiveness of screening. While Chiu et al. noted a reduction in advanced-stage cancers in the screened group compared to the unscreened groups, the authors highlighted the need for longer follow-up to address the lead-time bias inherent in the early phases of screening programmes.^(311, 312) Doubeni et al. commented on several of the other observational studies included in this review,⁽³¹³⁾ specifically those by Njor et al.,⁽³¹⁵⁾ Chiu et al. (2015 and 2021),^(311, 312) and Baldacchini et al.⁽³¹⁴⁾ The authors noted that these studies compared CRC mortality risk between screened and unscreened individuals, or people invited versus not invited to screening, in those aged 50–65 or 50–71 years, but that these studies did not verify eligibility in all individuals and or used incidence-based mortality rates, which may be subject to lead-time bias.⁽³¹³⁾

Non-random assignment to the screening group increases the probability that other important factors may differ between the two groups.⁽³⁴⁰⁾ Self-selection bias (often known as 'healthy screenee bias') occurs when studies are conducted in the context of population-based screening programmes, as those exposed to screening are those who voluntarily accept an invitation to participate, while those not exposed are those who decide not to take up the offer of screening.⁽³²⁷⁾ Since those who choose to participate in screening are likely to differ systematically from those who do not, the results are likely to be biased.⁽³⁴²⁾ Effect estimates reported by RCTs, on the other hand, are based on intention-to-treat analyses, whereby participants are maintained in their original, randomly assigned groups regardless of crossover between the groups,⁽³⁴⁰⁾ eliminating the impact of self-selection bias.

Two of the five FIT studies adjusted for self-selection bias,^(311, 312) informed by a method developed by Duffy et al., whereby an RCT intention-to-treat analysis is applied using the pre-screening group and natural incidence rate of CRC as a proxy to model the CRC mortality risk in an uninvited group.⁽³²⁷⁾ A similar method, described by Puliti et al.,⁽³²⁸⁾ was used by another of the included studies.⁽³¹⁴⁾ The differences in the adjusted and unadjusted effect estimates reported by two related publications based on a Taiwanese CRC screening programme demonstrate the

moderating effects of adjustment for self-selection bias and other potential confounders.^(311, 312) Chiu et al. (2021) reported a relative CRC mortality reduction of 0.60 (95% CI 0.57, 0.64) when adjusted for several potential confounding factors including selection bias, compared to an unadjusted estimate of 0.49 (95% CI 0.47, 0.51).⁽³¹¹⁾ However, adjustment is unlikely to fully account for confounding. The nested case-control study conducted by Doubeni et al. attempted to account for potential confounders through various methods; however, the authors noted that the potential for confounding by healthy screenee effects remains.⁽³¹³⁾

Other screening factors that can mediate the effectiveness of CRC screening

Intention-to-screen analyses may address the impact of self-selection bias on clinical effectiveness estimates; however, differences in uptake rates across studies may contribute to the heterogeneity in reported effect estimates, as the success of a screening programme depends on uptake among the eligible population. For example, Shaukat et al. (2021) reported a 16% relative reduction in CRC mortality among participants who underwent at least one screening procedure in the pooled analysis of data from the Minnesota and Funen trials, compared to a 10% reduction based on the pooled intention-to-treat analysis.⁽³¹⁸⁾

Similarly, the effectiveness of a stool-based screening programme is likely to vary depending on the number of screening rounds, as both CRC and pre-cancerous lesions tend to bleed intermittently. One of the five FIT-based studies included in this review reported outcomes based on a single round of screening.⁽³¹⁵⁾ More than one round of screening was reported in the other studies, but the upper limit of rounds was not reported.^(311, 312, 314, 316) As discussed by Njor et al. and acknowledged as a limitation of their study, the long-term effectiveness of FIT screening is increased through repeated screening rounds.⁽³¹⁵⁾ Multiple screening rounds increase the chances of catching previous false negative results in subsequent screening rounds, while the removal of adenomas will translate into cumulative mortality reductions over multiple screening rounds.⁽³¹⁵⁾ An editorial commenting on the findings of Baldacchini et al. suggested that the reduction in CRC incidence observed within the study likely reflects the detection and removal of adenomas within an organised screening programme that was running for more than 10 years at the time of analysis; that is, the findings represented repeated and regular return of participants for FIT screening.⁽³⁴³⁾

Two observational studies^(314, 315) and four RCTs^(84, 85, 317, 318) included in this review reported sex-stratified results. In five of these studies, screening was associated with greater reductions in CRC mortality in men than in women.^(84, 314, 315, 317, 318) Greater reductions in CRC incidence were reported for men in two studies that reported incidence outcomes.^(314, 317) The lower reduction in CRC incidence and mortality

associated with FIT-based screening programmes in women compared to men has been highlighted previously.^(296, 297) Strategies such as varying the FIT threshold for a positive result by sex have been implemented in Sweden, where a higher threshold is used for men, based on a higher faecal haemoglobin concentration compared to women.⁽¹⁰³⁾ However, it has been suggested that the use of sex-specific thresholds could introduce sex differences in positive and negative predictive values,⁽²⁸⁵⁾ and may disadvantage men.⁽²⁹⁶⁾ Any consideration of sex-specific screening strategies therefore warrants careful deliberation to avoid unintended consequences.

Relevance of evidence to the question concerning this HTA

While this review sought to assess the clinical effectiveness of screening with a starting age of 50 compared to screening at a later starting age, all included studies compared screening to no screening. Further, while two studies that reported results for people aged 50–54 were identified, the majority of the included studies did not present stratified results specifically for this age group. All included studies of the clinical effectiveness of screening with FIT used a threshold of 20µg/g to identify individuals for referral to colonoscopy. While BowelScreen initially commenced screening with FIT at a threshold of 20µg Hb/g faeces, this was increased to 45µg/g in 2014 to ease pressure on endoscopy capacity.^(18, 37, 60) The increased threshold resulted in lower positivity rates (from 8.6% to 4.1%) and fewer overall colonoscopy referrals.⁽⁶¹⁾ The CRC detection rate per 1,000 people screened also decreased from 3.8 per 1,000 at a FIT threshold of 20µg Hb/g to 2.3 per 1,000 at a threshold of 45µg Hb/g.⁽⁶¹⁾ In the Netherlands, an increase in the FIT threshold from 15 to 47µg/g similarly resulted in a decrease in age-adjusted detection rates (based on the number of positive FITs) from 5.8% to 4.4% for CRC and 30.8% to 20.6% for advanced adenomas.⁽¹³²⁾ Higher FIT thresholds result in the detection of fewer cancers; thus the clinical effectiveness estimates of FIT-based screening reported in this chapter may overestimate the effect. However, given the improved test accuracy of FIT for the detection of CRC relative to gFOBT, and the consistent evidence of clinical effectiveness of gFOBT screening, it is unlikely that screening with FIT at a threshold of 45µg/g would be less effective than screening with gFOBT. The test accuracy of FIT is discussed in more detail in Chapter 4.

5.5.4 All-cause mortality

Endpoints for assessing clinical effectiveness of screening programmes are necessarily selected based on the specific disease in question, such as CRC mortality and CRC incidence. It has been argued that the overall goal of healthcare and screening programmes should be to reduce the risk of death and improve the quality of life of patients more generally, rather than focusing on cancer-specific mortality.⁽³⁴⁴⁾ No significant reductions in all-cause mortality were reported by the four gFOBT and FSIG RCTs included in this review that reported it as an outcome.^{(84,}

85, 317, 320) The USPSTF review similarly reported that none of the included RCTs reported an association of gFOBT screening with all-cause mortality,⁽⁷³⁾ while the ECICC review did not consider all-cause mortality as an outcome.⁽⁸⁰⁾ Shaukat et al. (2021) reported no effect of gFOBT screening on 30-year all-cause mortality (RR 1.00, 95% CI 0.99, 1.00), based on an IPD meta-analysis that combined data from both the Funen and Minnesota Colon Cancer Control trials.⁽³¹⁸⁾

The absence of RCTs showing an effect on all-cause mortality may be due to a lack of sufficient power to detect small reductions in all-cause mortality.^(344, 345) Two modelling studies suggested that CRC screening trials would need a minimum follow-up time of 15–20 years and participant numbers between 500,000 and 1,200,000 to detect a 3% reduction in all-cause mortality.^(346, 347) A lack of consensus about what constitutes an acceptable reduction was highlighted, with Stang et al. suggesting that an absence of effect on all-cause mortality should not be mistakenly interpreted as an absence of effect for screening more generally.⁽³⁴⁶⁾

One of the five observational studies of FIT screening within the present review reported data for all-cause mortality.⁽³¹⁴⁾ While the sample size of this study was smaller than the suggested minimum participant size for this outcome, as mentioned above, it was larger than that of any of the RCTs. FIT screening in those aged 50–69, compared to no screening, was associated with significant reductions in all-cause mortality excluding CRC deaths in both men and women (men RR 0.46 [95% CI, 0.45 to 0.48], n=380,651 screened, n=327,100 unscreened; women RR 0.44 [95% CI, 0.42 to 0.45], n=1,681 screened, n=1,628 unscreened). However, the study authors noted that the difference in all-cause mortality between the screened and unscreened groups was likely to have been the result of self-selection or healthy screenee bias, as those attending health screening are likely to be more informed and engaged with screening programmes, and may also have fewer comorbidities resulting in a greater disparity between all-cause mortality rates in screened and unscreened groups.⁽³¹⁴⁾ Shaukat et al. (2021) similarly highlighted that the benefits among individuals who participate in screening may be due not only to screening, but also other health behaviours such as non-smoking, healthy diet or other lifestyle choices, which may contribute to lower risks of dying.⁽⁷⁶⁾

5.5.5 Harms of screening

Harms of colonoscopy

The USPSTF evidence review reported serious adverse events from a single screening colonoscopy as relatively uncommon, with a slightly higher rate for colonoscopy following abnormal stool tests.⁽⁷³⁾ This likely reflects the fact that those undergoing colonoscopy following a positive FIT have elevated f-Hb, which could be a marker of systemic inflammation or the presence or risk of other chronic conditions,⁽²⁸⁸⁻²⁹⁰⁾ all

of which may contribute to an increased likelihood of adverse events. Harms of stool testing itself were not specifically considered, but were assumed to be limited to the risk of missed cancers (false negatives). The review further reported that serious adverse events from colonoscopy, including perforation and bleeding, increased with increasing age, based on 23 studies.⁽⁷³⁾ Evidence relating to harms of screening with colonoscopy were rated within the USPSTF evidence review as 'consistent and precise', with 'moderate' strength.⁽⁸²⁾ The ECICC Working Group review, in comparison, judged the undesirable effects of screening to be variable. Rates of severe harms were judged as 'trivial' for bleeding and perforation and 'moderate' for pain; collectively, these were assessed as 'small' overall.⁽⁸⁰⁾ The ECICC guideline working group judged that the balance between desirable and undesirable effects favours screening.

Age-stratified data regarding harms of colonoscopy following a positive FIT result were limited to two studies included in the USPSTF review^(330, 331) and one study identified through the updated search.⁽³²⁵⁾ The study by Ibanez et al. reported harms with age-stratified results and associated numbers of colonoscopies; this reported increased rates of adverse events following colonoscopy for a positive FIT in older age groups.⁽³³⁰⁾ The study by Rim et al. found that increasing age was statistically significantly associated with increased rates of perforation.⁽³³¹⁾ The study identified through the updated search, by Denis et al., found that rates of AEs increased with age, from 1.34% among those aged 50–59 to 2.06% and 2.35% among those aged 60–69 and 70–75, respectively ($p=0.02$).⁽³²⁵⁾ Data from BowelScreen, for reference, show low rates of colonic perforation and post-polypectomy perforation overall, affecting fewer than 0.1% of index colonoscopies. These perforation rates are comparable with the pooled estimates of colonic perforation reported for colonoscopy following abnormal stool testing by the USPSTF review (0.54 perforations per 1,000 colonoscopies based on 12 studies) and ECICC review (0.79 perforations per 1,000 colonoscopies). A review of 31 studies by Chandan et al. similarly concluded that the overall risk of severe adverse events related to colonoscopy following a positive stool test was minimal, although no analysis was provided by age.⁽³⁴⁸⁾ The pooled incidence for perforations and bleeding related to diagnostic colonoscopy following a positive FIT was 0.01% (95% CI 0.00, 0.08) and 0.33% (95% CI 0.10, 0.62) respectively.⁽³⁴⁸⁾ The pooled incidence for perforation and bleeding following therapeutic colonoscopy following positive FIT test was 0.12% (95% CI 0.00, 0.19) and 0.71% (95% CI 0.20, 1.11) respectively.⁽³⁴⁸⁾

Psychosocial harms of colorectal cancer screening

Psychological harms were not considered as outcomes by the USPSTF or ECICC Working Group reviews. Three studies identified through the de novo searches reported on the impact of FIT screening on psychosocial outcomes, and one of these

considered age. Vermeer et al. reported that while age did not appear to be associated with changes in psychological consequences following colonoscopy, increasing age appeared to be associated with a slight decrease in cancer worry.⁽³²⁴⁾ Overall, participants did not regret their decision to participate in screening.⁽³²⁴⁾ A 2017 systematic review of CRC-screening related morbidity and mortality included 11 studies of psychological distress or morbidity following invitation to screening;⁽³⁴⁹⁾ however, potential differences in the experience of harms by age were not considered. A study of first-round invitees to the BowelScreen programme (aged 60–70+) reported that while those who had received a positive FIT result were significantly more likely to experience stress compared to those with a negative FIT, age did not appear to be associated with the likelihood of experiencing stress.⁽³³⁶⁾

Overdiagnosis and overtreatment in colorectal cancer screening

Not all precursor lesions or cancers detected through screening will clinically manifest and lead to symptoms during the lifetime of a patient. Overdiagnosis in cancer screening is defined as the detection of a lesion that would not have progressed to cancer or caused symptoms or death in the remaining lifetime of the individual who received the diagnosis.⁽³⁵⁰⁾ In the case of overdiagnosis, the associated cancer treatment may then be considered to be overtreatment. In this case, there is no added benefit to the patient, and the additional treatment may be considered a harm.⁽²⁴⁶⁾ Identifying which adenoma or CRC cases detected as a result of screening constitute overdiagnosis is challenging, due to the complex biological factors that may affect tumour development.^(246, 351) The USPSTF review of harms related to CRC screening did not identify any studies that directly assessed overdiagnosis, but cited a German modelling study that estimated the risk of overdiagnosis to be below 0.1% among men up to age 65 and among women up to age 71.^(73, 352) This gradually increased to 0.9% and 0.6% at age 80 in men and women, respectively, with 28% of all overdiagnosis estimated to occur in those aged over 75.⁽³⁵²⁾ The risk of overdiagnosis may be lower in younger age groups, which have a lower incidence of CRC. Further, older individuals are more likely to have other comorbidities that may limit their overall life expectancy.⁽²⁴⁶⁾

5.5.6 Use of decision models in evaluating the effectiveness of screening; case study of US recommendations

Decision models are a methodological approach that can be used to simulate the effects of screening on health outcomes in specific populations (for example, different screening starting ages). Parameters such as disease incidence, stage distribution and survival are combined to predict events and outcomes in a hypothetical population over a defined timeline. Modelling can potentially address questions that have not been, or cannot be, answered in clinical trials, and can be

used to supplement reviews of the clinical evidence (trials and observational studies), such as that carried out within this chapter.

There are various limitations, however, to the use of decision models. Existing models may not be transferable to the local decision context due to differences in aspects such as epidemiological parameters (for example, CRC incidence), or the exact interventions assessed (for example, alternative thresholds or screening intervals). Furthermore, the validity of a model used for its intended purpose is subject to important limitations; these include the assumptions used to model the natural history process, the screening process, and individual behaviour, as well as the possibility of producing results with misleading levels of precision.⁽³⁵³⁾

Nonetheless, decision models have been used, for example, by the USPSTF in the development of recommendations for various screening topics, including colorectal cancer,⁽³⁵⁴⁾ to supplement systematic reviews of the clinical evidence. The following section describes the findings of CRC screening modelling work to provide context for recommendations made by bodies such as the USPSTF with respect to the starting age for screening.

CRC modelling conducted to inform USPSTF recommendations

The USPSTF has used model results to inform its recommendations since 2008.⁽³⁵⁵⁾ To inform the 2016 update to the 2008 USPSTF recommendations, 204 screening strategies were evaluated through microsimulation modelling, with part of this work modelling different ages to begin screening (45, 50, and 55).⁽³⁵⁶⁾ A range of screening modalities, including FIT testing (with a threshold of 20µg/g), were examined, with all non-colonoscopy screening tests assumed to be followed up with colonoscopy in the event of abnormal results. Full adherence to tests was assumed. In initial analyses, for all modalities, strategies with screening beginning at age 45 years provided additional life years gained (LYG) at a lower number of additional colonoscopies than strategies with screening beginning at later ages. However, given limited empirical data to support screening from age 45, and given that the results showed a small increase in LYG relative to the additional number of colonoscopies, subsequent analyses were limited to strategies beginning screening at age 50 or 55. Within these analyses, screening from age 50 was found to be favourable.

To inform the 2021 update of its recommendations, the USPSTF requested an update to the 2016 modelling study.⁽⁴⁾ This incorporated recent evidence reporting increasing CRC incidence rates among recent US birth cohorts, and also considered whether results varied by race and sex. Model findings again suggested that screening from age 45 would be more 'efficient' (in terms of incremental LYG per additional colonoscopy) than screening from age 50. However, it is important to note that these results are influenced by modelling assumptions, and varied by individual

model. For example, one of the models (MISCAN), assumed that some adenomas are non-progressive, with the probability that an adenoma is non-progressive decreasing with age at onset; because of this age dependency, this model was found to estimate a smaller benefit from removing adenomas present at age 45 compared with the other two models.⁽⁴⁾ While these findings concern a question of screening at age 45 versus age 50 (as opposed to 50 versus 55), they are illustrative of the impact of choice of model assumptions.

Evidence to decision: USPSTF recommendations

In 2016, in an update to its 2008 CRC screening recommendations, the USPSTF concluded with high certainty that screening for colorectal cancer in average-risk, asymptomatic adults aged 50 to 75 years is of substantial net benefit, and that the harms in this group are small. The USPSTF issued a grade 'A' recommendation in favour of screening (across modalities) for this group.⁽³⁵⁷⁾ In this statement, the USPSTF noted that it had found convincing evidence that screening for colorectal cancer in adults aged 50 to 75 years reduces CRC mortality, although the individual tests were found to have varying levels of evidence supporting their effectiveness. Specifically in relation to stool-based tests, the statement noted that multiple RCTs had shown that screening with gFOBT reduces CRC deaths, and, separately, that available RCTs included participants with age ranges of 45 to 80 years, though the majority entered the trials at age 50 or 60.⁽³³⁷⁾ Considerations regarding a starting age of 45, versus 50, were additionally informed by results of the microsimulation analyses, as described above, and findings regarding an increased lifetime number of colonoscopies.

For the 2021 update, the USPSTF commissioned a systematic review of the benefits and harms of screening for CRC in adults 40 years or older (as updated in the present chapter) and also considered microsimulation model findings as described above.⁽⁸²⁾ In its assessment of this combined evidence, the USPSTF concluded with high certainty that screening for CRC (across modalities) in adults aged 50 to 75 years has substantial net benefit, and issued a grade 'A' recommendation in favour of screening for this group. The strength of evidence supporting this recommendation was rated as 'high' and considered to be 'consistent and precise' in showing reductions in CRC mortality through screening with gFOBT specifically. The evidence review, which included studies published through December 2019, highlighted, however, a lack of evidence for FIT-based screening;⁽⁷³⁾ the strength of evidence for clinical effectiveness of FIT screening (regardless of starting age) was rated as 'low', with no rating given for consistency or precision as only one cohort study with limited follow-up was included.⁽³³⁷⁾

The USPSTF additionally concluded, with moderate certainty, that screening in adults aged 45 to 49 has moderate net benefit, and issued a grade 'B' recommendation in

favour of screening for this group. Specifically in relation to FIT, the USPSTF concluded, based on microsimulation model findings, that screening with annual FIT provides an estimated greater LYG than annual high-sensitivity gFOBT, for example. The rationale provided was that a recent trend for increasing CRC had been observed in US birth cohorts of adults younger than 50 years. Additionally, it was stated that the benefit of reducing CRC deaths by screening in adults 50 years or older is well established through trial data; it was noted that some of the trials, specifically Faivre et al., Kronborg et al., and Scholefield et al., included adults younger than 50 years, though results were not reported separately for younger age groups.^(85, 319, 320)

It is important to note that not all recommendation bodies consider decision-modelling data within their assessments of net benefit; for example, the ECICC Working Group guidelines on CRC primary prevention, screening, and diagnosis considered modelling studies, but only in the context of assessment of cost-effectiveness.⁽⁸⁰⁾ As such, it is important to consider the nature of the evidence base underlying recommendations, and the assumptions informing the evidence.

5.5.7 Strengths and limitations

This review has a number of strengths. Two recent systematic reviews, conducted to inform recommendations of the USPSTF and the European Commission Initiative on Colorectal Cancer (ECICC) Working Group, were updated using comprehensive, systematic search strategies. Given the limited direct evidence for the clinical effectiveness of FIT-based screening, a range of different screening modalities was considered, including older gFOBT-based RCTs. This review also considered both disease-focused outcomes such as CRC mortality and incidence, and broader outcomes such as all-cause mortality and PROM-based studies reporting patient experiences.

A number of limitations should be noted. The present review updated the USPSTF and ECICC Working Group reviews and shares some limitations of these reviews. The updated search was conducted to identify cohort and case-control studies published since the last search of the USPSTF review (from 1 December 2019 to 12 July 2024); therefore, studies published prior to 1 December 2019, but not captured within the USPSTF and ECICC Working Group reviews, would not have been identified. The USPSTF review notes, for example, that it is possible that excluded well-designed nested case-control studies of colonoscopy or FIT may have had lower risk of bias than included prospective cohort studies. Also, given the volume of records returned by the update searches, titles and abstracts of identified records were screened by one reviewer only; as a result, it is possible that some studies may have been missed. In relation to harms, this review included the outcome of psychological harms, in contrast with the USPSTF and ECICC Working Group reviews. However, only studies of psychological harms that were published since the last search dates

of the USPSTF review were identified by the updated search. It is therefore possible that additional studies have explored potential associations between the experience of psychological harms of CRC screening and age. Further, the quality of the six studies of harms included in this review was not formally assessed.

5.5.8 Conclusion

The review presented in this chapter focused on studies that included participants specifically within the age range of interest, namely those aged 50 to 54. Age-stratified data on the clinical effectiveness and harms of colorectal cancer screening in those aged 50 to 54 were reported infrequently, and no studies were identified that directly compared the effectiveness of screening with a starting age of 50 to screening with a starting age of 55. There was consistent evidence, however, based on a range of screening modalities and study designs, that screening from age 50 reduces colorectal cancer mortality compared to no screening. There was some evidence to suggest that FIT screening may also reduce colorectal cancer incidence; however, this was based mainly on observational studies, which are at higher risk of bias. With respect to harms, the risk of adverse events of colonoscopy following a positive stool-based test appears to decrease with age. Direct evidence of the clinical effectiveness of screening with FIT specifically is based on observational studies; while these are subject to important biases, the evidence from these studies is consistent with a beneficial effect of screening.

6 Review of the cost effectiveness of extending BowelScreen to those aged 50 to 54 years

6.1 Key points

- This chapter reviewed the international evidence on the cost effectiveness of lowering the starting age of eligibility for population-based colorectal cancer (CRC) screening. The evidence review focused on European studies that examined expansion to the age range of interest (that is, the age range of 50 to 54). The potential relevance, credibility, and transferability of the findings to the Irish setting were considered.
- The review aimed to address whether, for the population in Ireland at average risk of colorectal cancer, providing two-yearly faecal immunochemical test (FIT)-based colorectal cancer screening at a FIT threshold of 45µg Hb/g faeces (FIT45) to persons aged 50 to 74 years, is likely to be cost-effective relative to screening those aged 55 to 74 years.
- A 2023 systematic review of the cost effectiveness of CRC screening was used as a key source of identification of relevant studies. An additional systematic search was performed to capture studies published since this systematic review.
- Eight studies met the inclusion criteria for the review. However, none of the studies directly reported the cost effectiveness of screening all adults aged 50–74, versus those aged 55–74, using a FIT45 threshold and two-yearly screening intervals.
 - Most studies reported costs and quality-adjusted life years gained (QALYs) for broadly similar strategies, where either the FIT threshold, screening interval, or age range varied; these strategies were used to consider the potential cost effectiveness of extending the age of eligibility for screening from 55–74 to 50–74 years in Ireland.
- Six studies were deemed sufficiently relevant to the present HTA. Among these, the validity, design, and choice of data inputs were largely robust and considered 'sufficiently credible' to support decision making in the context of Ireland.
- The six studies were largely considered to be of high quality overall. However, a number of concerns were identified in relation to the historical

nature of costs, scale of cost inputs, choice of utility weights, and lack of detailed reporting of data sources.

- Study results were disaggregated to examine the model findings for the effectiveness of screening from age 50 versus screening from age 55. Based on three studies, which modelled screening strategies that had a greater or lesser intensity to that used in the BowelScreen programme, estimates of CRC incidence reduction ranged from less than one to four additional CRC cases prevented per 1,000 people screened. For CRC mortality, these studies estimated between one and two additional CRC deaths avoided per 1,000 people screened. However, these estimates are uncertain and the applicability to Ireland is unclear.
- The cost per QALY could be estimated from four studies deemed sufficiently relevant to the present HTA. Incremental cost-effectiveness ratios (ICERs) ranged from €1,548 to €10,401 per QALY. The impact of the quality and transferability concerns identified is not expected to result in an ICER of above €20,000 per QALY.
- In the context of Ireland, the overall evidence suggests that screening all adults from age 50 to 74 years is likely cost-effective versus screening all adults from age 55 to 74 years, based on a willingness-to-pay threshold of €20,000 per QALY gained.

6.2 Introduction

The aim of this chapter was to assess whether, for the population in Ireland at average risk of colorectal cancer (CRC), it is cost-effective to provide two-yearly faecal immunochemical test (FIT)-based colorectal cancer screening at a FIT threshold of 45µg Hb/g faeces (FIT45) to persons aged 50 to 74 years, versus those aged 55 to 74 years. As described in Chapter 1, additional modifications to the screening programme were considered beyond the scope of this HTA.

The cost effectiveness of CRC screening overall has been well documented in the literature, including in a previous assessment by HIQA in 2009 that led to the introduction of the BowelScreen programme in 2012.⁽¹²⁾ For this reason, this chapter does not summarise the available evidence on the cost effectiveness of CRC screening generally. For the purposes of this HTA, the evidence on the cost effectiveness of lowering the starting age of CRC screening was reviewed, with a particular focus on the comparison of the cost effectiveness of the age ranges of 50–74 and 55–74.

6.3 Methods

6.3.1 Approach to study identification and selection

A detailed background to this review, and description of associated methods, is provided in the accompanying [protocol](#). Briefly, a review of cost-effectiveness literature was performed, focusing on model-based studies published since 2014 that estimated the cost effectiveness of FIT-based CRC screening strategies. Initial scoping indicated that a broad range of FIT-based strategies were examined in the primary literature, for example, variations in FIT thresholds, starting and finishing ages, and screening intervals. Also, there was heterogeneity in the parameters and parameter values used across studies, and a lack of studies specifically addressing the strategy of interest to this HTA. As such, it was considered necessary to apply a broad PICOS framework (Table 6.1) for the identification of studies to ensure a sufficient breadth of evidence.

As part of scoping, a systematic literature review published in 2023 was identified to be of particular relevance to the present review.⁽³⁵⁸⁾ As such, this systematic review was chosen as a key source for identification of cost-effectiveness analysis (CEA) studies. Studies included in the systematic review were examined for relevance according to the inclusion criteria specified in Table 6.1. An additional systematic search was performed between 23 and 31 January 2024 to identify studies published since the conclusion of the searches conducted as part of this review, and to search for grey literature. The complete electronic search strategy for all databases is available on Zenodo®.⁽³⁵⁹⁾ Study titles and abstracts were screened independently by two reviewers. The full texts of potentially eligible studies were retrieved and independently assessed for eligibility by two reviewers according to the criteria outlined in Table 6.1, with any disagreements resolved by discussion with a third reviewer.

Table 6.1 PICOS framework for review of cost-effectiveness studies

Inclusion criteria	
Population	Average-risk populations in European countries.
Intervention and comparator	<i>Ideal intervention and comparator for HTA research question:</i> Colorectal cancer screening using FIT-based strategies at starting age of 50 (with screening age up to 74), compared to a starting age of 55. Range of evidence to be considered: Colorectal cancer screening using FIT-based strategies with any screening interval (one-yearly, two-yearly or longer), where the intervention eligibility age incorporates people aged between 50 and 54 years with any finishing age, compared to a later starting age of screening. Evidence for consideration may include varying FIT thresholds.
Outcome	Measures of cost-effectiveness, for example, ICERs (cost per quality-adjusted life year) or measures of costs and health benefits expressed separately.
Study design	Full economic evaluations: - cost-utility analyses - cost-effectiveness analyses.
Exclusion criteria	
Population	Studies in populations at high genetic risk.
Intervention and comparator	Studies for which the only comparator is no screening.
Outcome	Studies not reporting measures of health benefits such as life years gained or ICERs, or not reporting both measures of costs and health benefits.
Study design	Studies published prior to 2014. Conference abstracts, comments and editorials.

Key: CRC – colorectal cancer, FIT – Faecal Immunochemical Test, ICER – incremental cost-effectiveness ratio.

6.3.2 Data extraction and management

A data extraction form was developed in Microsoft Excel and piloted. Data were extracted independently by two reviewers, with any disagreements resolved through discussion or with a third reviewer where necessary. The information extracted for each study is detailed in Appendix D.

6.3.3 Assessment of relevance, credibility, and methodological quality of studies

The ISPOR questionnaire on the relevance and credibility of model-based studies was used to inform the potential transferability of CEA studies to the Irish setting.⁽³⁶⁰⁾ As per the ISPOR questionnaire, questions on 'relevance' relate to population, intervention, and context, while questions on 'credibility' pertain to seven domains:

model validity, design, inputs, analysis, reporting, interpretation, and conflicts of interest. The overall relevance, along with the credibility, of a model was assessed as 'sufficient' or 'insufficient'. If the relevance of a study was deemed 'sufficient', its credibility was assessed. The questionnaire consists of 15 questions overall, where the individual response to each question is 'yes', 'no', or 'can't answer'. Each domain on credibility is assessed as a 'strength', 'neutral', 'weakness' or 'fatal flaw'. A response indicating 'fatal flaw' would suggest serious credibility issues associated with a model.

The methodological quality of studies deemed 'sufficiently relevant' to the present question, as per the ISPOR questionnaire, was then assessed using the Philips checklist.⁽³⁶¹⁾ Comprising 57 questions in total, the Philips checklist covers three key modelling domains: (1) structure; (2) data; and (3) consistency. For this review, an assessment of the methodological quality of existing evidence is crucial to understanding the strengths and limitations of potentially transferable evidence. The checklist does not provide a rating on the methodological quality of studies under consideration, or provide answers to the appropriateness of a model to inform decision-making in the present HTA. Rather, the framework and accompanying checklist serve as a guide to raise concerns regarding, or improve confidence in, the approaches used to (1) develop the model structure; (2) incorporate parameter inputs; and (3) ensure consistency in key findings.

Both assessments were performed by two researchers independently, with any disagreement resolved through discussion or a third reviewer where necessary.

6.3.4 Data synthesis

A narrative synthesis of the results of the included studies is presented, with a particular focus on studies deemed 'sufficiently relevant' to the present HTA, based on the assessment of relevance and credibility (above). Study results are summarised and presented in terms of 2023 Irish Euro (€) as described in the [protocol](#). Appendix D (section D.4) presents the consumer price index (CPI) and gross domestic product (GDP) purchasing power parity (PPP) data that were used to adjust and convert costs. Cost-effectiveness outcomes are summarised relative to commonly applied willingness to pay (WTP) thresholds of €20,000 and €45,000 per QALY gained in Ireland using summary estimates of incremental cost-effectiveness ratios (ICERs) and incremental net monetary benefits (INMBs).

6.4 Results

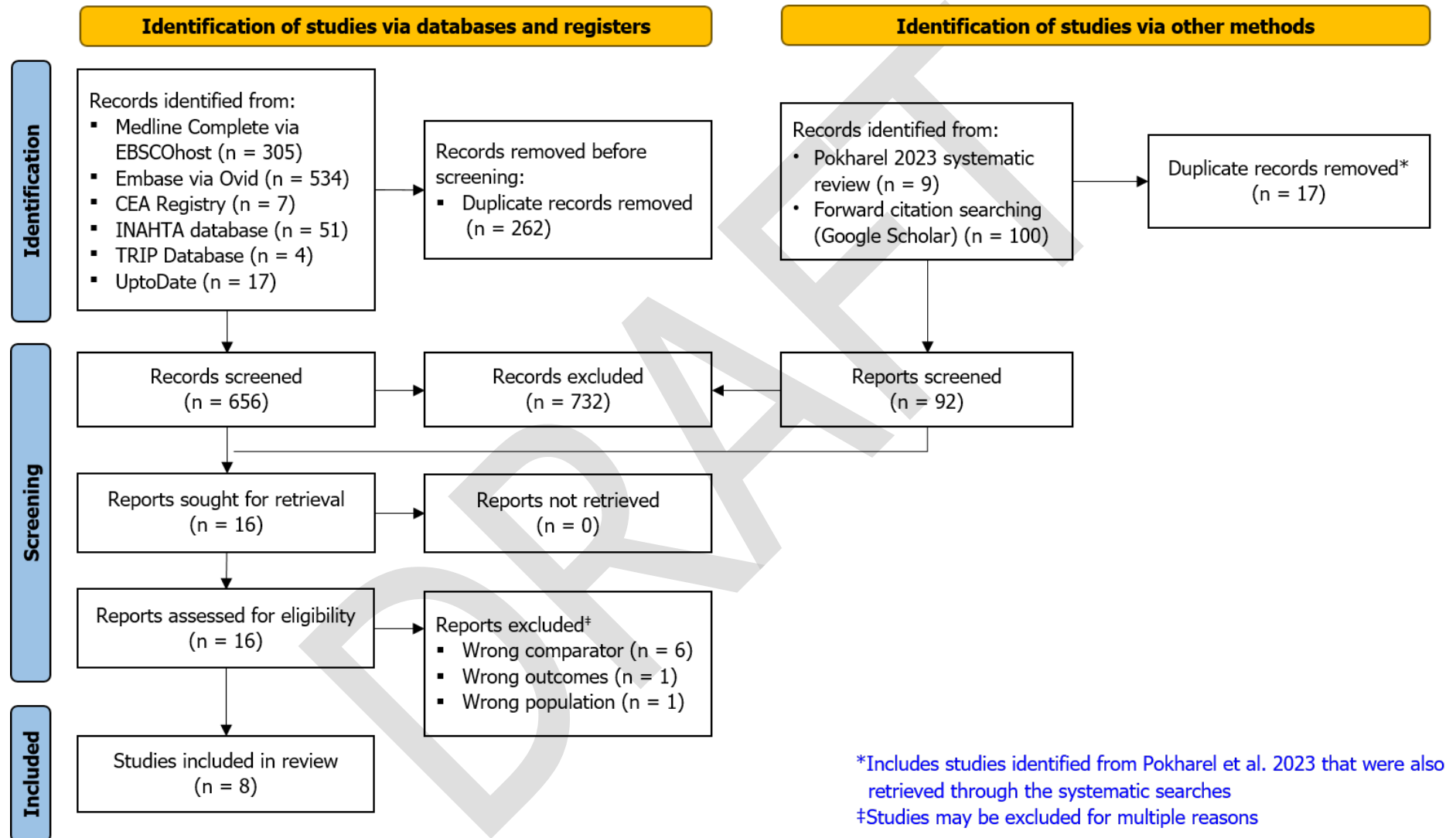
The PRISMA flow chart for the systematic search is presented in Figure 6.1. The electronic search returned 656 records for title and abstract screening after duplicates were removed. A forward citation search was also conducted. Sixteen full-

text articles were assessed for eligibility, of which eight met the inclusion criteria for this systematic review.

A brief overview of the included studies is provided in section 6.4.1. The relevance and credibility of these studies, based on the ISPOR questionnaire, is discussed in section 6.4.2. The methodological quality of studies deemed 'sufficiently relevant' to the present HTA, as assessed using the Philips Checklist, is presented in section 6.4.3. A detailed summary of these studies is then presented in sections 6.4.4, 6.4.5 and 6.4.6, where consideration is given to the potential transferability of the cost-effectiveness findings to the Irish setting.

DRAFT

Figure 6.1 PRISMA 2020 flow diagram of included studies



6.4.1 Overview of included studies

Of the 16 full text articles assessed, eight were deemed to meet the inclusion criteria for the review.⁽³⁶²⁻³⁶⁹⁾ One of the eight articles was published as a 'research letter' (or short research paper) (van de Schootbrugge-Vandermeer 2024).⁽³⁶⁹⁾ None of the studies specifically sought to establish whether lowering the starting age at which individuals at average risk of CRC are invited for screening is cost-effective. Instead, studies broadly compared the cost effectiveness of a wide range of age ranges (including those considered in this HTA), FIT thresholds, and screening intervals. An overview of the study characteristics is presented in Tables 6.2 to 6.5, encompassing study design (Table 6.2), screening strategies (Table 6.3), costs (Table 6.4), and analysis of uncertainty (Table 6.5).

Four studies considered the cost effectiveness of screening in the Netherlands (Lansdorp-Vogelaar 2018; McFerran 2022; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017);^(364, 365, 367, 369) two considered cost-effectiveness in England (Thomas 2021 and Whyte 2021);^(366, 368) and one study each considered cost-effectiveness in Finland (Heinävaara 2022)⁽³⁶²⁾ and Germany (Ladabaum 2014),⁽³⁶³⁾ respectively. Four studies considered cost-effectiveness in the context of colonoscopy capacity constraints (McFerran 2022; Thomas 2021; van de Schootbrugge-Vandermeer 2024; Whyte 2021).^(365, 366, 368, 369) Three studies specifically evaluated the cost effectiveness of sex-stratified screening (Heinävaara 2022; Thomas 2021; van der Meulen 2017).^(362, 366, 367) One study evaluated the cost effectiveness of hybrid screening strategies involving both FIT and colonoscopy screening (Ladabaum 2014).⁽³⁶³⁾ Another study sought to identify the maximum unit cost of a hypothetical biomarker test, such that the test could be considered cost-effective compared with FIT-based screening (Lansdorp-Vogelaar 2018).⁽³⁶⁴⁾

Cost-effectiveness was typically expressed using cost per QALY gained (that is, cost utility analysis, CUA) (Ladabaum 2014; McFerran 2022; Thomas 2021; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017),^(363, 365-367, 369) though two studies expressed cost-effectiveness using cost per life year (LY) gained (Heinävaara 2022 and Lansdorp-Vogelaar 2018) (that is, cost-effectiveness analysis, CEA)^(362, 364) and two studies summarised cost-effectiveness in terms of net monetary benefit (NMB) (Thomas 2021; Whyte 2021).^(366, 368) Net monetary benefit represents the value of an intervention in monetary terms at a given willingness-to-pay (WTP) threshold for a unit of benefit (for example, €20,000 per QALY gained). A positive NMB suggests an intervention is cost-effective at the assumed WTP threshold, while a negative NMB suggests the opposite.

Given the typically high number of screening strategies considered in each study (see Table 6.2), the most cost-effective strategy was identified using information on: (1) the cost-effectiveness efficiency frontier (Heinävaara 2022; van de Schootbrugge-

Vandermeer 2024; van der Meulen 2017);^(362, 367, 369) and, (2) NMB (Thomas 2021 and Whyte 2021),^(366, 368) or net health benefit (NHB) (McFerran 2022),⁽³⁶⁵⁾ where strategies with the highest NMB/NHB were considered 'optimal' strategies. van de Schootbrugge-Vandermeer 2024 additionally sought to identify the optimal strategy among efficient strategies based on the maximum QALYs gained given a €20,000 WTP threshold.⁽³⁶⁹⁾

Individual-level microsimulation models were typically used to simulate screening outcomes (Heinävaara 2022; McFerran 2022; Thomas 2021; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017; Lansdorp-Vogelaar 2018),^(362, 364-367, 369) though two studies used state transition models (Ladabaum 2014 and Whyte 2021).^(363, 368) The widely validated MISCAN-Colon microsimulation model was used in five studies (Heinävaara 2022; McFerran 2022; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017; Lansdorp-Vogelaar 2018).^(362, 364, 365, 367, 369)

Table 6.2 Overview of study characteristics

Author Year	Country	Type of analysis	Outcome(s)	Model structure	Model name	Perspective	Time horizon	Discount rate (%)	Price year Currency
Heinävaara 2022 ⁽³⁶²⁾	Finland	CEA	LYs	Microsimulation	MISCAN-Colon	Healthcare payer	Lifetime (50 years)	3%	2019 EUR (€)
Ladabaum 2014 ⁽³⁶³⁾	Germany	CUA	QALYs	Markov	-	Healthcare payer	30 years	3%	2011 EUR (€)
Lansdorp-Vogelaar 2018 ⁽³⁶⁴⁾	Netherlands	CEA	LYs	Microsimulation	MISCAN-Colon	(Modified) Societal	Not reported	3%	2013 EUR (€)
McFerran 2022 ⁽³⁶⁵⁾	Netherlands	CUA	QALYs	Microsimulation	MISCAN-Colon	Not reported†	Lifetime	3%	2010* EUR (€)
Thomas 2021 ⁽³⁶⁶⁾	England	CUA	QALYs, NMB	Microsimulation	MiMiC-Bowel	Healthcare payer	Lifetime	3.5%	2017/18 Sterling (£)
van der Meulen 2017 ⁽³⁶⁷⁾	Netherlands	CUA	QALYs	Microsimulation	MISCAN-Colon	Healthcare payer	Lifetime (75 years)	3%	2012 EUR (€)
van de Schootbrugge- Vandermeer 2024 ⁽³⁶⁹⁾	Netherlands	CUA	QALYs	Microsimulation	MISCAN-Colon	Not reported†	Lifetime	3%	2018 EUR (€)
Whyte 2021 ⁽³⁶⁸⁾	England	CUA	QALYs, NMB	State transition cohort model	SCHARR Bowel Cancer Screening Model	Healthcare payer	Lifetime	3.5%	2014/15 Sterling (£)

* Price year used in McFerran 2022 was unclear; since these derive from a 2011 publication, costs were assumed to reflect 2010 prices.

† Although the assumed perspective was not reported, it was consistent with a healthcare payer perspective.

Key: CEA – cost-effectiveness analysis, CUA – cost-utility analysis, LYs – life years, NMB – net monetary benefit, QALYs – quality-adjusted life years, SCHARR – School of Health and Related Research (University of Sheffield).

Table 6.3 Overview of included studies: screening details

Author, year	Target population	Number of screening strategies	FIT threshold(s) (µg Hb/g)	Screening interval(s)	Screening start age(s)	Screening stop age(s)	Screening uptake / adherence
Heinävaara 2022 ⁽³⁶²⁾	Adults aged 50+ without CRC	362	10, 25, 40, 55, 70	1, 2, 3 years	50, 55, 60, 65	69, 74, 79	100%
Ladabaum 2014 ⁽³⁶³⁾	Persons at average risk of CRC from the ages of 50 to 75 years	NR	NR	1 year (50-54) and 2 years (55-75)	50	75	NR
Lansdorp-Vogelaar 2018 ⁽³⁶⁴⁾	Cohort of average risk individuals	3,000	10	1, 1.5, 2, 3, 5, 7, 10 years	45, 50, 55, 60	70, 75, 80	100%
McFerran 2022 ⁽³⁶⁵⁾	Single birth cohort of average-risk individuals (aged 45+ without CRC)	526	10, 15, 20, 30, 40	1, 2, 3, 4, 5 years	45, 50, 55, 60, 65, 70	70, 75, 80	100%
Thomas 2021 ⁽³⁶⁶⁾	Normal colorectal epithelium at model start (aged 30 at model start)	NR	20, 80, 120	2 years	48, 50, 52, 54, 55, 56, 58, 60 (men); 50, 52, 54, 56, 58, 60, 61, 62 (women)	73, 74 (men); 74, 75 (women)	NR
van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾	One birth cohort born in 1968	588	15, 20, 47, 60	1, 2, 3 years	50, 52, 54, 55, 56, 58 or 60 years	70, 72, 74, 75, 76, 78, or 80 years	100%
van der Meulen 2017 ⁽³⁶⁷⁾	Dutch population aged 25-85 years in 2015	960	10, 15, 20, 30, 40	1, 1.5, 2, 3 years	40, 45, 50, 55, 60, 65	70, 75, 80, 85	100%
Whyte 2021 ⁽³⁶⁸⁾	Cohort of 50-year-old adults in the general population	60,221	Any integer between 20-180	1, 2, 3, 4, 5, 6 years	50-60	Up to 74	90% (65% on average over all rounds)

Key: CRC – colorectal cancer, FIT – faecal immunochemical test, NR – not reported.

Table 6.4 Overview of included studies: costs

Study ID	Costs included	Cost sources
Heinävaara 2022 ⁽³⁶²⁾	- FIT test - colonoscopy with or without polyp removal - colonoscopy with complications - cancer care per life year initial and ongoing stage I-IV, and cancer care in terminal year stage I-IV.	Healthcare providers and published studies
Ladabaum 2014 ⁽³⁶³⁾	- test cost (e.g., FIT) - colonoscopy - colonoscopy with lesion removal - major haemorrhage after colonoscopy - perforation after colonoscopy - cancer care (localised, regional, distant; initial, continuing, and CRC death).	Healthcare providers, published studies, and DRGs
Lansdorp-Vogelaar 2018 ⁽³⁶⁴⁾	- FIT test (including organisational costs [administration, education, and QA], test kit and patient time) - colonoscopy with polyp removal - colonoscopy without polyp removal - colonoscopy with complications - colonoscopy with CRC diagnosis - cancer care (treatment-related): stage I-IV (initial, continuous, death due to CRC and death due to other causes (terminal care)).	Goede 2013 (scope costs taken from Dutch Erasmus medical centre [unpublished data])
McFerran 2022 ⁽³⁶⁵⁾	- FIT test (cost per invitation and cost per attendee) - colonoscopy polyp - colonoscopy without polyp removal - colonoscopy with complications - cancer care: stage I-IV (initial, continuous, death due to CRC and death due to other causes).	Healthcare providers, published studies, and DBC (i.e., DRG)
Thomas 2021 ⁽³⁶⁶⁾	- FIT test (cost per invitation, additional cost of FIT performed and FIT positive result) - colonoscopy without polyp removal - colonoscopy with polyp removal - cost of CTC - cost of treating bowel perforation (major surgery).	Healthcare providers, published studies, and NHS reference costs

Study ID	Costs included	Cost sources
	- cost of admittance for bleeding (overnight stay on medical ward) - pathology cost - cancer care (treatment costs) by cancer stage (Dukes' A-D), age group and years since diagnosis.	
van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾	- FIT test (participation, non-participation, consult by phone) - colonoscopy without polypectomy - colonoscopy with polypectomy - colonoscopy with complications - cancer care per life year initial and ongoing stage I-IV - cancer care in terminal year stage I-IV.	FIT costs and scopes from Dutch National Institute for Public Health and the Environment 2018; Treatment costs from National Health Care Institute Netherlands 2018
van der Meulen 2017 ⁽³⁶⁷⁾	- FIT test (including a single kit, packing material, material and personnel costs of the analysis, postage costs, and organisational costs) - colonoscopy with polyp - colonoscopy without polyp (negative) - colonoscopy with complications - cancer care (treatment-related): stage I-IV (initial, continuous, death due to CRC and death due to other causes (terminal care).	Pilot study, published studies, and DBC (i.e., DRG)
Whyte 2021 ⁽³⁶⁸⁾	- FIT test (noncompliers, normal result and positive result) - colonoscopy without polyp removal - colonoscopy with polyp removal - colonoscopy with complications (treating perforation - major surgery) - admittance for bleeding (overnight stay on medical ward) - pathology cost for adenoma - pathology cost for cancer - CTC cost - cancer care (treatment-related costs) by cancer stage (Dukes' A to Dukes' D).	Healthcare providers, published studies, and NHS reference costs

Key: CRC – colorectal cancer, CTC – computed tomography colonography, DBC – Diagnose Behandelings Combinatie (i.e., Diagnosis Treatment Combination), DRG – diagnostic related group, FIT – faecal immunochemical test, QA – quality assurance, NHS – National Health Service.

Table 6.5 Overview of included studies: analysis of uncertainty

Author, year	PSA	OWSA	Scenarios investigated
Heinävaara 2022 ⁽³⁶²⁾	No	No	- increased cancer care costs by 50% and 100% - assumed same FIT performance for both sexes - no restrictions on colonoscopy resources and total costs - incomplete adherence to screening.
Ladabaum 2014 ⁽³⁶³⁾	Yes	Yes	- imperfect and differential utilisation and per-cycle adherence - threshold analyses on influential parameters (specific to methylated Septin 9 DNA 3-well assay).
Lansdorp-Vogelaar 2018 ⁽³⁶⁴⁾	No	No	- adjusted quality of life effects of CRC screening and treatment - evaluated the effect of limited colonoscopy capacity (i.e., limited to 40, 30, 20, or 10 colonoscopies per 1,000 persons per annum) - reduced screening uptake with FIT (to 60%) and biomarker (40% and 80%) - increased cost effectiveness threshold to €100,000 - applied test characteristics of FIT20 - increased and decreased the costs of colonoscopy and CRC treatment - replaced all CRC screening and treatment costs with US costs.
McFerran 2022 ⁽³⁶⁵⁾	No	Yes	- incidence (50% below and 50% above) - FIT screening participation (50% and 80%) - discount rate (1.5% and 5%) - test performance matched to Whyte et al.
Thomas 2021 ⁽³⁶⁶⁾	Yes	No	- sex-stratification with lower FIT thresholds (FIT80 and FIT20) - a younger mean start age (age 54 or age 50) - lower FIT threshold and younger mean start age (FIT20 at age 50) - a different number of years (2, 4, 6 or 8) between the starting age for screening in men and women - a different discount rate for costs and QALYs (1.5% and 5%, compared to the 3.5% used in the base case analysis).
van de Schootbrugge-	Yes	No	- scope capacity restricted to 20% extra capacity compared to current Dutch programme - age-dependent QoL.

Author, year	PSA	OWSA	Scenarios investigated
Vandermeer 2024 ⁽³⁶⁹⁾			compared screening outcomes for the optimal strategy at 100% vs 70% adherence to primary screening.
van der Meulen 2017 ⁽³⁶⁷⁾	No	No	- assumed only specificity differed between men and women - assumed only sensitivity differed between men and women - assumed no difference between men and women in sensitivity and specificity - assumed a difference between men and women in sensitivity for colorectal cancer similar to the difference in sensitivity for advanced adenomas - assumed that sensitivity of FIT in women is primarily lower for progressive adenomas and to a lesser extent for nonprogressive adenomas - assumed that a percentage of adenomas do not bleed and can therefore never be detected by FIT, unless they grow - a similar analysis where the percentage of adenomas that do not bleed was higher in women than in men - differential attendance for men and women (59.8% and 64.6% [screening], 97.1% and 95.6% [diagnostic], and [joint] 80% [surveillance]) - double/quadruple colonoscopy costs - half/double cancer care costs - no discounting/1.5% of QALYs and 4% on costs - societal costs.
Whyte 2021 ⁽³⁶⁸⁾	Yes	No	- discount rates set to 1.5% - reduced CRC treatment costs - reduced and increased colonoscopy costs - different screen and colonoscopy uptake rates - reduced screening test performance - increased symptomatic presentation rates - varying cancer risk by sex.

Key: CRC – colorectal cancer, FIT – faecal immunochemical test, OWSA – one-way sensitivity analysis, QALY – Quality-adjusted life year, QoL – quality of life, PSA – probabilistic sensitivity analysis.

6.4.2 Relevance and credibility: ISPOR Questionnaire

To support decision-making on the potential transferability of cost-effectiveness evidence to the Irish setting, the relevance and credibility of all eight studies was assessed using the ISPOR questionnaire,⁽³⁶⁰⁾ as described in section 6.3.3. Appendix D (section D.2) reports the responses to the ISPOR questionnaire for each study.

Two studies were deemed insufficiently relevant to the present HTA (Ladabaum 2014 and Lansdorp-Vogelaar 2018).^(363, 364) Ladabaum 2014 compared the cost effectiveness of hybrid screening strategies involving both FIT and colonoscopy screening,⁽³⁶³⁾ while Lansdorp-Vogelaar 2018 aimed to establish what the maximum unit cost of a hypothetical biomarker test would be for it to be considered cost-effective compared with FIT screening.⁽³⁶⁴⁾ As such, the economic endpoints, or outcomes, were not relevant to support decision making on the potential cost effectiveness of an age extension to CRC screening in Ireland.

Credibility was assessed for the remaining six studies, which were deemed sufficiently relevant to the present HTA. The validity, design, and data inputs across the six studies were largely characterised as a 'strength'. Inadequate assessment of uncertainty or limited reporting of cost-effectiveness findings resulted in some studies being characterised as 'neutral' or 'weakness' on the 'analysis' and 'reporting' domains. In particular, reporting by van de Schootbrugge-Vandermeer 2024 was characterised as a 'weakness' because the source for the majority of parameter inputs was not reported (largely due to being a 'research letter' with limited information).⁽³⁶⁹⁾ None of the studies were assessed as having a 'fatal flaw' on any of the seven domains.

The overall credibility of one study was deemed potentially insufficient, largely due to the lack of reporting of relevant results to the present HTA (van der Meulen 2017).⁽³⁶⁷⁾ Although the authors used the previously validated MISCAN-Colon model, internal validation (and additional external validation) was not reported and could not be assessed appropriately. Potential conflicts of interest were also unclear. In all other studies, the overall credibility was assessed as 'sufficient'. Therefore, the evidence could potentially support decision making on the cost effectiveness of lowering the starting age of screening in Ireland.

6.4.3 Assessment of methodological quality: Philips Checklist

The methodological quality of the six studies deemed sufficiently relevant to the present HTA (following application of the ISPOR questionnaire) was assessed using the framework and accompanying checklist for good practice in decision-analytic modelling in HTA proposed by Philips et al.⁽³⁶¹⁾ The findings from the assessment are summarised according to the three key domains below. Responses to the checklist for each study are provided in Appendix D (section D.3).

Structure

Across most studies, there was a clear statement of the decision problem and the perspective assumed was commonly that of the healthcare system. The primary decision-maker was only specified in Whyte 2021,⁽³⁶⁸⁾ where the analyses were undertaken to inform a decision on screening in England by the UK National Screening Committee. The choice of model inputs largely aligned with the specified decision-maker (where stated), perspective, and stated objectives of each study, with the exception of McFerran 2022.⁽³⁶⁵⁾ McFerran 2022 sought to explore the potential for improved effectiveness and cost-effectiveness within a capacity-constrained (that is, colonoscopy-constrained) system using Ireland (and its recent policy changes) as a case study. However, the authors assumed the Netherlands' health system perspective by adopting costs and CRC incidence information and economic evaluation guidelines from the Netherlands. While the analysis uses Irish policy changes to identify more optimal strategies or alternatives than those proposed in Ireland, the findings are illustrative of the potential impact of changes to screening in the Netherlands. As such, use of Ireland as a 'case study' may be considered inconsistent with the decision problem.

There were no major issues identified with the choice of model structure used to simulate patient outcomes across the six studies. Four studies used the widely validated MISCAN-Colon microsimulation model to simulate outcomes (Heinävaara 2022; McFerran 2022; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017).^(362, 365, 367, 369) Whyte 2021 used a previously developed School of Health and Related Research (SchARR) state-transition bowel cancer screening model that was both internally and externally validated.⁽³⁶⁸⁾ Thomas 2021 developed a *de novo* microsimulation model (MiMiC-Bowel), which ultimately resembled MISCAN-Colon.⁽³⁶⁶⁾ In each case, the model structure comprised a natural history of CRC component (reflecting adenoma onset, progression, CRC incidence, progression, and death) and a screening part that effectively interrupted CRC development.

Data

Data input choices were largely transparent and justified across studies. Incorporated costs were generally comprehensive and consistent, with most studies including costs associated with the FIT test, colonoscopy procedure (with or without polyp removal and with or without complications), and cancer care treatment (across all four stages of cancer). Three studies additionally considered terminal care costs (McFerran 2022; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017).^(365, 367, 369) FIT test costs typically included the cost of the invitation and the kit costs. Three studies also separately modelled the cost of compliers and noncompliers (Thomas 2021; Whyte 2021; van de Schootbrugge-Vandermeer 2024),^(366, 368, 369) while two studies additionally considered the cost of a positive result (Thomas 2021 and Whyte

2021).^(366, 368) Pathology costs were also considered in Thomas 2021 and Whyte 2022,^(366, 368) suggesting the cost inputs were perhaps more comprehensive in these studies.

Although the range of incorporated costs was generally comprehensive and consistent across studies, these were often historical in nature. Despite publishing in 2022, McFerran 2022 applied costs from a 2011 publication by Wilschut,⁽³⁷⁰⁾ without adjusting for inflation, suggesting costs may date back to 2010. Although Whyte 2021 published its economic model in 2021, costs were based on 2014/15 prices. A similar gap was observed in van der Meulen 2017 and van de Schootbrugge-Vandermeer 2024, which used 2012 and 2018 prices, respectively. This may raise some concerns about the applicability of the estimated costs and cost-effectiveness findings in these studies.

Cost inputs were considerably higher in van de Schootbrugge-Vandermeer 2024 than in other Netherlands-based evaluations, including McFerran 2022 and van der Meulen 2017. For example, the cost of 'colonoscopy with complications' using data from the Dutch National Institute for Public Health and the Environment was €2,735 in van de Schootbrugge-Vandermeer 2024; in contrast, the cost of the same procedure using Diagnosis Treatment Combination (DBC) tariffs in the Netherlands in McFerran 2022 and van der Meulen 2017 was €1,250 (2010 prices) and €1,372 (2012 prices), respectively. Adjusted to 2018 prices using the consumer price index (CPI) for health in the Netherlands, the cost of colonoscopy with complications would be €1,260 and €1,377 based on McFerran 2022 and van der Meulen 2017, respectively. Large differences in the cost of colonoscopy, with and without polypectomy, were also observed between van de Schootbrugge-Vandermeer 2024 and both McFerran 2022 and van der Meulen 2017, adding uncertainty about the validity of the cost estimates used in van de Schootbrugge-Vandermeer 2024.

With the exception of McFerran 2022 and van de Schootbrugge-Vandermeer 2024, utility values were referenced and largely justified in each of the CUAs (Thomas 2021; van der Meulen 2017, and Whyte 2021). For instance, utility values specific to CRC in Thomas 2021 and Whyte 2021 were derived from a meta-analysis published in 2014.⁽³⁷¹⁾ Van der Meulen 2017 similarly applied utility values specific to CRC health states using evidence derived from a 1999 study of patient-reported CRC utilities.⁽³⁷²⁾ Although the utility values were CRC stage-dependent, they were derived from a 1999 publication when the treatment landscape for CRC was considerably different from today and the associated impact of treatment on a patient's quality of life may be considered comparably different, raising some concerns over the relevance of these historical utility values. McFerran 2022 did not report the source nor the values used to inform utilities in the economic model, which raises some concerns over the validity of the utility values used in the study. In contrast, van de

Schootbrugge-Vandermeer 2024 reported the utility values used in the model but not the source.

Analysis of uncertainty was typically limited to (1) parameter uncertainty and (2) uncertainty in heterogeneity. Three studies performed probabilistic sensitivity analysis (PSA), which has the advantage of jointly reflecting uncertainty in each input parameter (Thomas 2021; van de Schootbrugge-Vandermeer 2024; Whyte 2021).

Consistency

There were no major issues identified with consistency checks in included studies. Four studies relied on the previously validated MISCAN-Colon model, where CRC incidence data were typically calibrated to the country-specific population, with no issues identified in three studies (Heinävaara 2022; McFerran 2022; van der Meulen 2017). Due to minimal reporting by van de Schootbrugge-Vandermeer 2024, it is unclear whether the calibrated data in this study were consistent with local CRC incidence and mortality data. Whyte 2021 used the SchARR Bowel Cancer Screening Model, which had also been validated, both internally and externally. In contrast, Thomas 2021 developed a *de novo* microsimulation model (MiMiC) and did not report undertaking any internal or external validation. However, the model has sufficient face validity as it essentially mimics the MISCAN-Colon model.

Given the difference in total screening costs between McFerran 2022 (which were found to be net costly versus no screening) and Whyte 2021 (net saving versus no screening), McFerran 2022 conducted a scenario analysis, in which the authors applied the FIT performance characteristics from Whyte 2021, to attempt to resolve the difference in net costs. However, their findings remained unchanged. Consistent with Whyte 2021, van de Schootbrugge-Vandermeer 2024 found certain strategies were net saving versus no screening, including screening all adults from age 50–75 years using two-yearly intervals. Van der Meulen 2017 also found screening was either net costly or net saving versus no screening, depending on the sex of individuals, with cost savings more pronounced when screening men from age 50–75 years using 1.5 to one-yearly intervals. In contrast, screening men from age 40–80 years using one-yearly intervals was most costly. The somewhat divergent conclusions regarding the total cost of screening versus no screening may raise some concerns over the consistency of findings in published cost-effectiveness estimates.

6.4.4 A narrative summary of cost-effectiveness findings

Three studies specifically evaluated the cost effectiveness of sex-stratified screening (Heinävaara 2022; Thomas 2021; van der Meulen 2017). Across each study, FIT screening was more effective in men than in women due to the higher disease burden in men. While sex-stratified screening produced more QALY gains and reductions in CRC incidence and mortality in men, optimal screening strategies were

often similar in both sexes with respect to interval, age range, and FIT cutoff, favouring uniform screening over sex-stratified screening. Within sex-stratified screening, Heinävaara 2022 found that an annual screening strategy with a cut-off of 25µg/g at 50–79 years was optimal in men, while a cut-off of 10µg/g at 55–69 years was optimal in women. Where resources are constrained and it is not feasible to screen everyone from the same age (for example, from age 58 years), Thomas 2021 found that starting screening at a younger age for men (for example, at age 56 years) than women (for example, age 60 years) would reduce the disproportional disease burden in men, generate more health benefits overall, and still be considered cost-effective.

Four studies considered cost-effectiveness in the context of colonoscopy capacity constraints (McFerran 2022; Whyte 2021; Thomas 2021; van de Schootbrugge-Vandermeer 2024). McFerran found more lives and health services costs could be saved (based on inputs from the Netherlands setting) within existing colonoscopy capacity constraints if a lengthening of the screening interval was traded off against an increase in population coverage and the adoption of a more sensitive FIT cutoff. For instance, relative to a strategy involving a FIT40 threshold with two-yearly screening of adults aged 60–70 years, McFerran 2022 found extending the interval to four years using a reduced FIT10 threshold and an age range of 60–72 years would require 6% fewer colonoscopies, reduce net costs by 23%, prevent 15% more CRC deaths and save 16% more QALYs. Relative to the same strategy, screening adults aged 50–80 years with a one-yearly interval and FIT10 threshold would produce favourable net health benefits (increase QALYs gained by 163%), but would lead to a substantial increase in costs (320% increase) and colonoscopies required (691% increase).

Whyte 2021 found the optimal screening age range varied in England by endoscopy capacity but generally started at age 50/51 years and ranged to age 70 years, or 74 years if capacity allowed. The authors found the optimal screening interval was every two years using a FIT threshold of 127 to 166µg Hb/g. Screening strategies involving three-yearly screening with a lower FIT threshold (that is, with higher sensitivity) were less cost-effective. With a high screening referral colonoscopy capacity, annual screening became optimal. Screening all adults aged 50–74 using two-yearly screening and a FIT threshold of 74 to 105 was optimal at high levels of colonoscopy capacity. If endoscopy capacity is constrained, Thomas 2021 found screening men from age 56 years, but keeping the screening start age at 60 years for women, was more cost-effective than reducing the starting age to 58 years for all adults in England.

If colonoscopy capacity were limited, van de Schootbrugge-Vandermeer 2024 found decreasing the starting age to 50 years (from 55 years) was cost-effective in the Netherlands using two-yearly screening and a FIT47 threshold at a WTP threshold of

€20,000 per QALY gained. However, increasing the stopping age to 80 years (from 75 years) was more efficient (that is, produced more QALYs gained per additional Euro spent), but would require 124% extra colonoscopy capacity. If colonoscopy capacity was restricted to 20% extra capacity only, two-yearly screening from age 52 to 74 years at a FIT cutoff of 20µg Hb/g faeces was optimal.

6.4.5 Assessment of transferability

Before considering the potential cost effectiveness of lowering the age range for screening in the context of Ireland, this section first considers the potential transferability of available evidence to the Irish setting. The purpose of the section is to identify potential differences between key model inputs used in included studies and those that would be applied in an Irish-specific model that could unduly affect the transferability of cost-effectiveness evidence to the Irish setting. In particular, the section focuses on three key parameters: (1) CRC incidence and mortality; (2) costs; and (3) FIT performance characteristics. This section is distinct from the assessment of relevance and credibility, as per the ISPOR questionnaire, and assessment of methodological quality, as per the Philips Checklist.

CRC incidence and mortality

Cancer incidence and mortality data from three countries were used to inform the economic models in the included studies. To replicate the situation without screening, the authors used national cancer incidence data prior to the introduction of screening in each country. For example, Heinävaara 2022 and van der Meulen 2017 used cancer incidence data from 1999–2003 for Finland and the Netherlands, respectively, as this preceded the introduction of colorectal cancer screening in these countries. McFerran 2022 also used data from the Netherlands; however, the authors did not specify the years to which these data related. Whyte 2021 used data from the first round of CRC screening in England, which dates from 2009; this was supplemented with data from Cancer Research UK from 2015. Thomas 2021 also used data from Cancer Research UK.

A review of CRC incidence in Europe from 2000–2018 showed that age-standardised incidence rates of CRC in Ireland were similar to those of the Netherlands.⁽²³³⁾ However, McFerran 2022 highlighted that, prior to the introduction of BowelScreen, Ireland had a higher level of stage IV disease and a lower level of stage I disease compared to the Netherlands. The incidence of CRC in Scotland is similar to that of Ireland, while England and Wales have a lower incidence of CRC compared to Ireland and the Netherlands.⁽³⁷³⁾ Finland also has a lower age-standardised incidence rate of CRC compared to Ireland and the Netherlands. This suggests transferring evidence from the Netherlands to Ireland may be appropriate in terms of disease burden. All else being equal, transferring evidence from England and Finland might understate the health benefits (and cost-effectiveness) expected in Ireland due to the higher

levels of disease burden relative to those settings (that is, higher CRC detection rates expected in Ireland).

Costs

The studies included in this review considered various cost parameters in their analyses. Colonoscopy costs varied across the studies, ranging from €192 (van der Meulen 2017) to €686 (van de Schootbrugge-Vandermeer 2024) for colonoscopies without polypectomy, and €329 (van der Meulen 2017) to €981 (van de Schootbrugge-Vandermeer 2024) for colonoscopies where polypectomy was performed. Exact values (that is, microcosted values) for colonoscopy costs associated with the Irish screening programme were not readily available at the time of writing. The BowelScreen programme, as screening commissioner, provides a contribution for services provided (including colonoscopy) to individual hospitals; as of 2024, the contribution for colonoscopy amounted to €650 (BowelScreen, personal communication). Separately, the 2024 Activity Based Funding (ABF) Admitted Patient Price List quoted a cost of €1,001 or €1,067 per colonoscopy for a minor or major complexity procedure performed on a day case basis, respectively (G48B and G48A).⁽³⁷⁴⁾ These costs are more aligned with van de Schootbrugge-Vandermeer 2024. The cost of a colonoscopy with complications was €2,735 in van de Schootbrugge-Vandermeer 2024. The cost of the same procedure in van der Meulen 2017 was €1,372.

Information relating to the cost of FIT-based screening was provided as a total cost in some studies or disaggregated by the cost of the FIT test and FIT processing by others. Overall, the total costs for FIT testing including invitation to screening, postage and processing ranged from £7.06 (Whyte 2021 and Thomas 2021) to €22 (van der Meulen 2017 and van de Schootbrugge-Vandermeer 2024). This is equivalent to a range of €9 to €25 in 2023 Irish Euro and is in line with the estimated cost of FIT testing in Ireland, which was approximately €18 in 2024 (including postagepackaging, and processing).

The studies included in this review categorised colorectal treatment care costs into initial treatment costs, ongoing care, and terminal care costs. In four of the included studies, costs were presented as the cost per person per year. In contrast, Whyte 2021 presented CRC treatment costs as the cost per patient's lifetime. In all five studies, treatment costs varied according to stage at diagnosis, with higher treatment costs for later stage disease and for terminal care. Overall, the estimated care costs ranged from €2,888 to €5,665 per year for stage I–IV CRC and a range of €12,884 to €32,860 per year for terminal care. McFerran 2022 and van der Meulen 2017 used similar treatment and continuous care costs, which varied by stage of disease at diagnosis. Thomas 2021 presented costs for the initial nine years after diagnosis and grouped Dukes' stages A&B together as one category, with Dukes'

C&D as the other category for treatment costs. The authors also assumed that treatment costs were higher for those diagnosed under the age of 64 years compared to those aged 65 years and over, and similar to the other studies, the cost of treating those diagnosed with later stage disease (Dukes' C&D) was higher than early stage disease (Dukes' A&B). Heinävaara 2022 used CRC treatment costs that were lower than all of the other studies (for example €2,888 to €5,665 per annum stage I–IV).

It is difficult to establish whether CRC treatment costs used in included studies are comparable with costs in Ireland in the absence of Irish data by cancer stage per annum. Research by Tilson et al. in 2008 found that the average lifetime cost of managing a case of CRC in Ireland was €39,607. Costs were lower for stage I CRC at €23,668 compared to €48,835 for stage III disease, and costs were most sensitive to recurrence rates and the use of biological agents.⁽³⁷⁵⁾ Treatment costs in Ireland are likely to have increased in the intervening years since this study was completed in line with inflation and changes in treatment such as increased use of biologic agents (Chapter 3, section 3.6).

FIT Threshold

Several scenarios of interest to this HTA were identified in the included studies. However, different FIT thresholds were used in each of the studies. This is relevant when considering the transferability of the findings, as the FIT sensitivity and specificity for adenomas and CRC will vary according to the threshold used.⁽⁴⁰⁾ Specifically, FIT sensitivity decreases as the FIT threshold increases, while specificity increases as the FIT threshold increases. As a result, while lower FIT thresholds will pick up more cases of CRC and adenomas, they will also result in more false positives. Ireland currently uses the OC-Sensor™ FIT device with a threshold of 45µg Hb/g for the BowelScreen programme. Therefore, studies that include a FIT threshold that is close to the threshold used in Ireland are of most relevance.

However, it is important to note that the estimates of sensitivity for a given FIT threshold varied widely between the included studies (from 24% to 82.5% for thresholds between 40 and 47µg Hb/g). Estimates of the sensitivity and specificity of FIT to detect CRC may be expected to vary according to the disease and demographic characteristics of the screened population, as well as the reference standard and FIT device used. A 2019 meta-analysis of eight studies with FIT thresholds >30µg Hb/g (although it was not clear what range of thresholds >30µg Hb/g were included in the analysis) reported a pooled estimate of sensitivity for CRC and advanced adenoma of 66% (95% CI: 55, 75) and 19% (95% CI 14, 25), respectively, with an estimated specificity of 97% (95% CI 96, 98) for CRC and advanced adenoma combined.⁽⁴⁰⁾ Estimates of the sensitivity of the OC-Sensor™ FIT device for CRC at a threshold of 40µg Hb/g ranged from 60% (95% CI: 26%, 88%)

to 80% (95% CI 35%, 100%), and specificity from 95% to 97%, in studies with a colonoscopy reference standard included in the review of test accuracy reported in Chapter 4.^(277, 279) Based on data from the Danish CRC screening programme with a registry reference standard, sensitivity of OC-Sensor™ for the detection of CRC at a threshold of 45µg Hb/g in participants aged 50–74 was 76% (95% CI: 74%, 77%), with a specificity of 96% (95% CI: 96%, 96%).⁽²⁷⁵⁾

Van de Schootbrugge-Vandermeer 2024 reported results from scenarios that used a FIT threshold of 47µg Hb/g, as well as comparing the age ranges relevant to this HTA. Whyte 2021 included a FIT threshold of 45µg Hb/g in their scenarios; however, the results for the strategies relevant to this HTA were not reported in the paper. Thomas 2021 reported strategies that included age ranges of interest; however, these strategies used FIT thresholds of 20µg Hb/g and 120µg Hb/g. van der Meulen 2017 also included strategies with age ranges of interest with a FIT threshold of 10µg Hb/g and Heinävaara for 25µg Hb/g.

6.4.6 A consideration of cost-effectiveness in the context of Ireland

This section considers the potential cost effectiveness of lowering the starting age of eligibility for CRC screening from age 55 to 50 years in Ireland based on studies deemed sufficiently relevant to the present HTA.

None of the studies considered 'sufficiently relevant' directly reported the cost effectiveness of screening all adults from age 50–74 versus age 55–74 years using a FIT45 threshold and two-yearly intervals (that is, strategies relevant to the present HTA). In some cases, for example, Whyte 2021, the strategies of interest were considered in an incremental analysis, but the ICERs, net monetary benefit or incremental costs and QALYs were not reported for these strategies. However, most of the eight studies reported costs and QALYs for broadly comparable strategies, where either the FIT threshold, interval, or age range varied. In particular, van de Schootbrugge-Vandermeer 2024 reported the (incremental) costs and QALYs of screening all adults from age 50–74 years, as well as 55–75 years, using a FIT47 threshold and two-yearly intervals (versus no screening). Combined, these studies provide an opportunity to estimate the potential cost effectiveness of lowering the starting age of screening in Ireland, with some adjustments to costs and QALYs, where applicable.

Based on evidence from van de Schootbrugge-Vandermeer 2024, screening all adults from age 55–75 years using a FIT47 threshold and two-yearly intervals would be less costly and more effective than no screening. Lowering the age range to 50–74 years increases costs, but results in more favourable QALY gains than screening from age 55–75 years (in practice, the last screen for two-yearly screening from 50–75 would be at age 74; personal communication with the author). Compared directly, screening from age 50–74 years would be considered cost-effective versus screening

from age 55–75 years with an estimated ICER of €8,977 (see Table 6.6). Assuming a WTP threshold of €20,000 and €45,000 per QALY gained, the strategy had an INMB of €105 and €342 per person, respectively. These findings were supported by sensitivity analysis in which quality of life was assumed to be age-dependent (that is, deteriorating over time due to increasing comorbidities). However, it is unclear what additional benefits in terms of CRC incidence and mortality reductions could be achieved by lowering the age range from 55–74 to 50–74 years using evidence from van de Schootbrugge-Vandermeer 2024.

Table 6.6 Summary of cost-effectiveness findings based on van de Schootbrugge-Vandermeer 2024⁽³⁶⁹⁾

Outcome	Base case (main) analysis		Sensitivity analysis with age-dependent QoL scores	
	FIT47, 55-75 2 years	FIT47, 50-74 2 years	FIT47, 55-75 2 years	FIT47, 50-74 2 years
Cost (per 1,000 persons)*	-€7,743	€77,543	-€7,743	€77,543
QALYs (per 1,000 persons)*	83.1	92.6	67.5	75.7
ICER	NA	€8,977	NA	€10,401
INMB at €20,000 (per person)	NA	€105	NA	€79
INMB at €45,000 (per person)	NA	€342	NA	€284

Note: Numerical results were not reported in full in the published research letter but were provided by the author upon request.

* Versus no screening

Key: FIT – faecal immunochemical test, ICER – incremental cost-effectiveness ratio, INMB – incremental net monetary benefit, NA – Not applicable, QALYs – quality-adjusted life years, QoL – quality of life.

Thomas 2021 compared the cost effectiveness of starting screening at age 50 years versus 60 years using a FIT20 threshold with a two-yearly interval. The authors also compared the cost effectiveness of starting screening at age 50 years against starting screening at 54 years using a FIT120 threshold with the same two-yearly screening interval. As detailed in Table 6.7, screening those aged 50–74 was considered cost-effective compared to both screening those aged 60–74 (FIT20) and those aged 54–74 (FIT120) years; the estimated ICERs were €1,550 and €3,962 for FIT20 and FIT120, respectively. Assuming a WTP threshold of €20,000 per QALY gained, the strategies had an INMB of €179 and €42, respectively. At the higher WTP threshold of €45,000, more favourable net benefit results would be observed. Using

a FIT20 threshold produced marginally more QALY gains than a FIT120 threshold and resulted in more favourable reductions in CRC incidence and mortality. However, the age range for the comparator differed in both scenarios (FIT20 was relative to 60–74 age range, while FIT120 was relative to 54–74 age range).

It is possible to attempt to estimate outcomes for a 55–74 year age range for the FIT20 scenario using linear interpolation on costs and QALYs for the 50–74 and 60–74 year age ranges. As detailed in Table 6.7, screening all adults from age 50–74 would be considered cost-effective, compared with screening all adults from age 55–74, using two-yearly intervals and a FIT threshold of 20, with an estimated ICER and INMB (at €20,000 per QALY gained threshold) of €1,548 and €90 (Table 6.5). However, it is important to highlight that these estimates are based on approximated costs and QALYs for the 55–74 age range using linear interpolation. The relationship between the 50–74 and 60–74 age ranges in terms of the impact on costs and QALYs may not be linear, so these figures should be considered with caution. Nevertheless, the results suggest that lowering the age range for screening is likely cost-effective at either low or high FIT thresholds.

Evidence from the other studies broadly supports the findings that screening adults from age 50 years is cost-effective versus screening adults from age 55 years. For instance, based on evidence from McFerran 2022, screening all adults from age 50–76 would be cost-effective compared with screening all adults from age 55–75 years using a FIT40 threshold and two-yearly intervals, with an estimated ICER and INMB (at €20,000 per QALY gained threshold) of €5,895 and €113 (Table 6.8). Based on evidence from Heinävaara 2022, screening all adults from age 50–74 versus age 55–74 years using a FIT25 threshold and two-yearly intervals could be considered cost-effective as the lower age range produces more favourable LY gains and CRC incidence and mortality reductions (Table 6.8). However, as the evaluation did not include QALYs, the results cannot be directly compared against accepted WTP thresholds.

Based on van der Meulen 2017, there is further evidence to suggest screening adults from age 50–74 would be cost-effective compared with screening adults from age 55–74. This evidence was based on a FIT10 threshold and 1.5-year intervals, producing an estimated ICER and INMB (at €20,000 per QALY gained threshold) of €4,332 and €94, respectively (Table 6.8). Although the study used a FIT10 threshold, it is unlikely that a FIT45 threshold and a longer screening interval would have resulted in less favourable cost-effectiveness outcomes for the 50–54 age range. As demonstrated in Thomas 2021, a lower screening starting age produces more favourable outcomes (such as QALY gains and reductions in CRC incidence and mortality) at marginally higher cost, irrespective of the FIT threshold, while differences in estimated ICERs between low and high thresholds (for example, FIT20 and FIT120 threshold) are minimal.

While Whyte 2021 considered the costs and consequences of screening adults aged 50–74 and 55–74 years using a FIT45 threshold and two-yearly intervals, the outcomes associated with these age ranges and FIT threshold were not reported in the paper. This was due to the vast number of strategies simulated ($N = 60,221$) and the finding that other strategies produced more optimal results (that is, higher INMB versus no screening). The authors found that the optimal screening age range varied by endoscopy capacity but generally started at age 50/51 years and ranged to age 70 years, or 74 years if capacity allowed, suggesting screening adults aged 50–74 years may be more cost-effective than screening adults aged 55–74 years.

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Table 6.7 Summary cost-effectiveness findings based on Thomas 2021⁽³⁶⁶⁾

Outcome	FIT20		FIT120		FIT20 – linear interpolation by age*	
	60-74, 2 yrs	50-74, 2 yrs	54-74, 2 yrs	50-74, 2 yrs	55-74, 2 yrs	50-74, 2 yrs
Cost (per person)	€595	€610	€614	€625	€603	€610
QALYs (per person)	19.8317	19.8414	19.8293	19.8319	19.83655	19.8414
Total CRC incidence (per 100,000)	5,548	4,800	6,336	6,186	5,174	4,800
Total CRC mortality (per 100,000)	2,513	2,067	2,924	2,813	2,290	2,067
ICER	NA	€1,550	NA	€3,962	NA	€1,548
INMB at €20,000 (per person)	NA	€179	NA	€42	NA	€89
INMB at €45,000 (per person)	NA	€421	NA	€107	NA	€211
Total CRC incidence reduction (%)	NA	13%	NA	2%	NA	7%
Total CRC mortality reduction (%)	NA	18%	NA	4%	NA	10%

* Age range 55-74 approximated using linear interpolation based on age 60-74 and 50-74.

Costs rounded to the nearest Euro

Key: CRC – colorectal cancer, FIT – faecal immunochemical test, ICER – incremental cost-effectiveness ratio, INMB – incremental net monetary benefit, NA – not applicable, QALYs – quality-adjusted life years.

Table 6.8 Summary cost-effectiveness findings based on McFerran 2022, Heinävaara 2022, and van der Meulen 2017

Outcome	McFerran 2022 ⁽³⁶⁵⁾		Heinävaara 2022 ⁽³⁶²⁾		van der Meulen 2017 ⁽³⁶⁷⁾	
	FIT40 55-75, 2 years	FIT40 50-76, 2 years	FIT25 55-74, 2 years	FIT25 50-74, 2 years	FIT10 55-75, 1.5 years	FIT10 50-75, 1.5 years
Cost (per 1,000 persons)	€108,198	€155,408	€1,095,268	€1,140,212	€20,293	€46,283
QALYs (per 1,000 persons)	51.7847	59.7929	41*	48*	86	92
ICER	<i>NA</i>	€5,895	<i>NA</i>	€6,421†	<i>NA</i>	€4,332
INMB at €20,000 (per person)	<i>NA</i>	€113	<i>NA</i>	NA	<i>NA</i>	€94
INMB at €45,000 (per person)	<i>NA</i>	€313	<i>NA</i>	NA	<i>NA</i>	€244
Total CRC incidence reduction (per 1,000)	<i>NA</i>	<i>NR</i>	<i>NA</i>	<1	<i>NA</i>	<i>NR</i>
Total CRC mortality reduction (per 1,000)	<i>NA</i>	1	<i>NA</i>	1	<i>NA</i>	<i>NR</i>

* Based on life years (LYs) gained.

† Cost per LY gained.

Key: CRC – colorectal cancer, FIT – faecal immunochemical test, ICER – incremental cost-effectiveness ratio, INMB – incremental net monetary benefit, NA – not applicable, NR – not reported, QALYs – quality-adjusted life years.

6.4.7 A consideration of the modelled comparative effectiveness in the context of Ireland

The results presented thus far represent the characteristics and qualities of the studies examined, and the cost-effectiveness findings. The study results may however be disaggregated to examine the model findings for the effectiveness of the intervention, in terms of QALYs and other clinical outcomes such as CRC cases and deaths avoided. As expected, all studies showed that screening was clinically effective. However, no measures of uncertainty were reported by the study authors. In the absence of this information and in light of the variety of model inputs used by the different studies, and the uncertainty of the underlying input parameters, the applicability of the numerical estimates of comparative effectiveness presented below to the context in Ireland should be considered with caution.

Van de Schootbrugge-Vandermeer 2024 examined a screening intensity similar to Ireland, that is a FIT threshold of 47µg Hb/g and a screening interval of every two years, versus 45µg Hb/g every two years as used in Ireland. Based on a discount rate of 3% per annum, the authors estimated that lowering the starting age of screening from age 55 to 50 years was associated with a QALY gain of 9.5 or 8.2 QALYs per 1,000 people screened, depending on the utility assumptions used (Table 6.6).⁽³⁶⁹⁾ Undiscounted QALY gains are more relevant from a clinical perspective, but they were not reported by the study authors.⁽³⁶⁹⁾ The associated reductions in CRC incidence or mortality were also not reported.⁽³⁶⁹⁾ Heinävaara 2022 and McFerran 2022 based their analysis on the same MISCAN-colon model as that used by van de Schootbrugge-Vandermeer 2024, albeit they employed different assumptions.^(362, 365, 369) As Heinävaara 2022 and McFerran 2022 reported the clinical benefits of an age extension at a more intense screening strategy than that used in Ireland, information on the direction of clinical benefit can be inferred.^(362, 365) Heinävaara 2022 and McFerran 2022 both estimated one death averted per 1,000 persons screened while Heinävaara 2022 estimated a 1% reduction in incidence, which is equivalent to less than one CRC case prevented per 1,000 people screened (Table 6.8).^(362, 365)

In contrast, if the Irish age extension were modelled using the MiMiC-Bowel model employed by Thomas 2021, the modelled clinical benefits would be expected to be larger than those estimated by Heinävaara 2022.⁽³⁶⁶⁾ As the Irish FIT threshold of 45µg Hb/g lies between the FIT thresholds of 20 and 120µg Hb/g reported and interpolated from data presented by Thomas 2021, the expected reduction of CRC deaths would lie between one and two CRC deaths avoided per 1,000 persons screened, while the incidence reduction would lie between two and four CRC cases prevented per 1,000 persons screened (Table 6.7).⁽³⁶⁶⁾

6.5 Discussion

The purpose of this chapter was to assess whether, for the population in Ireland at average risk of CRC, it is cost-effective to provide two-yearly FIT-based CRC screening at a FIT threshold of 45µg Hb/g (FIT45) to persons aged 50 to 74 years, versus persons aged 55 to 74 years. To address this question, a systematic literature review was conducted to identify evidence on the cost effectiveness of lowering the starting age of CRC screening, in particular from age 55–74 years to 50–74 years using FIT-based screening.

A summary of the findings of the review is presented below in section 6.5.1, followed by a critical appraisal of the quality and transferability of available evidence to inform a decision on the potential cost effectiveness of lowering the age range for screening in Ireland in section 6.5.2. The limitations of the review are discussed in section 6.5.3. Lastly, in the context of the review's findings, the potential benefits of developing (or adapting) an economic model to address the question of cost effectiveness are considered in section 6.5.4.

6.5.1 Summary of review findings

The review identified eight studies that considered the cost effectiveness of different age ranges using FIT-based screening and two-yearly intervals (that is, criteria relevant to the present HTA). Based on the assessment of relevance and credibility to the present decision problem, six of the studies were deemed 'sufficiently relevant' to support decision making on the costs and consequences of lowering the age range for screening in Ireland. None of these studies specifically sought to establish whether lowering the starting age at which individuals at average risk of CRC are invited for screening is cost-effective. Instead, they aimed to (1) identify efficient or optimal strategies among a wide range of screening options involving different age ranges, FIT thresholds and screening intervals (McFerran 2021, Thomas 2021, van de Schootbrugge-Vandermeer 2024; Whyte 2021), or (2) establish whether sex-specific screening would be more cost-effective than uniform screening (Heinävaara 2022, Thomas 2021, and Van der Meulen 2017). Nevertheless, each study reported important information on strategies that closely resemble those of interest to the present HTA.

For the six studies that were deemed 'sufficiently relevant', the validity, design, and choice of data inputs were largely characterised as a 'strength'. Five studies were considered sufficiently credible to support decision-making in the context of Ireland. Only one study was deemed non-credible, largely due to the lack of reporting of relevant results to the present HTA (van der Meulen 2017).

The overall quality of the six studies that were deemed sufficiently relevant, based on the framework and accompanying checklist proposed by Philips et al.,⁽³⁶¹⁾ was

regarded as strong. However, a number of key concerns were identified. These related to:

- the historical nature of costs in two studies (McFerran 2022 and Whyte 2021)
- source and scale of costs in one study (van de Schootbrugge-Vandermeer 2024)
- choice of utility weights in one study (van der Meulen 2017), along with lack of reporting of utility sources in another study (McFerran 2022)
- lack of internal and external validation in one study (Thomas 2021).

Nevertheless, there were a number of key strengths associated with the included studies. For instance, studies largely used previously validated models, such as the MISCAN-Colon model, to simulate patient outcomes and compare costs and consequences (Heinävaara 2022; McFerran 2022; van de Schootbrugge-Vandermeer 2024; van der Meulen 2017). Whyte 2021 adapted a previously developed SchARR model and internally and externally validated its predictions. Thomas 2021 developed a *de novo* microsimulation model (MiMiC-Bowel), which essentially mimicked MISCAN-Colon, ensuring sufficient face validity.

Incorporated costs were broadly consistent and comprehensive across studies. These were also largely relevant to, and comparable in price with, the Irish context. Lastly, a number of studies considered the potential implications of capacity constraints (that is, endoscopy constraints) (McFerran 2022, Thomas 2021; van de Schootbrugge-Vandermeer 2024; Whyte 2021). Capacity constraints have historically been and continue to be a consideration in Ireland and other countries. In response to endoscopy capacity challenges in Ireland, in 2014 the BowelScreen FIT threshold was raised from 20 to 45µg Hb/g, resulting in lower positivity rates and fewer overall colonoscopy referrals.⁽⁶¹⁾ In the Netherlands, the FIT threshold was similarly increased from 15 to 47µg Hb/g in an effort to relieve pressure on colonoscopy capacity within the CRC screening programme.⁽¹⁰⁹⁾

6.5.2 Critical appraisal of existing evidence to inform cost-effectiveness in Ireland

Although none of the studies directly reported the cost effectiveness of screening all adults from age 50–74 years versus age 55–74 years using a FIT45 threshold and two-yearly intervals, most reported outcomes for broadly comparable strategies (in particular, van de Schootbrugge-Vandermeer 2024) that provide some indication of the potential cost effectiveness of lowering the age range for screening in Ireland. Overall, the evidence consistently suggests that lowering the age range for screening from age 55–74 years to 50–74 years would likely be cost-effective. The lower starting age for screening appears to produce more favourable QALY gains and reductions in CRC incidence and mortality, albeit at marginally higher cost due to increased overall duration of screening.

The most relevant evidence on the potential cost effectiveness of lowering the screening age to 50 likely derives from van de Schootbrugge-Vandermeer 2024. The authors reported the (incremental) costs and QALYs of screening all adults from age 50–74 years, as well as 55–75 years, using a FIT47 threshold and two-yearly intervals (that is, strategies closely resembling those of relevance to the present HTA). The evidence suggests screening from age 50–74 years would be considered cost-effective versus screening from age 55–75 years with an estimated ICER of €8,977. The strategy also had an INMB of €105 and €342 at commonly-assumed WTP thresholds of €20,000 and €45,000 per QALY gained, respectively. However, although the strategies evaluated in van de Schootbrugge-Vandermeer 2024 most closely resemble the strategies of relevance to the present HTA, the methodological quality of the evidence is uncertain and could not be fully assessed. Since the evidence was published as a research letter, which, by default, contains minimal information, there is some uncertainty over the appropriateness of certain data sources and inputs, particularly in relation to costs in the context of the Netherlands, which were higher than other evaluations conducted in the same setting. However, the cost estimates were broadly aligned with those in Ireland, which lends more weight to the applicability of the evidence from van de Schootbrugge-Vandermeer 2024 to support decision making on the cost effectiveness of lowering the screening age in Ireland.

Similarly relevant evidence also derives from Thomas 2021, which was also considered to be of high methodological quality, as per the Philips Checklist. The authors compared screening all adults from age 50–74 years with screening all adults from age 60–74 years using a FIT threshold of 20µg Hb/g, as well as from age 54–74 years using a FIT threshold of 120µg Hb/g, each with two-yearly intervals. At both FIT thresholds, screening from age 50 years was considered cost-effective, resulting in higher QALY gains and reductions in CRC incidence and mortality and a low ICER (€1,550 and €3,962 for FIT20 and FIT120, respectively) relative to the commonly used €20,000 per QALY gained WTP threshold in Ireland. This suggests that at a FIT45 threshold, similar results might be expected for the same age range.

Evidence from McFerran 2022 supports the conclusion that screening from age 50 years is likely cost-effective versus screening from age 55 years. Using a FIT40 threshold and two-yearly intervals, screening adults from age 50–76 is likely more cost-effective than screening adults from age 55–75, with an estimated ICER of €5,895. Evidence based on Heinävaara 2022 suggests screening adults from age 50–74 years versus 55–74 using a FIT25 threshold and two-yearly intervals produces more LYs gained and reductions in CRC incidence and mortality, consistent with Thomas 2021 and McFerran 2022.

Van der Meulen 2017 similarly found that screening from age 50–74 is cost-effective relative to screening from age 55–74 years. However, the results have somewhat less generalisability to Ireland as the findings are based on a FIT10 threshold and 1.5-yearly screening intervals. Hence, the evidence from van der Meulen 2017 was considered non-credible to support decision-making in the context of Ireland, as per assessment of relevance and credibility using the ISPOR questionnaire.

Among a large number of strategies explored (N=60,221), Whyte (2021) generally found that the most cost-effective strategies were those where screening starts at age 50 or 51 and extends to age 70 or 74. While they did not report the specific outcomes for 50–74 and 55–74 years using a FIT45 threshold at two-year intervals, their finding is consistent with the assertion that screening adults aged 50–74 years is more cost-effective than screening those aged 55–74 years.

Although it may be assumed that thresholds closer to the threshold of 45µg Hb/g used in Ireland would be most transferable to the Irish context, this may not be the case. This is due to the wide range of sensitivity estimates for a given FIT threshold among the studies included in this review, and the absence of data on the sensitivity of FIT at a threshold of 45 in Ireland. While there remains some uncertainty regarding the exact cost effectiveness of lowering the age range from 55–74 to 50–74 using a FIT45 threshold and two-yearly intervals, the overall evidence suggests that lowering the age range from 55–74 to 50–74 is likely to be cost-effective.

6.5.3 Limitations

This review was subject to several limitations. Firstly, the inclusion criteria were limited to European studies. Therefore, the review could have missed evidence relevant to the present HTA published elsewhere (for example, evidence specifically on the cost effectiveness of lowering the age range of screening from age 55–74 years to 50–74 years using a FIT45 threshold with two-yearly intervals). However, the extent to which evidence (for example, epidemiological and cost data) from a non-European country could be transferable to Ireland is questionable. An advantage of limiting the inclusion criteria to European-based studies was that there are inherent similarities between Ireland and many European countries in terms of population characteristics, disease burden, health systems, and use of population-based screening programmes, as well as similarities in guidelines on economic evaluation.

Next, the scope of the review (and HTA more broadly) was limited to assessing whether, for the population in Ireland at average risk of CRC, it is cost-effective to provide two-yearly FIT-based screening at a FIT threshold of 45µg Hb/g (FIT45) to persons aged 50 to 74 years, versus persons aged 55 to 74 years. While the available evidence suggests lowering the age range for screening would likely be cost-effective, there may be more efficient screening combinations than screening all

adults from age 50–74 using a FIT45 threshold and two-yearly intervals. As illustrated by McFerran 2022, extending the screening interval to four years, reducing the FIT cutoff to 10µg Hb/g, and limiting the age range for screening to 60–72 years could provide a screening strategy that returns maximum net health benefit within finite capacity constraints. In contrast, Whyte 2021 found that the 20 most cost-effective strategies (that is, optimal strategies with the highest NMB at £20,000 per QALY gained threshold) involved starting screening at age 50 to 53 years, using two-yearly intervals with seven or eight rounds of screening, and a FIT threshold of 127 to 166µg Hb/g. However, the difference between strategies may be marginal, as in Whyte 2021 where the percentage difference in NMB between the highest and lowest strategy (among the top 20 most cost-effective strategies) was 10%. Furthermore, the available evidence presented here suggests starting screening earlier is likely cost-effective at commonly assumed WTP thresholds in Ireland.

In all included studies that reported the uptake rate of the screening programme, the assumed value was higher than that observed in the real-world setting (assumed values of 90 to 100% compared to 39.2 to 49.9% in Ireland; Chapter 2, section 2.4.3), while uptake rates were not reported in Ladabaum 2014 and Thomas 2021. Nonetheless, the uptake rate likely has a negligible influence on the interpretation of the cost effectiveness in the context of lowering the starting age of colorectal cancer screening: this is because the uptake rate affects both the benefits and costs of screening.⁽³⁷⁶⁾ In a circumstance, however, where the real-world uptake rates are exceptionally low, the screened population may represent the 'worried well', who are generally at lower risk. In such instances, higher uptake, which in turn extends screening to higher-risk individuals, could improve cost-effectiveness.

Lastly, none of the included studies directly reported the cost effectiveness of screening all adults aged 50–74 years, versus those aged 55–74 years, using a FIT45 threshold and two-yearly screening intervals. However, most studies reported costs and consequences for broadly similar strategies, where either the FIT threshold, screening interval, or age range varied. For the purposes of this review, ICERs were in some cases calculated by the review team using absolute results presented by study authors for strategies comparing to 'no screening'. These values were used to calculate an ICER for the comparisons of interest to this review. As such, the review did not primarily focus on the ICERs presented by the study authors in relation to their specific review questions, that is, comparisons involving strategies that are not currently under consideration in Ireland.

Notwithstanding the above limitations, combining the evidence presented directly by study authors, and the ICERs calculated by the review team for the specific strategies of interest to this HTA, the evidence suggests lowering the starting age for

screening from 55–74 years to 50–74 years is likely cost-effective using two-yearly screening with either low or high FIT thresholds.

6.5.4 Assessing the benefits of further evidence

In order to inform decision-making by the National Screening Advisory Committee, it is necessary to establish whether extending BowelScreen to those aged 50 to 54 is likely to be cost-effective. In the absence of transferable evidence on cost-effectiveness to the Irish setting, an economic model would be required to assess the costs and consequences of extending CRC screening in Ireland.

Although there remains some uncertainty regarding the generalisation of international evidence to the Irish setting (particularly generalisation of population outcomes, costs, and FIT performance characteristics), there is likely sufficient evidence to suggest lowering the age range from 55–74 years to 50–74 years would be cost-effective in the context of Ireland. While it is possible that developing a bespoke economic model would reduce uncertainty, it is also necessary to evaluate the benefit of developing a new model against the resources required. In the present review, the key finding – that is, lowering the starting age of CRC screening to 50 (from 54, 55, or 60) is cost-effective – was consistent across studies regardless of the geographical context and FIT threshold. Therefore, it is unlikely that an Ireland-specific model would lead to a different conclusion. Consequently, the cost of developing an economic model likely outweighs the potential benefits of reduced uncertainty in the present context. The benefits of developing an economic model would be more pronounced if the existing evidence differed, for example, or if there were sufficient grounds to suggest results would differ considerably in an Irish setting.

6.6 Conclusion

Based on available and relevant evidence to the Irish setting, the findings from this review suggest lowering the age range for CRC screening from 55–74 to 50–74 is likely to be cost-effective. Although extending BowelScreen to those aged 50 to 54 years may be more costly versus the current strategy, it is also likely more effective and would result in more favourable QALY gains due to an expected reduction in CRC incidence and mortality. As would be expected when considering the transferability of international evidence on cost-effectiveness, there remains some uncertainty regarding the generalisation of population outcomes, costs, and FIT performance characteristics to the Irish setting. Nonetheless, the five European studies deemed sufficiently credible and relevant to the Irish context were consistent in their findings that lowering the starting age of CRC screening to 50 (from 54, 55, or 60) is likely cost-effective.

7 Resource and budget impact of extending BowelScreen to those aged 50 to 54 years

7.1 Key points

Background

- This chapter presents an analysis of a cohort model of the natural history of colorectal cancer (CRC) to examine the resource implications of extending CRC screening to ages 50–74, compared to screening those aged 55–74. The analysis estimated changes in CRC incidence, additional resources required (endoscopy, laboratory testing, radiology, treatments), and the incremental costs of the proposed extension. Several scenarios were considered, involving different paces of expansion (that is, immediate, 1-yearly, and 2-yearly expansions), and varying assumptions about programme uptake and migration projections.
 - It should be noted that the aim of this model was not to predict the clinical effectiveness or cost-effectiveness associated with an age extension. The resource and budget impact model considers a ten-year time horizon with expansion assumed to commence from 2031. The model indicates the initial effects of screening in terms of early identification of CRC cases, but does not capture the longer-term benefits.

Additional resource requirements

- Lowering the starting age of CRC screening from 55 to 50 would increase the eligible population by 27% (over 400,000 additional people) when fully implemented, necessitating careful planning and allocation of health service resources to accommodate the larger eligible population.
- In both the immediate and 1-yearly expansion scenarios, the incremental number and rate of CRC in those aged 50–54 were predicted to peak within a 10-year time horizon, stabilising at around 40 to 60 additional cases (10 to 15 cases per 100,000) per year by 2040.
- The expanded programme (to ages 50–54) may generate up to approximately 2,100 additional screening colonoscopies and 800 additional participants requiring histopathology tests annually. Additionally, up to 600 more colonoscopies may be required in a given year for the surveillance of high-risk adenomas. Since surveillance colonoscopies follow on from initial screening, the years with the highest

resource requirements for screening and surveillance colonoscopies may be different.

- The primary aim of BowelScreen is early detection of cancer. The model predicts that expanding the screening programme to include those aged 50–54 would extend the benefits of early detection, resulting in fewer advanced-stage CRC cases (stages III and IV). As a result, fewer resources would be needed for treatment of such cases. By the 10th year, advanced stage cancers are expected to reduce by 34, 26 and 14 cases annually for the immediate, 1-yearly and 2-yearly expansion scenarios.
- FIT-based CRC screening additionally identifies and removes pre-cancerous polyps before they develop into cancer, potentially reducing the incidence of CRC. The model projects that immediate and 1-yearly expansion to those aged 50–54 could lead to an overall reduction in CRC cases within 10 years. By the 10th year, the overall cases reduced by 38 and 22 annually for the immediate and 1-yearly expansion scenarios. The 2-yearly expansion scenario did not reduce cases within 10 years, but a decrease is expected in the longer-term due to declining incremental case numbers in the latter half of the period.
- Expanded screening increases the demand for diagnostic tests and procedures including colonoscopy, CT colonography, and examination of samples taken during colonoscopy. However, for resources relating to cancer staging and grading (for example, diagnostic radiology and further histological examination), the increased demand from patients identified through screening will be partially offset by the reduced demand from patients presenting in the symptomatic services.
- All expansion pace scenarios showed similar trends, but scenarios of faster implementation achieved full effects of expanded screening sooner at the expense of larger initial resource needs. While faster implementation is expected to lead to greater health gains, slower implementation may be necessary to build capacity.

Cost implications

- Faster implementations incurred higher cumulative incremental costs over 10 years, with immediate, 1-yearly, and 2-yearly expansions costing an additional approximately €66 million, €57 million, and €45 million, respectively, compared to screening at ages 55–74.
- Immediate implementation incurred the highest initial cost, amounting to approximately €9.2 million in incremental costs in the first year versus screening only in those aged 55–74. This can be compared to an

incremental cost of €2.1 million for the 1-yearly and 2-yearly expansion strategies. By the 10th year, the annual incremental cost of the immediate expansion pace scenario was lower than that of slower expansion scenarios, although the analysis did not indicate cost savings within the first 10 years regardless of the pace of intervention.

- The largest drivers of overall incremental costs were related to colonoscopy (45%), treatments (25%), FIT tests (19%), histopathology (4%), BowelScreen contribution to related services (4%) and additional programme staff (3%).
- Once established, the overall incremental cost is expected to decline over time due to earlier cancer detection, which reduces the need for more costly advanced-stage treatments.

Scenario analysis

- CRC screening uptake rates in Ireland have been relatively low, ranging from 38.1% among those aged 60–64 to 49.9% among those aged 65–69 years. Achieving the target uptake of 60% would reduce CRC cases, but would require greater resources, costing an estimated additional €5 to €10 million by 2040.
- Higher inward migration scenarios predicted a larger population, leading to more CRC cases, and increased resource and budgetary requirements. The high and low migration scenarios are estimated to cost up to plus or minus €3 million by 2040, respectively, compared to the moderate migration scenario.

Conclusion

- In summary, over the 10-year period, the model estimated the incremental budget impact associated with immediate, 1-yearly and 2-yearly expansions as €66, €57, and €45 million, respectively. These values are influenced by the assumed pace of expansion, programme uptake and migration projections as well as uncertainty in the underlying data used to inform them. Therefore, the figures provided should be viewed as broad indications rather than precise estimates.
- Expanding BowelScreen to include those aged 50–54 is expected to lead to population health benefits by reducing CRC cases and detecting cancers at less advanced stages. This expansion will inevitably place substantial demands on health service resources and budgets. Slower implementation options may be necessary to manage the initial resource requirements.

7.2 Introduction

Screening aims to detect cancer at early stages. By identifying cancer before symptoms appear, screening can decrease the number of cases diagnosed through symptomatic presentation. This early detection helps prevent severe disease and reduces the need for resource-intensive and costly treatments associated with advanced-stage cancers, thereby incurring benefits both at the patient and health service level. Additionally, screening for colorectal cancer (CRC) has the benefit of enabling the removal of pre-cancerous polyps, which can prevent the development of cancer altogether. However, a screening programme incurs additional resource requirements on the health system, as additional resources are needed for screening, diagnosis and treatment of CRC identified through the programme.

The ability to deliver the necessary health service resources is crucial for the successful implementation of a screening programme. For example, previous resource modelling studies have concluded that colonoscopy capacity is a pivotal factor for resource planning in CRC screening programmes.^(377, 378) In Ireland, concerns have been raised regarding the capacity of endoscopy, histopathology and radiology services in light of the proposed BowelScreen expansion (Chapter 8).

Ireland's CRC screening programme, BowelScreen, was introduced in October 2012 with the aim of offering free screening to people aged 55–74.⁽¹⁴⁸⁾ Implementation progressed on a phased basis, commencing with those aged 60–69. In 2012–2013, invitations initially focused on older clients who would soon exceed the eligible age range. The National Cancer Strategy 2017–2026 and 2020 Programme for Government included a commitment to expand screening to those aged 55–74:^(1, 2) the expansion commenced in October 2023, lowering the starting age from 60 to 59.⁽³⁷⁹⁾ The 2025 HSE National Service Plan outlined the expansion of the programme to include those aged 58 to 70 years on an incremental basis by 2026 as a key area of focus;⁽¹⁵⁾ as of April 2025, screening is available to people aged 59–70. The scope of the present HTA is to assess the impact of a further extension of the programme to include those aged 50–54.

The present chapter reports on a cohort model devised to examine the resource and budget impact of lowering the starting age of BowelScreen from 55 to 50; the impacts are presented over a ten-year time horizon. This model considers various consequences of the programme expansion, including the increased number of individuals eligible for screening, the potential for earlier cancer detection, and the subsequent effects on treatment and patient follow-up. In doing so, the present model aimed to quantify the resources required for expanding the screening programme to a younger population. The aim of this model was not to predict the clinical effectiveness or cost-effectiveness associated with lowering the screening age from 55 to 50; the ten-year time horizon indicates the initial effects of screening

in terms of early identification of CRC cases, but does not capture the long-term benefits. This is described further in Section 7.6. Chapter 5 (Review of clinical effectiveness) and chapter 6 (Review of cost-effectiveness) provide detailed information on the expected clinical benefits and consideration of the cost effectiveness of an age extension, respectively.

The analysis focused on the comparison between the proposed extension scenario (that is, screening 50–74) and the age range already committed to (that is, screening 55–74).⁽¹⁾ The model estimates the potential reductions in CRC incidence, the additional resources required (including those involved in endoscopy, laboratory testing, radiology and treatments) and the incremental costs of the proposed extension.

7.3 A summary of the analysis

This section provides a high-level summary of the model structure and analysis employed in this chapter. Detailed descriptions of the model equations, parameters, and specific methodologies are provided in Appendix E.1.

7.3.1 Cohort model of colorectal cancer screening

A cohort model of CRC screening in Ireland was devised, with each cohort stratified into four categories according to the CRC natural history:

1. No CRC or adenoma
2. Non-high-risk adenoma(s)
3. High-risk adenoma(s)
4. CRC

This natural history reflects terminology used within the BowelScreen programme, which distinguishes between 'high-risk findings' and 'no high-risk findings'; these adenoma categories (that is, non-high-risk and high-risk) were differentiated to reflect the different surveillance pathways (see Chapter 2, section 2.4.2).⁽⁶⁶⁾ The heterogeneities in the TNM cancer stages (that is, I, II, III, and IV) and cancer sites (that is, colon or rectum) were incorporated indirectly using data from the National Cancer Registry Ireland.

Each cohort in the model represents a cohort of average-risk people born in a particular year, who were assumed to varyingly experience five annual events describing processes of demography, CRC natural history and health services in Ireland. These included a) CRC disease progression, b) symptomatic presentation, c) eligibility-based screening, d) death and e) net migration. Throughout the simulation, the cohort sizes were scaled to CSO estimates of past population size and future population projection.^(380, 381)

The cohorts were simulated from 2013 (that is, the first full year of BowelScreen), taking into account the historical change in the eligibility and pattern of invitation in screening-eligible cohorts. The historical context of CRC screening was required to reflect the interaction between health services and epidemiology (for example, previously screened cohorts have a reduced CRC risk) and resources incurred through the follow-up of previously detected cases. The BowelScreen programme launched in October 2012, initially targeting individuals aged 60–69. Initially, invitations were prioritised for older clients nearing the upper limit of the eligible age range. Based on the current rate of expansion and consultation with the programme, the ongoing expansion to 55–74 was anticipated to be completed by 2030. As of April 2025, those aged 59–70 are eligible, while a further expansion to 58–70 is planned for 2026.⁽¹⁵⁾ Upon consultation with the BowelScreen programme, 2031 was chosen as the intervention base year (that is, the start of the rollout) for the proposed expansion to 50–54. A 10-year time horizon was chosen, such that the present analysis focused on the time period between 2031 and 2040 inclusive.

The analysis considered biennial screening for those aged 55–74 as the baseline or comparator, while extending screening to those aged 50–54 served as the intervention. To avoid fluctuating resource demands from biennial screening, it was assumed that half of the newly eligible population would be invited to participate in their first year of eligibility, with the remaining half invited the following year.

The analysis examined alternative scenarios regarding the pace of extension, FIT uptake rate, and migration projections as modelled by the CSO.⁽³⁸²⁾ Table 7.1 summarises the modelled scenarios.

Table 7.1 Alternative modelled scenarios in the pace of expansion, FIT uptake rate and migration scenarios

Scenario	Description
Expansion pace	
Immediate expansion	Instantaneous implementation from the base year.
One-yearly expansion	Lowering the starting age by one every year from the base year.
Two-yearly expansion	Lowering the starting age by one every two years from the base year.
FIT uptake rate	
Empirically-informed*	Observed rate in Ireland and Canada (Canadian rate used for age groups currently not yet screened in Ireland; (Appendix E.1, Table E.5)
Quality assurance standard	The achievable quality assurance standard set by BowelScreen ⁽³⁰⁵⁾ : 60%
Migration	
High	Net migration begins at +75,000 in 2022, gradually decreases to +45,000 per year by 2027, and remains at this level until 2057.
Moderate*	Net migration begins at +75,000 in 2022, gradually decreases to +30,000 per year by 2032, and remains at this level until 2057.
Low	Net migration begins at +75,000 in 2022, gradually decreases to +10,000 per year by 2032, and remains at this level until 2057.

Note: All three expansion pace scenarios are presented together.

* Where applicable, the asterisk indicates the base-case scenario assumed for the analysis. Migration projection scenarios were calibrated by CSO.⁽³⁸²⁾

7.4 Health outcomes

The number and incidence rate per 100,000 of CRC and adenomas were estimated by the model. In addition, the number of individuals that experience a bowel perforation and major bleeding during colonoscopy was estimated (further details provided in Section 7.4.3).

7.4.1 Resources and associated costs

Resources required in CRC-related health services, including screening, symptomatic detection, treatment, and patient follow-up were estimated by the model. Based on input from the BowelScreen programme, most capital investment was assumed to take place in advance to support the ongoing expansion to those aged 55–74. The provision of endoscopy rooms is likely to represent the most significant form of capital investment required for an expansion. The potential number of additional endoscopy rooms required to support the additional colonoscopy procedures projected by this model is explored in Chapter 8. While these costs are expected to be substantial, there is considerable uncertainty, for example, because it remains unclear whether the provision of additional rooms would take place as part of other planned building works or as a standalone project. As such, the analysis does not include any additional capital investment for extending BowelScreen to those aged 50–54.

The BowelScreen programme is supported by administrative staff based in the NSS. The additional administrative staff required to support expansion is described in Chapter 8 (Section 8.6.1). Compared to the 55–74 scenario, the model accounts for the cost of one additional clinical co-ordinator and two additional staff officers. Table 7.2 below presents the price per resource item along with the corresponding source of cost information.

Table 7.2 Unit cost data included in the model

Description	Price (€)	Source
Home screening test		
FIT invitation	1.70	NSS
FIT kit, packaging, postage and processing	17.60	BowelScreen
Additional BowelScreen Programme administrative annual staff costs	261,058	BowelScreen, HSE Staff costs. ⁽³⁸³⁾
Clinical diagnostic procedures and tests		
Outpatient clinic visit	220	HPO
Emergency department visit	464	HPO
Colonoscopy clinic visit	1,007	DRG: weighted average of day-case colonoscopy (DRG G48A and G48B) ⁽³⁷⁴⁾
CT colonography visit	550	St Vincent's Private Hospital website ⁽³⁸⁴⁾
Cost of perforation during colonoscopy	13,822	DRG: weighted average of inpatient small and large bowel procedures (DRG G05A and G05B) ⁽³⁷⁴⁾
Cost of major bleeding during colonoscopy	4,047	DRG: weighted average of inpatient gastrointestinal haemorrhage (DRG G61A and G61B)
Histopathology (H&E)	710 [#]	Laboratory Services Reform Programme (HSE)
Further histopathology (immunohistochemistry & special histochemistry)	440 [#]	Laboratory Services Reform Programme (HSE)
Molecular tests (colorectal panel: KRAS, NRAS and BRAF)	550	Laboratory Services Reform Programme (HSE)
Blood tests (Blood count, coagulation, CEA)	100	Commercial provider ⁽³⁸⁵⁾ ; Laboratory Services Reform Programme (HSE)
CEA test	15	Laboratory Services Reform Programme (HSE)
CT scan during diagnosis	400	St Vincent's Private Hospital website ⁽³⁸⁴⁾
PET scan during diagnosis	1,800	Personal communication ⁽³⁸⁶⁾
MRI pelvis during diagnosis (rectal cancer)	475	St Vincent's Private Hospital website ⁽³⁸⁴⁾
Rigid sigmoidoscopy during diagnosis (rectal cancer)	1,135	DRG: day case digestive malignancy (Day Case DRG G60) ^{\$(374)}
Patient care	Base-case	CPI Sensitivity Analysis
Treatment of Stage I CRC	22,030	30,793
Treatment of Stage II CRC	39,071	54,615
Treatment of Stage III CRC	53,925	75,377
Treatment of Stage IV CRC	39,969	55,870

Tilson et al. 2012^{(375)*}

Description	Price (€)	Source
BowelScreen contribution		
Towards colonoscopy	650	BowelScreen
Towards CTC	650	
Towards histopathology	100	
Towards surgery	5,000	

+ The estimation of additional BowelScreen programme administrative costs is detailed in Appendix E.2.

* The costs from Tilson et al. 2012 were inflated to 2024 Irish Euro.

\$ A large majority (over 91%) of rigid sigmoidoscopy performed on rectal cancer patients in 2022–2023 were classified as day case DRG G60.

The estimation of the cost of histopathology per case (which integrates the staffing costs) is detailed in Appendix E.2.

Key: ABF – activity based funding; BRAF – proto-oncogene B-Raf; CEA – carcinoembryonic antigen; CRC – colorectal cancer; CT – computed tomography; CTC – computed tomography colonography; DRG – diagnosis-related group; FIT – faecal immunochemical test; KRAS – Kirsten rat sarcoma; H&E – haematoxylin and eosin stain; HPO – Healthcare Pricing Office; HSE – Health Service Executive; MRI – magnetic resonance imaging; NRAS – neuroblastoma rat sarcoma; NSS – National Screening Service; PET – positron emission tomography.

7.4.2 Home screening test

Initial invitation

People eligible for BowelScreen receive a letter of invitation to participate in screening. Related costs include paper and outward postage for all invitations.

FIT test kit and processing

When an eligible person responds affirmatively, they are sent a FIT kit. Relevant costs include the FIT test kit, packing and postage (returned invitations and onward kit delivery). The processing cost relates to the test returned by participants, including return postage, analysis, quality control, and result reporting.

7.4.3 Clinical diagnostic procedures and tests

Colonoscopies are used during symptomatic presentation, screening, high-risk adenoma surveillance and subsequent surveillance of CRC survivors (Appendix E.1, Figure E.1). CT colonography (CTC, also known as virtual colonoscopy) is offered as an alternative to colonoscopy in the event of an incomplete colonoscopy, or if an individual refuses colonoscopy or is deemed unsuitable (for example, as a result of poor health or a higher risk of perforation). The BowelScreen 2022–2023 programme report documented that 2.1% of participants were referred for CTC following a positive FIT result.⁽¹⁴⁹⁾ During screening, an additional colonoscopy, following an index colonoscopy, may be required due to inadequate bowel preparation, the

participant's tolerance level for the first procedure, the requirement to have a second colonoscopy to check a site previously examined or resected, or a clinical decision to perform colonoscopy over two visits instead of surgery.⁽¹⁸⁾ In 2022–2023, 13.7% of index colonoscopies were followed by such an additional procedure.⁽¹⁴⁹⁾ During colonoscopy, polyps are removed and sent for histopathological examination (Haematoxylin and eosin stain, or H&E). If safe endoscopic removal is not possible (such as due to size and or complexity), biopsies are taken and sent for histopathological examination.

Colonoscopy complications – including perforation and bleeding – occur in a small number of cases and there are additional costs associated with their management (Table 7.2). In BowelScreen between 2022 and 2023, colonic perforation occurred in 0.8 per 1,000 colonoscopies and post-polypectomy perforation and major bleeding occurred in 0.3 and 1.0 per 1,000 procedures where polypectomy was performed, respectively.⁽¹⁴⁹⁾

For staging and grading cancer, additional tests are conducted, including further histopathology (histochemistry and immunohistochemistry), blood tests (complete blood count, coagulation, and carcinoembryonic antigen [CEA]), molecular testing (colorectal panel), and a CT scan. PET scans are ordered for up to 15% (estimated based on personal communication with EAG members) of CRC-confirmed patients. Additionally, an MRI of the pelvis and rigid sigmoidoscopy are ordered for rectal cancer.⁽¹⁷⁵⁾

Hospital visit at symptomatic diagnosis

For symptomatic diagnosis, 30% of symptomatic persons were assumed to present as emergency cases via the emergency department, while the remainder were assumed to have been referred to a hospital outpatient clinic via their general practitioner. This assumption was corroborated by a recent study in Canada, which reported that roughly 30% of symptomatic CRC patients present to the emergency department.⁽³⁸⁷⁾

7.4.4 High-risk adenoma surveillance

Those who enter the high-risk adenoma surveillance pathway were assumed to undergo a colonoscopy (or CTC in rare cases as described above) three years after the index colonoscopy.⁽⁶⁶⁾

Adenoma surveillance participation rate

High-risk and intermediate-risk adenomas previously, between 2012 and 2022, underwent follow-up at 1 and 3-year intervals as part of the BowelScreen surveillance pathway. Thus, there were roughly two years between a person with either a high- or intermediate-risk adenoma being referred for surveillance

colonoscopy. Using the surveillance referral data from 2014–2021 and surveillance colonoscopy data from 2016–2023, the surveillance uptake rate was calculated as the proportion of the total surveillance colonoscopies carried out over the total number referred. The estimated proportion of 0.851 closely matches the figure reported by the UK CRC screening programme (0.872).⁽³⁶⁸⁾

Probability of high-risk adenoma recurrence three years following a resection of a high-risk finding

An international meta-analysis of adenoma recurrence reported a local recurrence rate of 11.0% for polyps ≥ 10 mm at up to 12-month follow-up.⁽³⁸⁸⁾ At 10mm, an adenoma is classified as advanced and having ≥ 2 adenomas (including one advanced) is one definition of high-risk findings according to the BowelScreen surveillance guideline.⁽⁶⁶⁾ Scaling up the 12-month local recurrence rate to three years, assuming a constant rate process, the probability of high-risk adenoma recurrence three years following resection of a high-risk finding equates to 0.295. The subsequent recurrent events were modelled with this same probability until the time horizon was reached.

Probability of cancer detection following a resection of a high-risk finding

A small proportion of people under surveillance after resection of a high-risk finding subsequently may develop CRC: an international meta-analysis reported that 0.63% of people developed CRC over three years following resection of a high-risk finding.⁽³⁸⁹⁾ These cases were considered in the model by incrementing CRC incidence three years from the initial resection.

7.4.5 Patient care

When CRC is confirmed (either through a symptomatic presentation or screening), the patient goes through a treatment regimen and a subsequent surveillance protocol, as described below.

Treatments

Treatment events were considered in aggregate per cancer stage, including surgery and radiology. Further details on the receipt of treatment in Ireland can be found in Chapter 3 on Epidemiology. As the CRC stages were not modelled explicitly, the cancer stages were assigned retrospectively based on the mode of detection according to NCRI data (Table 7.3): CRC cases detected via screening are found in earlier stages than those that present symptomatically.

Table 7.3 Stage distribution of colorectal cancers detected in Ireland by screening and symptomatic presentation from 2012 to 2020 in those aged 60–69

Mode of detection	Stage I	Stage II	Stage III	Stage IV
Symptomatic service	14%	24%	36%	26%
Screening programme	41%	22%	30%	7%

Source: NCRI.

Note: BowelScreen has been available since October 2012 for people aged 60 to 69 years old.

Key: NCRI – National Cancer Registry Ireland.

CRC patient follow-up

CRC patients are monitored in hospital outpatient clinics to detect early signs of recurrent or metastatic disease. However, follow-up protocols are heterogeneous among hospitals in Ireland and individualised to specific patient needs.^(390, 391) As part of the previous HTA which HIQA published in 2009 before the introduction of BowelScreen, the evaluation team carried out a survey of follow-up protocols from three hospitals.⁽¹²⁾ Following the same framework as the 2009 HTA, the present work assumes the same resource requirement matrix produced as a result of the survey and a maximum follow-up duration of five years for Stage I–III patients and 15 months for Stage IV patients (Table 7.4). Those who are diagnosed with CRC were assumed to participate in the follow-up protocols in the year of diagnosis, while a proportion of patients were removed from follow-up due to mortality.⁽²¹²⁾

Table 7.4 Assumed resource requirements during five-year follow-up surveillance of colorectal cancer patients

Time (months)	CEA test	CT scan	Colonoscopy	Outpatient visit
12	3	1	1	3
24	2	1	0	2
36	1	0	1	1
48	1	0	0	1
60	1	1	1	1
Total	8	3	3	8

Source: HIQA HTA (2009).⁽¹²⁾

Note: The model time step is in the unit of 12 months.

Key: CEA – carcinoembryonic antigen; CT – computed tomography

7.4.6 BowelScreen contributions

BowelScreen-participating hospitals receive a 'contribution for services' for the purpose of service development, for each of the following:

- Colonoscopy: €650
- CTC: €650
- Histopathology: €100
- Surgery: €5,000

It is noted that the BowelScreen contributions are not designed to cover the costs of the procedures. While appropriate deductions may be applied to ABF budgets to avoid double payments,⁽³⁹²⁾ information on potential deductions were not available at the time of the assessment. As such, these amounts were accounted for in addition to the unit costs (Table 7.2); therefore, the overall cost of screening-associated procedures may be overestimated.

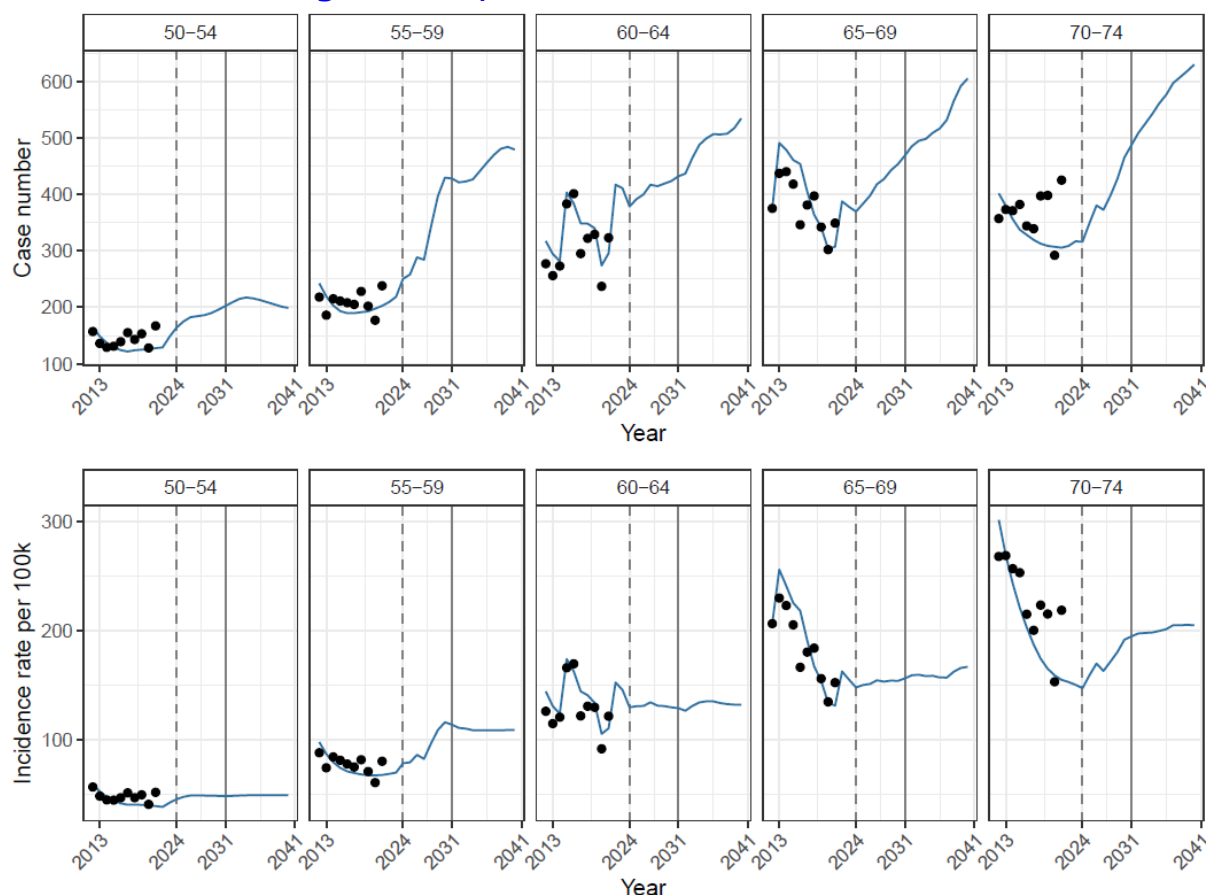
7.5 Estimated colorectal cancer epidemiology and resource requirements

This section presents estimates based on the base-case scenarios, which assumed the empirically-estimated screening uptake rate and moderate migration, as detailed in Table 7.1. The outcomes for alternative scenarios, including screening uptake rates meeting QA standards, and varying migration scenarios (low and high), are detailed in Section 7.5.5. Detailed model outputs of the epidemiology, resource use, and costs across all intervention, uptake and migration scenarios are included in Appendix E.3.

7.5.1 Colorectal cancer epidemiology

The cohort model of CRC natural history and health services adequately captured the time course of the CRC case number and incidence rate from 2013 to 2021 (Figure 7.1), with the differences between the model predictions and the observed data generally balanced around zero (Appendix E.4). Under the comparator, where those aged 55–74 are eligible for screening, CRC cases were projected to rise in age groups with growing populations (that is those over 60),⁽³⁸¹⁾ while incidence rates were expected to remain relatively stable across age groups (Figure 7.1).

Figure 7.1 Estimated and observed incidence of colorectal cancer: number (top) and rate per 100,000 (bottom) under the comparator screening scenario, 55–74

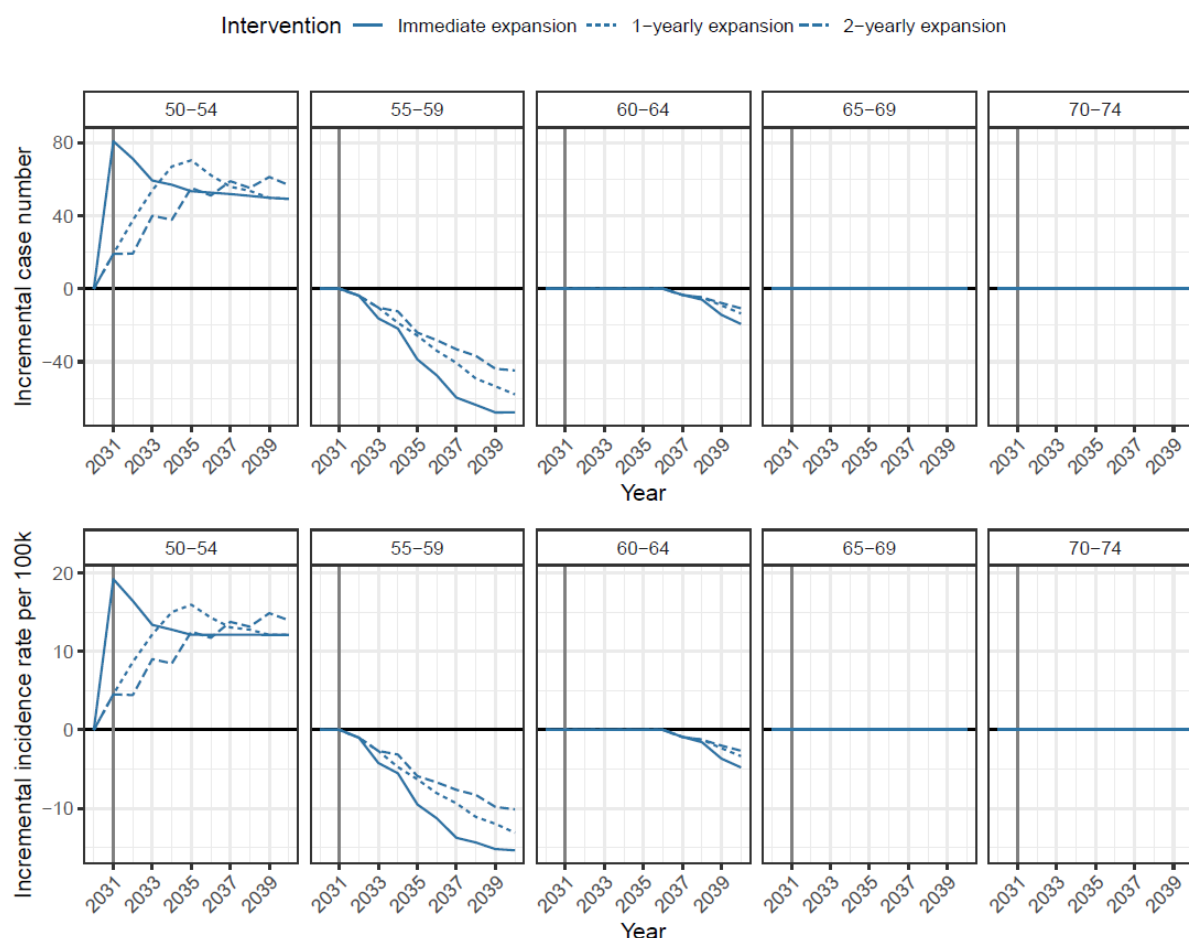


Source: NCRI

Note: Model estimates and observed data are indicated by blue lines and black dots, respectively. Dashed and solid vertical line indicate the start of the current expansion to 55–74 (2024; that is, rounded up from October 2023) and the intervention base year (2031), respectively.

In comparison to screening those aged 55–74 only, the number of CRC cases detected among individuals aged 50–54 was predicted to initially increase regardless of the pace of expansion (Figure 7.2). In both the immediate and 1-yearly expansion scenarios, the incremental number and rate in this age group were predicted to peak within the 10-year time horizon, stabilising at around 40 to 60 incremental cases (10 to 15 cases per 100,000) per year by 2040. As the newly screened cohort matures, the model predicted an offset of a similar magnitude in CRC presentations in the cohorts that had undergone screening at ages 50–54 (that is, a subsequent decline in CRC cases in the 55–59 and 60–64 age groups; Figure 7.2). No change is expected in age groups older than 64 within the 10-year time-horizon because the oldest newly screened cohort, that is those aged 54, would be 64 in the 10th year.

Figure 7.2 Estimated incremental incidence of colorectal cancer by age group: number (top) and rate per 100,000 (bottom) of the three expansion pace scenarios



Note: The solid horizontal line at 0 indicates the comparator scenario. The solid vertical line indicates the start of the intervention year (2031).

The primary aim of a FIT-based CRC screening programme is to detect cancer early, allowing for earlier treatment and improved prognosis. Expanding the programme from ages 55–74 to 50–74 was predicted to effectively achieve this aim by reducing the number of advanced cases (found in stages III and IV) compared to the comparator under all three intervention scenarios within the 10-year time horizon (Figure 7.3). By 2040, advanced stage cancers (that is, stage III and IV) were predicted to reduce by 34, 26 and 14 cases that year for the immediate, 1-yearly and 2-yearly expansion scenarios, respectively (Figure 7.3). However, in the context of all advanced stage cancers diagnosed that year ($n=1,806$, 1,815, and 1,827, respectively), these reductions represent a small proportional decrease of less than 2%. The incremental number of stage I cases was estimated to be higher than the comparator across every year of the 10-year time horizon examined. However, the

size of the increase was predicted to decline following full implementation (Figure 7.3).

Figure 7.3 Estimated incremental case number of colorectal cancer by cancer stages under the three expansion pace scenarios

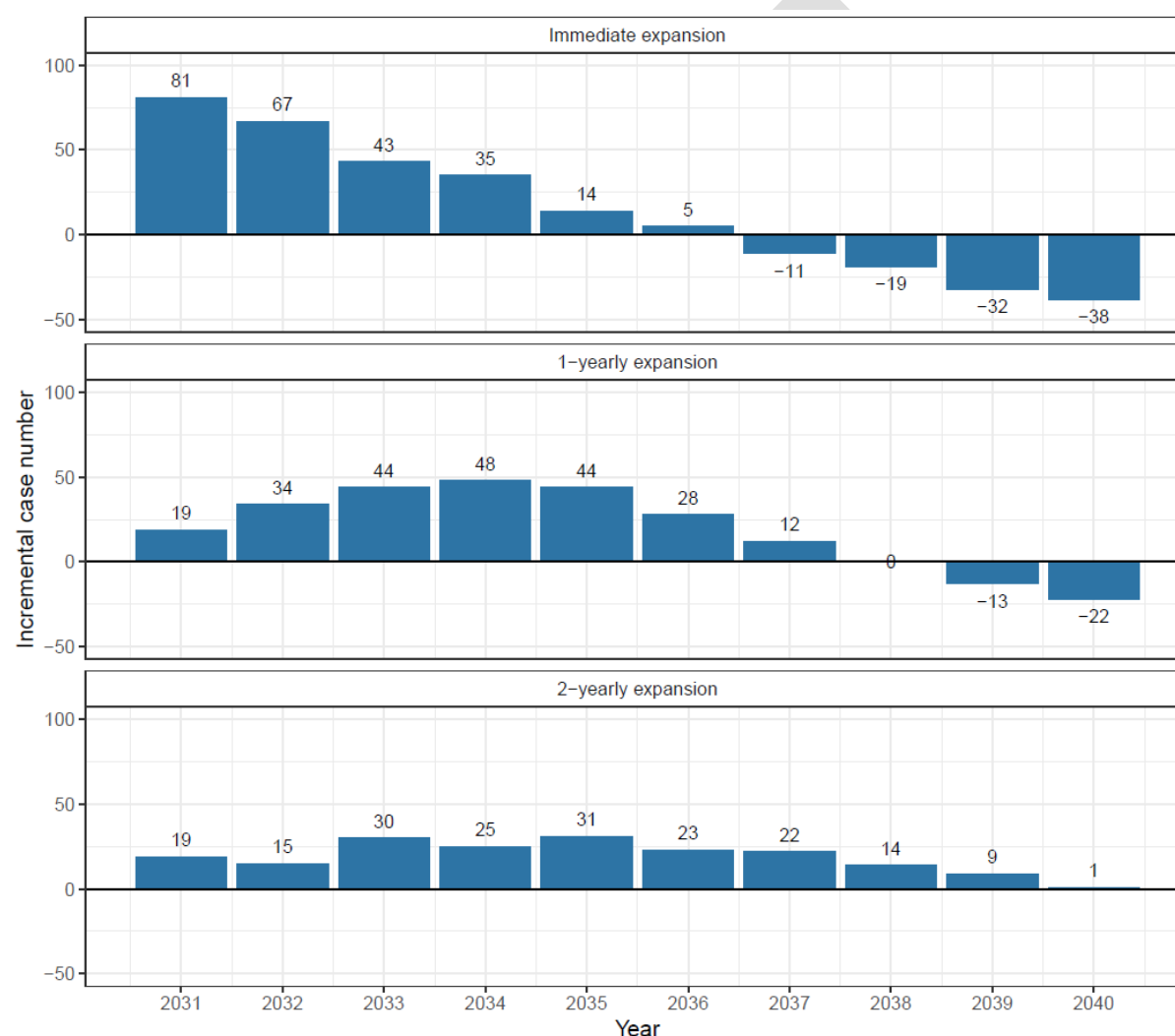


Note: The solid horizontal line at 0 indicates the comparator scenario. Colorectal cancer stages were extrapolated from the mode of detection and NCRI data linking the mode of detection to cancer stages. Details are found in Chapter 3 (Epidemiology).

Although FIT sensitivity with respect to detection of pre-cancerous polyps is low (see Chapter 4 on Test Accuracy), an additional intended benefit of FIT-based CRC screening is to identify and remove pre-cancerous polyps before they develop into cancer, thereby preventing new cases from arising. Aggregating over the whole population, the immediate and 1-yearly expansion scenarios were projected to result in an overall reduction in cases compared to the comparator scenario by the seventh and ninth years of intervention, respectively (Figure 7.4). By 2040, 38 (1.1%) and 22 (0.7%) fewer annual cases were predicted, respectively, as a result of the

immediate and 1-yearly expansion. The 2-yearly expansion scenario did not result in case reduction within the 10-year time frame, though a longer-term decrease is anticipated based on the declining incremental case numbers observed in the latter half of the period (Figure 7.4). Therefore, the model estimates that lowering the starting age of CRC screening to 50 may reduce the overall cancer burden in the population.

Figure 7.4 Estimated incremental case number of colorectal cancer across all ages modelled (50-84) under the three expansion pace scenarios



Note: The solid horizontal line at 0 indicates the comparator scenario.

7.5.2 Resource requirements

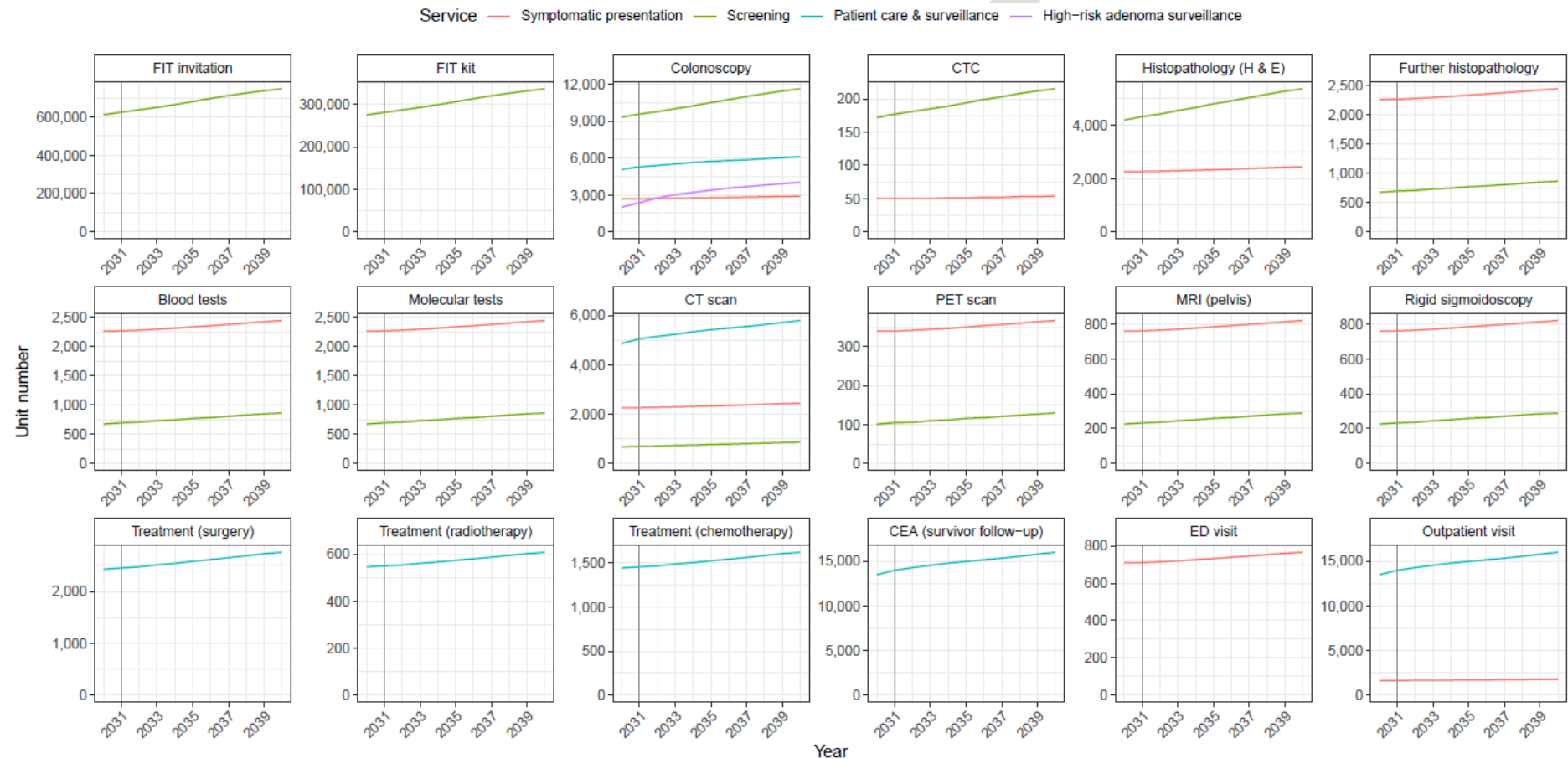
This section considers the expected CRC health service resource requirements. Staffing requirements are discussed further in the Organisational considerations chapter (Chapter 8).

The cohort model effectively captured the historical observed time course of the number of FIT invitations, FIT returns, FIT positives, and BowelScreen colonoscopies, from 2013 to 2023 (Appendix E.4). Under the comparator scenario (that is, screening 55–74), resource requirements for CRC-related health services were generally expected to increase over the 10-year time horizon due to the growth and ageing of the BowelScreen-eligible population (Figure 7.5).

Lowering the starting age of BowelScreen from 55 to 50 would increase the population eligible for screening by 27% if fully implemented by 2040.⁽³⁸¹⁾ As such, the intervention screening scenarios (that is, screening from 50) are expected to increase the demand for screening resources (Figure 7.6). Notably, the model predicted that the expansion to ages 50–54 may generate up to approximately 2,100 additional screening colonoscopies (including index and additional planned procedures), 40 additional CTCs, and 800 additional people requiring histopathology (H&E) tests annually in the screening programme. Furthermore, up to 600 additional colonoscopies may be required each year for the surveillance of high-risk adenomas (Figure 7.6). Since surveillance colonoscopies follow on from initial screening, the years with the highest resource requirements for screening and surveillance colonoscopies may be different. The increases in demand outweigh any reduction in resources used to determine for symptomatic cases whether a patient has cancer (including colonoscopy, CTC and histopathology [H&E]) (Figure 7.6 & Figure 7.7). This is because the expanded screening for those aged 50–54 would bring more people into the health system than would have presented symptomatically in this age group.

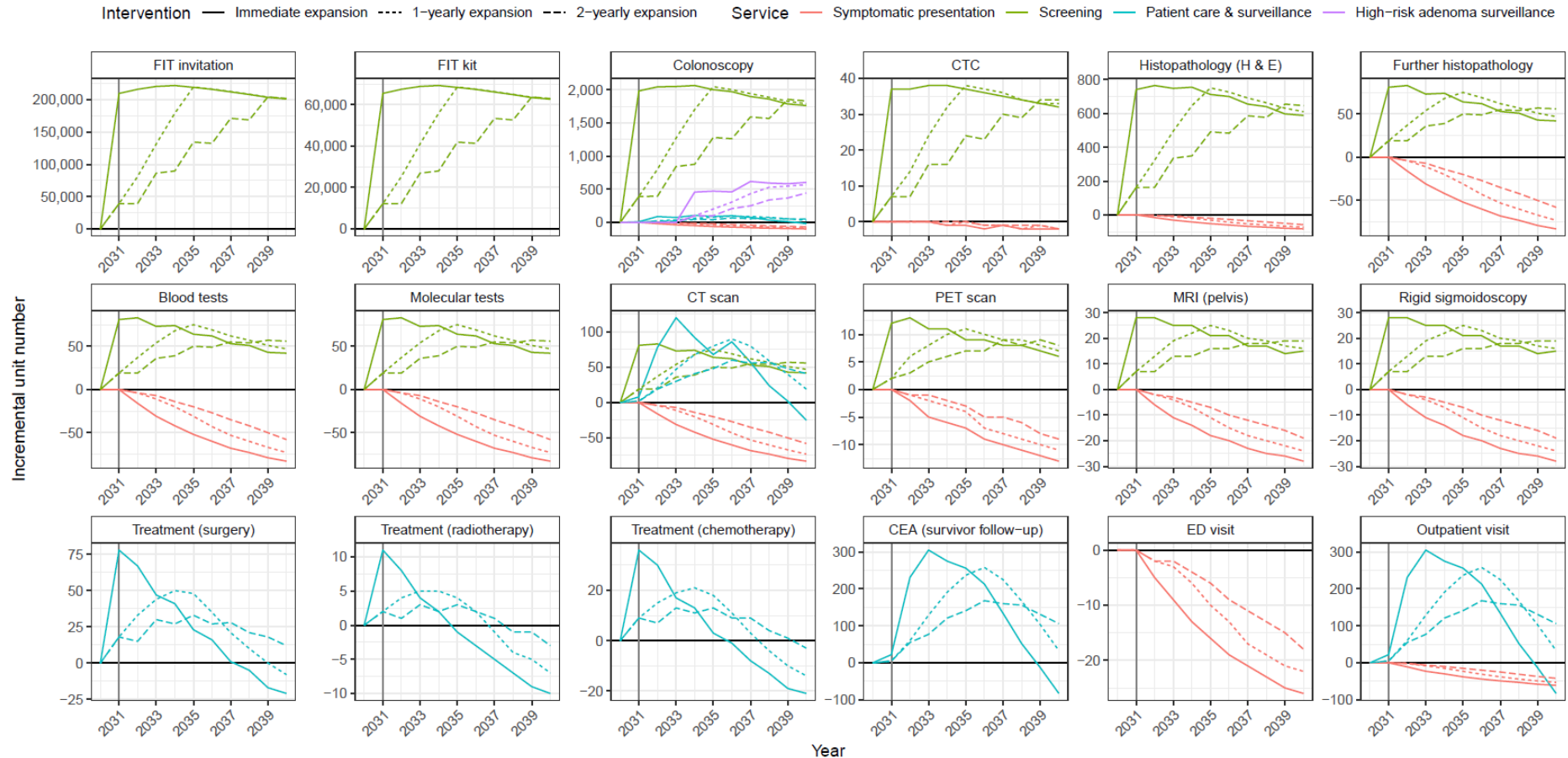
For diagnostic resources required for those highly suspected and confirmed as having CRC, such as for cancer staging and grading (including further histopathology tests such as immunohistochemistry, blood tests, molecular testing, CT scan, PET scan, MRI and rigid sigmoidoscopy), a short-term increase in the demand is expected following the expansion to 50–54 (Figure 7.6). However, the model predicted an offset from symptomatic services later in the time horizon. This offset was predicted to be comparable in magnitude to the increased demand generated by the expanded screening service (Figure 7.6 & Figure 7.7). This is because screening enables earlier detection of cases that would have presented symptomatically at a later stage.

Figure 7.5 Estimated resource requirements associated with colorectal cancer services under the comparator screening scenario



Note: For diagnostic tests, treatments and hospital visits, the unit number refers to the number of people requiring the service. For other services, the unit number refers to the number of procedures. Key: ED – emergency department; CEA – carcinoembryonic antigen; CT – computed tomography; CTC – computed tomography colonography; FIT – faecal immunochemical test; H&E – haematoxylin and eosin stain; MRI – magnetic resonance imaging; PET – positron emission tomography

Figure 7.6 Estimated incremental resource requirements associated with colorectal cancer services under the intervention screening scenarios

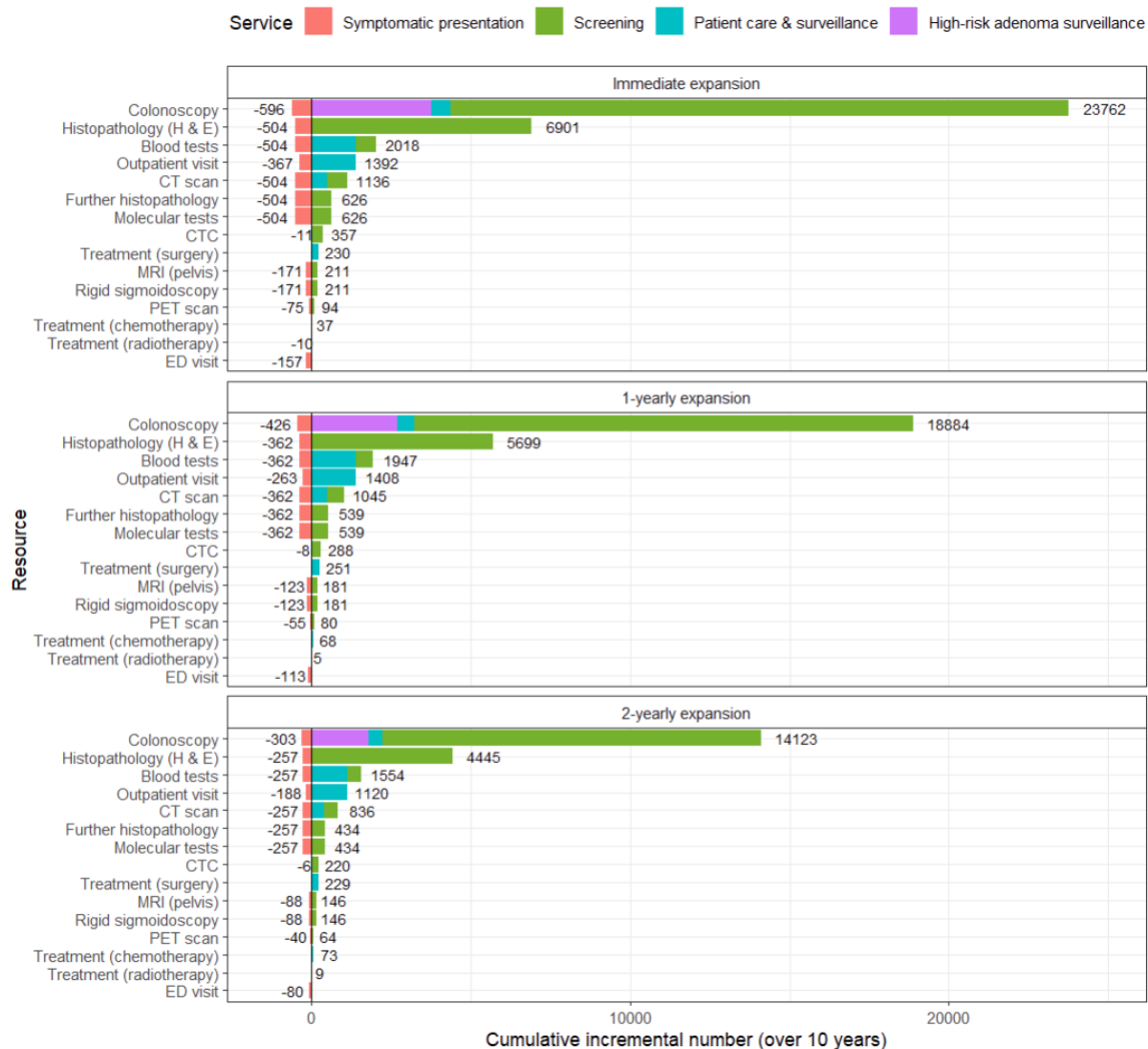


Note: For diagnostic tests, treatments and hospital visits, the unit number refers to the number of people requiring the service. For the others, the unit number refers to the number of procedures. Key: ED – emergency department; CEA – carcinoembryonic antigen; CT – computed tomography; CTC – computed tomography colonography; FIT – faecal immunochemical test; H&E – haematoxylin and eosin stain; MRI – magnetic resonance imaging; PET – positron emission tomography

As screening results in a higher number of cancers detected initially after the intervention (Figure 7.4), lowering the starting age from 55 to 50 was predicted to increase the number of surgeries and slightly increase chemotherapy usage over the 10-year time horizon (Figure 7.7). Conversely, screening results in earlier detection and shifts the cancer stage distribution at detection to less advanced stages (Figure 7.3). As a result, lowering the starting age of screening was predicted to reduce the number of radiotherapy treatments (Figure 7.7). Admissions to the emergency department were also predicted to decrease as the expansion of the screening programme is expected to reduce the number of symptomatically detected cases. However, outpatient visits were predicted to increase due to more follow-up appointments for CRC patients detected through the expanded screening (Figure 7.6 & Figure 7.7).

While all three scenarios showed similar trends, slower expansions were expected to incur smaller initial requirements at the expense of achieving the full effect of the intervention at a later time.

Figure 7.7 Estimated cumulative incremental resource requirements over 10-year time-horizon



Note: For diagnostic tests, treatments and hospital visits, the unit number refers to the number of people requiring the service. For the others, the unit number refers to the number of procedures. Blood test numbers are inclusive of CEA tests during patient follow-up.

Key: ED – emergency department; CEA – carcinoembryonic antigen; CT – computed tomography; CTC – computed tomography colonography; H&E – haematoxylin and eosin stain; MRI – magnetic resonance imaging; PET – positron emission tomography

7.5.3 Harms

Due to the increase in colonoscopies performed, a small rise (zero to two cases per year) in complications such as colonic perforation and major bleeding was predicted by the model (Table 7.5).

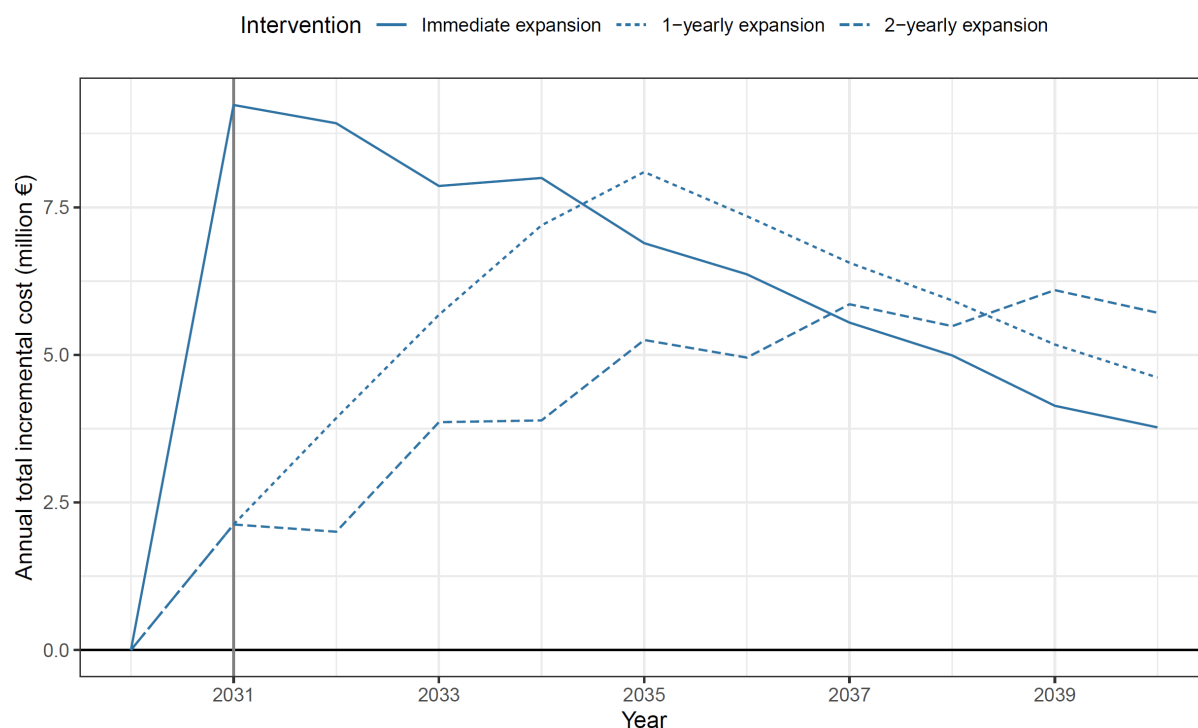
Table 7.5 Estimated incremental numbers of people experiencing harms of screening under the three expansion pace scenarios

	Intervention	Year 1	Year 5	Year 10
Colonic major bleeding	1-yearly expansion	0	1	0
	2-yearly expansion	0	0	0
	Immediate expansion	1	1	0
Colonic perforation	1-yearly expansion	1	2	2
	2-yearly expansion	1	1	2
	Immediate expansion	2	2	2

7.5.4 Incremental cost of intervention

The budget impact analysis projected that faster implementations would incur higher cumulative incremental costs. Over the 10-year period, immediate, 1-yearly and 2-yearly expansions were estimated to cost approximately €66, €57, and €45 million in addition to the comparator screening strategy (that is, screening those aged 55–74). The immediate implementation also incurred the highest initial cost, with incremental costs approximating €9.2 million in the first year, versus screening only those aged 55–74. The corresponding incremental cost for the 1-yearly and 2-yearly strategies amounted to €2.1 million (Figure 7.8). Once the programme is established, the overall incremental cost is expected to decline over time. By year 10, the annual incremental cost of the immediate expansion scenario was lower than that of the slower expansion scenarios, although the analysis did not indicate cost savings within the first 10 years regardless of the pace of intervention (Figure 7.8).

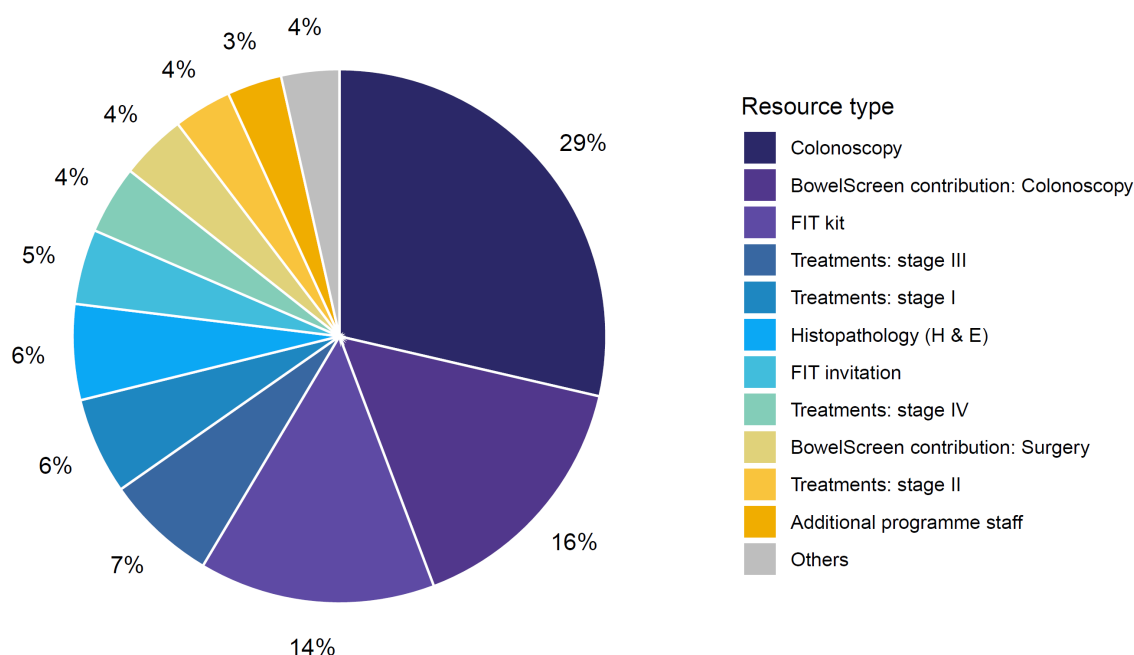
Figure 7.8 Time course of the total incremental cost of the three expansion pace scenarios



Note: The solid horizontal line at 0 indicates the comparator scenario. The solid vertical line indicates the start of the intervention year (2031).

The largest drivers of the overall incremental costs were related to colonoscopy, with the cost of colonoscopy and BowelScreen's monetary contribution for colonoscopy collectively accounting for approximately 45% of the total. Treatment-related costs were also major contributors, with stages I, II, III, and IV accounting for 6%, 4%, 7%, and 4%, respectively (Figure 7.9). BowelScreen's monetary contribution for surgery accounted for a further 4% of costs. Together, treatment-related costs accounted for 25% of the overall incremental costs. The costs associated with FIT invitations and kits (including posting, packaging and processing) were also large contributors, collectively accounting for 19% (Figure 7.9). Histopathology (H&E) and additional programme costs were the final key drivers, accounting for approximately 4% and 3%, respectively (Figure 7.9).

Figure 7.9 Relative contribution to the total incremental costs

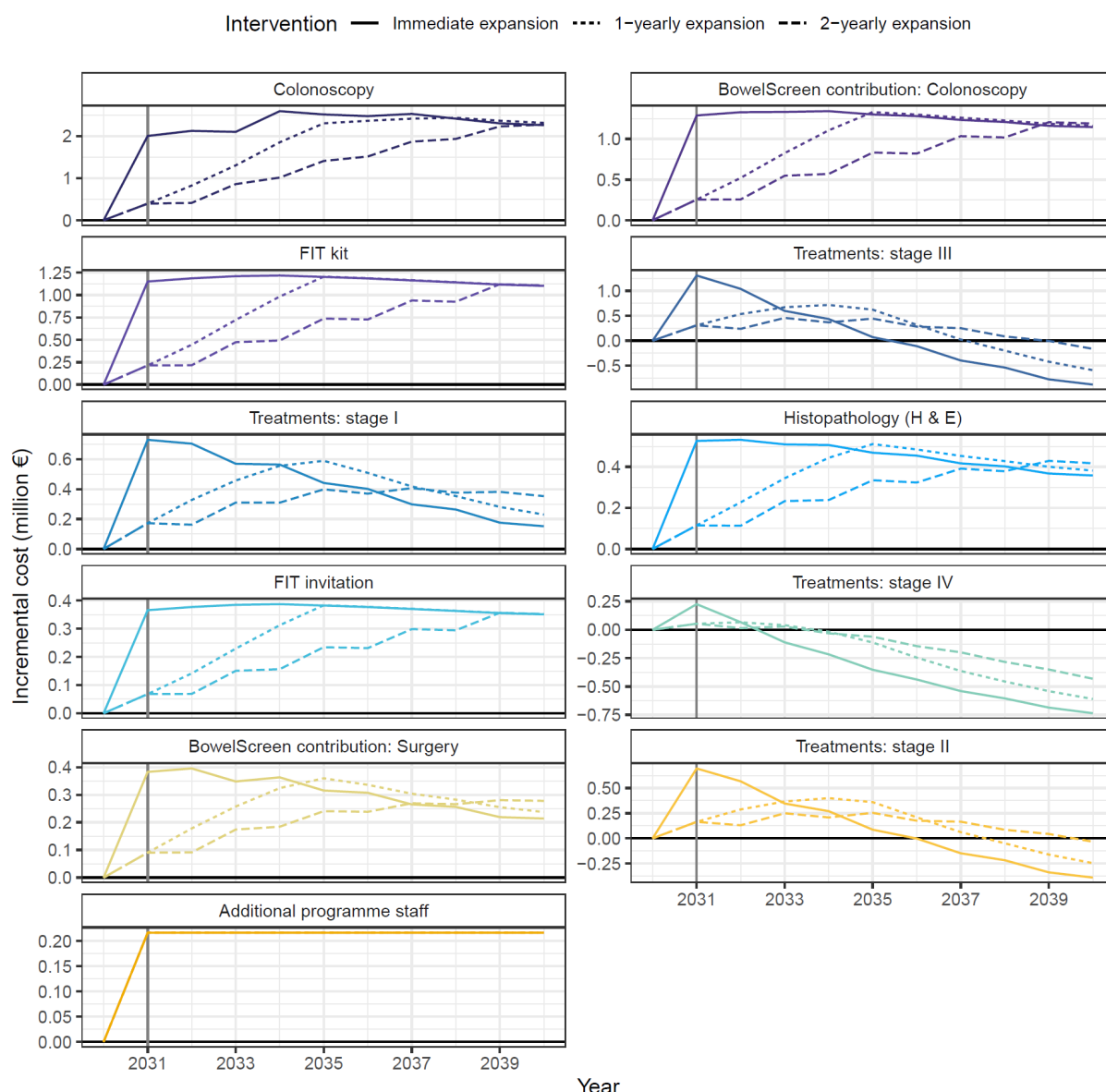


Note: The most influential resource items, which are shown in colour, collectively account for over 95% of the absolute cost differences from the comparator, totalled across three expansion pace scenarios. The items are ordered from the largest to smallest influence in a clockwise fashion. Others refer to other resource types that collectively account for less than 5% of the overall incremental costs.

Key: FIT – faecal immunochemical test; H&E – haematoxylin and eosin stain

Examining the time course of incremental costs for the most influential drivers revealed that the projected overall decline in costs post-implementation was largely driven by a reduction in treatment-related expenses (Figure 7.10). This is because the expanded screening programme is expected to lead to earlier cancer detection (Figure 7.3), which shifts the treatment landscape and reduces the need for costly interventions at advanced stages (Figure 7.3).

Figure 7.10 Time course of incremental costs of the most influential resource items



Key: FIT – faecal immunochemical test; H&E – haematoxylin and eosin stain

Note: The items listed here collectively account for over 95% of the total incremental costs.

7.5.5 Scenario analysis

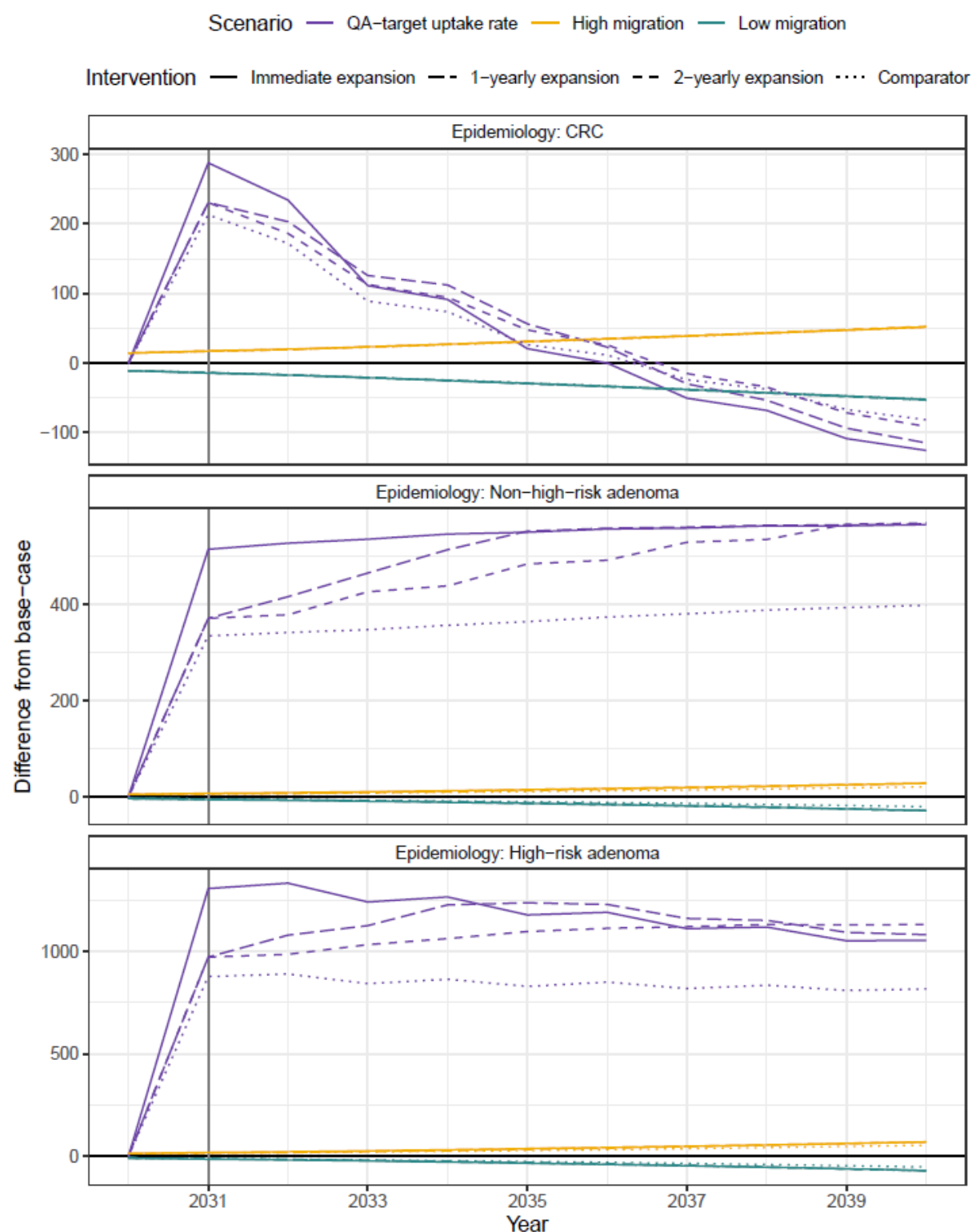
Scenario analyses were conducted to assess the influence of assumptions around the FIT uptake rate and migration projections on the estimated CRC epidemiology and resource requirements.

The base-case uptake rate was based on empirical data observed in Ireland and Canada (for age groups currently not screened in Ireland). Alternatively, assuming the 'achievable' BowelScreen quality assurance (QA) target uptake rate of 60% magnified the impact of screening, resulting in a higher initial increase in CRC cases

detected, a larger reduction in CRC cases over time, and greater resource requirements and costs (Figure 7.11 & Figure 7.12). Notably, the QA target scenario is expected to require up to approximately 170,000 additional FIT kits, 6,500 additional colonoscopies, and 2,100 additional people requiring histopathology (H&E) annually, compared to the empirically-estimated uptake rate (Figure 7.12). As a result, increasing the uptake rate to 60% would also entail greater costs, with the total cost estimated to be approximately €15 million to €25 million higher in the first year and €5 million to €10 million higher in 2040 (Figure 7.13) depending on the pace of expansion.

Migration scenarios were based on CSO projections, assuming low, moderate, and high inward migration to Ireland, with the moderate projection set as the base-case. High and low migration scenarios introduced uncertainty in model predictions around the base-case (moderate migration), due to variations in population size related to migration, which increase over time. By the end of the time horizon in 2040, annual variations were predicted to reach approximately plus or minus 50 CRC cases, 21,000 FIT invitations, and €3 million in total cost (Figure 7.11, Figure 7.12 & Figure 7.13). All expansion pace scenarios were similarly affected by changes in the migration assumption.

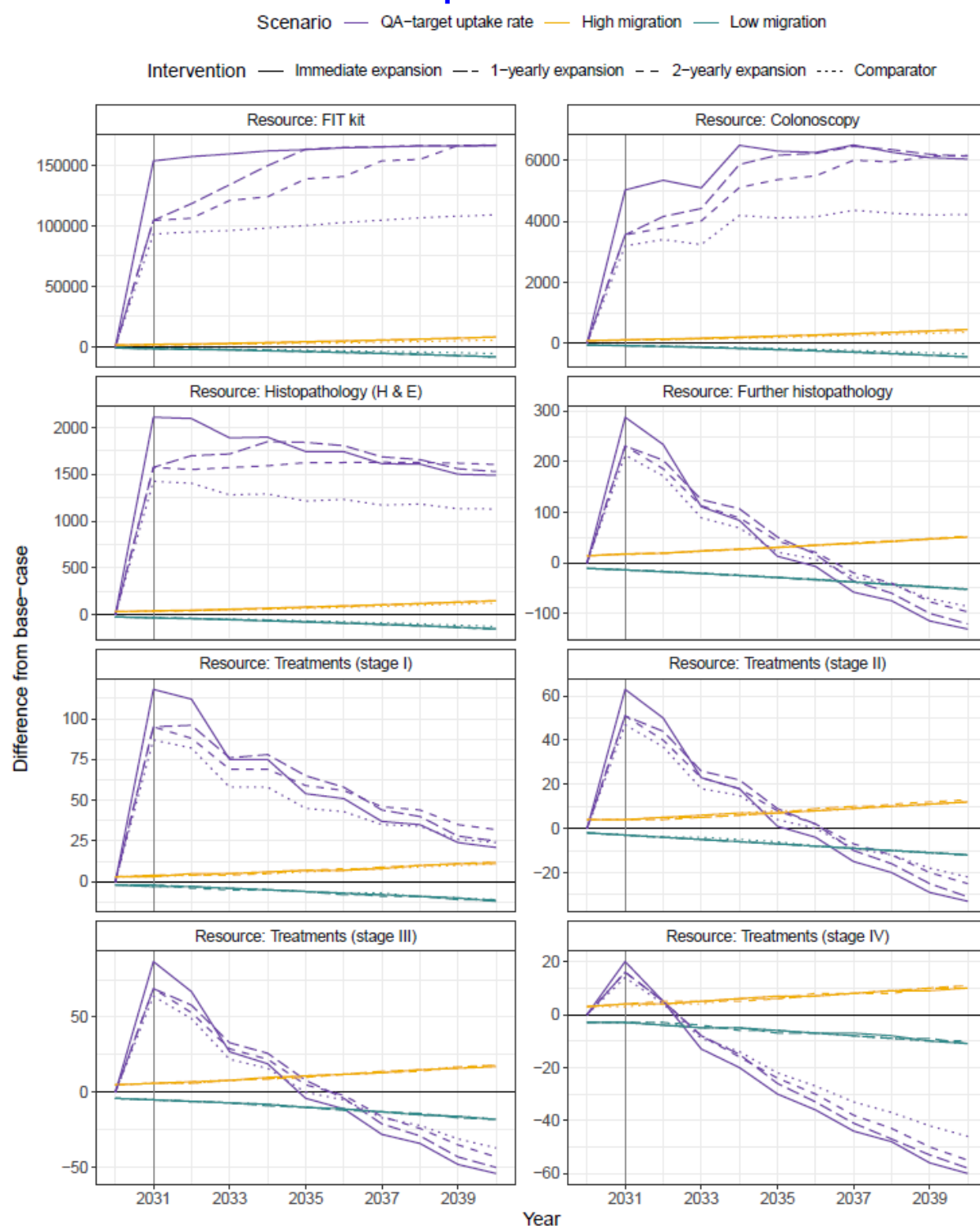
Figure 7.11 Scenario analysis. Difference from base-case scenario in estimated epidemiological outcomes



Note: Adenoma numbers are those detected from screening only as the model assumes no incidental or symptomatic adenoma detection. Y-axis reflects the number of people with each outcome.

Key: CRC – colorectal cancer

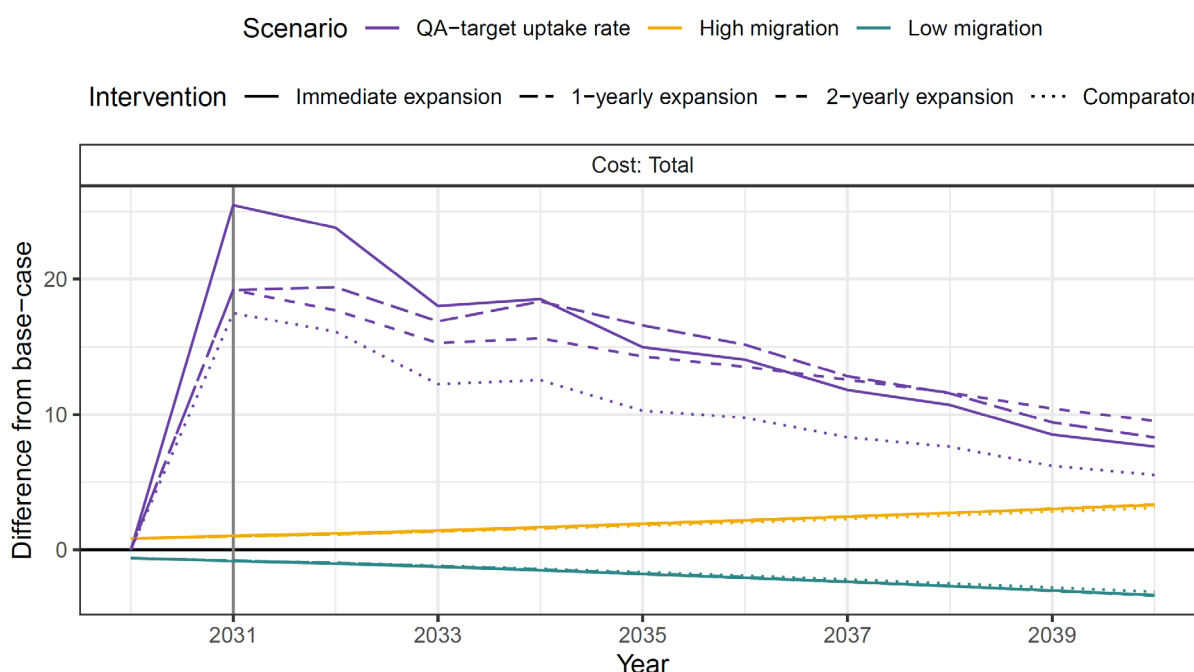
Figure 7.12 Scenario analysis. Difference from base-case scenario in estimated resource requirements



Note: Shown are the most influential items which collectively account for over 95% of the total absolute incremental costs. For FIT and colonoscopy, the y-axis reflects the number of units required for each resource, for example, the number of colonoscopies required. For histopathology and treatment, the y-axis represents the number of people requiring the procedure.

Key: CRC – colorectal cancer; FIT – faecal immunochemical test; H&E – haematoxylin and eosin stain.

Figure 7.13 Scenario analysis. Difference from base-case scenario in estimated total cost



Note: Costs (y-axis) are in millions of euros.

7.5.6 Sensitivity analysis

As described in Chapter 2, there have been significant developments in the pharmacological treatments available to patients with advanced CRC in recent years. To account for the resulting uncertainty in stage IV treatment costs, a sensitivity analysis was conducted assuming that stage IV treatment costs were double (that is, 100% higher than) the CPI-adjusted value of those calculated within the Tilson study.⁽³⁷⁵⁾ Under this assumption, the cumulative incremental costs over 10 years were estimated at €62 million, compared to €66 million under the base case. Higher stage IV treatment costs were associated with a reduction in the overall cost because the screening intervention would prevent more advanced cases, leading to a greater offset in treatment costs. Nonetheless, the intervention was not projected to be cost-saving within 10 years, as stage IV treatment accounted for a relatively small proportion of total costs (4% based on CPI-adjusted Tilson et al. estimates and 8% under the double-cost scenario).

Another potentially influential source of uncertainty is healthcare inflation which affects costs across all four cancer stages. The treatment costs reported by Tilson et al.⁽³⁷⁵⁾ (based on 2008 data) were adjusted to 2024 values using the Consumer Price Index (CPI) for health. While the CPI for health tracks the change in private healthcare costs, the costs incurred in the publically funded health system may not follow the same pattern.⁽³⁹³⁾ Therefore, a sensitivity analysis was conducted where treatment costs across all cancer stages (stage I to IV) were further inflated. This

analysis examined a scenario where the level of healthcare inflation between 2008 and 2024 was equivalent to the observed increase in the inpatient DRG costs used to capture colon and rectal resection costs (Inpatient DRG G01 and G02) during this period. Using this measure, inflation was estimated at 66.0% as opposed to the 18.8% observed in the CPI for health. Under this assumption, the cumulative incremental costs over 10 years were estimated at €67 million, representing a 1.5% increase over €66 million calculated in the base-case.

7.6 Discussion

7.6.1 Synthesis of key findings

To assess the expansion of the BowelScreen programme to include those aged 50–54, a model was developed to estimate the impact on population health gains, as well as resource and budgetary requirements. The analyses considered several intervention scenarios, differing in the pace of expansion and varying assumptions about programme uptake and migration projections. In all cases, the expansion was predicted to improve health outcomes, though the extent of health gains and resource and budgetary burdens varied depending on the assumed intervention pace, uptake rate, and migration scenarios.

Key drivers of the incremental cost following an expansion included costs related to colonoscopy, treatments, FIT tests (including invitation, FIT kits, and posting, packaging and processing), histopathology, BowelScreen contributions to support the development of related services, and additional programme staff. First, the expansion will involve inviting a larger number of people to FIT-based screening, albeit at relatively small unit costs of home screening. Second, demands for diagnostic resources such as colonoscopy and histopathology are expected to increase due to a larger number of returned FIT tests from the expansion. Third, treatment costs will initially rise due to the increased number of detected cases following the expansion. However, in the longer term, the expansion partially offsets the costs by detecting cancer at earlier, less advanced stages, where treatments are significantly less expensive. Finally, the cost of BowelScreen programme staff and contribution for services including those paid for cases involving colonoscopy, CTC, laboratory tests, and surgery, are all predicted to increase due to the expansion to those aged 50–54. It is worth noting, however, that some cancerous polyps can be safely resected as day case procedures due to advancements in endoscopic techniques such as endoscopic mucosal resection (EMR). The increasing adoption of these advanced techniques may significantly reduce the demand for inpatient admissions and operating theatre time for surgical resections in the future (see further discussion in Chapter 8).

The present analysis considered three intervention scenarios with different paces of expansion: immediate, 1-yearly, and 2-yearly expansions. While all three scenarios

were expected to produce similar outcomes, faster implementation was predicted to achieve an earlier reduction in CRC cases at the expense of higher initial resource and budgetary burdens; though the incremental (not absolute) resource requirements and costs were expected to decline over time. For instance, the total incremental cost in the first year was estimated at approximately 4.4 times higher in the immediate expansion compared to the gradual expansion scenarios. If the capacity to meet all CRC-related health service requirements is available at the time of intervention, the strategy that yields the greatest health gains would be preferred. However, if capacity building requires more time, slower implementation options may be necessary to manage initial resource requirements more effectively. Existing capacity constraints and resource requirements for an extension of the BowelScreen programme are discussed further in Chapter 8.

Screening uptake rates differ across countries. High uptake rates have been observed in the the UK (where uptake rates have ranged from 62% to 70%⁽⁹⁰⁻⁹²⁾), the Netherlands, (approximately 70%),⁽⁸⁸⁾ and Sweden (71%).⁽⁸⁹⁾ However, lower uptake rates have been reported in France (28.9%) and Spain (45.9%).^(93, 94) Compared with the international context, CRC screening uptake rates in Ireland have been relatively low, ranging from 38.1% among those aged 60 to 64 years to 49.9% among those aged 65 to 69 years. Thus, BowelScreen aims for higher participation, setting a quality assurance standard target of 60%.⁽³⁰⁵⁾ The present analysis predicted that achieving this target would result in a relative reduction in CRC cases compared to the base-case uptake scenario that assumed empirically observed rates in Ireland (and rates observed in Canada for those age groups not yet eligible for screening in Ireland). However, increasing the uptake rate to 60% would also entail greater resource and budgetary requirements, with the total cost estimated to be approximately €15 million to €25 million higher in the first year and €5 million to 10 million higher in 2040 depending on the pace of expansion. Similarly, the colonoscopy uptake rate following a positive FIT result is observed at approximately 80%, which falls slightly below the BowelScreen QA target (minimum standard $\geq 85\%$; achievable standard $>90\%$).⁽³⁰⁵⁾ If these QA performance thresholds were met, the number of colonoscopies required would increase further.

The present model incorporated net migration, aligning the overall population size with the CSO projected population size. A key source of uncertainty in population projections is the extent of inward migration. The CSO has published projections based on three migration scenarios: high, moderate, and low.⁽³⁸²⁾ While the present analysis adopts the moderate migration projection as the base-case, scenario analysis revealed that migration assumptions present a source of uncertainty. Higher migration scenarios predicted a larger projected population size, which in turn results in more CRC cases, increased resource needs, and higher budgetary requirements with the high and low migration scenarios estimated to cost up to plus or minus €3 million of the base-case scenario in 2040. Therefore, it is essential to

consider the findings of this chapter within the context of uncertainties in migration assumptions.

7.6.2 Comparisons with previous resource and budget analyses

Resource modelling was carried out as part of the 2009 HIQA HTA and related publications to inform the rollout of the BowelScreen programme in Ireland.^(12, 378) Both the present analysis and these previous assessments indicate that while FIT-based screening yields positive health outcomes, its heavy demands on endoscopy, pathology, diagnostic imaging, radiotherapy, and colorectal surgery need to be assessed in light of resource availability. The present analysis is also in agreement with these assessments that gradual implementation could alleviate the initial demand and may help ramp up resource capacity to meet programme needs.

The present analysis differs from the earlier Irish resource analyses in several ways. Firstly, there was no CRC screening programme in Ireland at that time, thus the comparator in those studies was no screening. In contrast, the present analysis compares the extension of an existing programme, the implementation history for which has been explicitly modelled. The existing programme also allowed this work to be closely parameterised with screening data from the Irish context. Notably, the uptake rates for FIT and colonoscopy were based on information provided by the BowelScreen programme. Additionally, the previous analyses were conducted from a screening programme perspective, considering costs from screening tests to colorectal resections. In contrast, the present analysis adopted the HSE perspective, taking into account the overall costs to the public healthcare system, including treatment and follow-up surveillance costs.

A separate budget impact analysis was published in 2008 by the National Cancer Screening Service (NCSS),⁽¹⁶²⁾ which envisaged a new CRC screening programme distinct from the existing symptomatic services, with significant capital investment to support the programme, including four new screening centres. An alternative budgetary model for CRC screening was proposed in 2010 by HIQA,⁽¹³⁾ which forecasted lower budgetary requirements by assuming that key resource capacities may be shared with symptomatic services, requiring minimal capital investment at the beginning of the programme.

In comparison to these pre-implementation budgetary studies, the present analysis reflects the current funding model of the BowelScreen programme, including the programme's contributions to procedures within the screening programme (including colonoscopy, CTC, histopathology, and surgery). The costs of initial investments, of updating infrastructure, and building costs were not considered in this assessment, as the scope of the present study was to assess the expansion to ages 50–54 and it was unclear in what context additional capital investment would be provided. In May 2025, a new endoscopy unit with two procedure rooms, six recovery bays, a

discharge lounge and a reception area opened in Bantry General Hospital. The cost of the project was reported to be in excess of €8 million.⁽³⁹⁴⁾ If capacity remains constrained at the time of implementation, one additional endoscopy procedure room may be sufficient to support the BowelScreen age extension (see Chapter 8). Methodologically, unlike the NCSS and previous HIQA reports,^(13, 162) the present analysis devised a dynamic cohort model to incorporate the history of screening, feedback between screening and cancer risks, and net migration.

Existing resource and budgetary impact analyses of FIT-based CRC screening cover various geographical contexts (for example, Spain,⁽³⁹⁵⁾ UK,⁽³⁹⁶⁾ US⁽³⁹⁷⁻³⁹⁹⁾), time horizons (one to 40 years), and model assumptions about treatment costs (that is initial year, lifetime or no treatment costs).⁽⁴⁰⁰⁾ Previous analyses focused on comparing a screening scenario to the status quo of no screening or modifications to an existing programme (for example, targeted screening⁽³⁹⁷⁾ and FIT outreach).⁽³⁹⁹⁾ However, there is a scarcity of published resource and budgetary impact analyses that examine the expansion of FIT-based screening to specific age groups, in spite of several cost-effectiveness studies that have addressed such expansions (see Chapter 6 for a review of cost-effectiveness). It is also worth noting that the resource and budget impact of CRC screening likely differs between countries due to variations in demography, cancer epidemiology, and financial landscape. With these caveats noted, these studies generally reported that increased screening coverage leads to a budget increase, though others reported cost savings within 10 years.⁽³⁹⁵⁾ Key cost drivers identified by these studies included FIT sensitivity, colonoscopy uptake rates, proportion of high-risk participants, frequency of screening and unit costs of colonoscopy and treatment.⁽³⁹⁶⁻³⁹⁸⁾

The results of the model presented in this chapter are not intended to be used to assess the clinical effectiveness or cost effectiveness of screening. Cost-effectiveness analysis rather than budget impact analysis is the appropriate method to compare the costs and benefits of an intervention in the longer term. The present model primarily serves to estimate the resource and budget impact from the point of view of estimating requirements over the first ten years. The systematic review presented in Chapter 6 found that expansion of the programme to those aged 50 to 54 is likely to be cost-effective, and the review presented in Chapter 5 indicated the likely clinical effectiveness of screening from the age of 50. In contrast, the analyses conducted with a 10-year time horizon presented here do not provide direct comparisons of the cases or costs. The analyses present the initial effects of screening in terms of early identification of CRC cases, but do not capture the long-term benefits. The observed CRC cases found earlier and the costs of treating these cases are captured in the age extension scenario. However, these cases will not be recorded in the comparator scenario unless they occur within the time horizon of the model (2031 to 2040 inclusive). For example, in the age extension scenario, a patient diagnosed in 2039, as a result of screening, with stage III CRC, is recorded.

In the comparator scenario, where the patient may have only been diagnosed at, for example, stage IV in 2041, they would not have been recorded within the model, as the case occurs beyond the time horizon of the model.

7.6.3 Limitations

The present analysis has several limitations that warrant careful interpretation of the findings. These limitations include the omission of cancer sites, cancer stages, sex differences, and the serrated pathway, as well as the exclusion of routine colonoscopies for non-CRC-related reasons.

Scenario analyses were conducted for key parameters in the model including expected future migration and programme uptake. However, one way sensitivity analysis was not conducted. This is an important limitation given the parameter uncertainty and the unclear transferability of the data used to inform many of the model inputs. However, in many cases, lack of data would mean that appropriate upper and lower bounds would not have been empirically informed, limiting the ability of one way sensitivity analysis to characterise uncertainty. Conducting sensitivity analyses would not be expected to change the conclusion that the budget impact figures and resource requirements characterised in this analysis are very uncertain. To maintain the relative simplicity of the model, a pragmatic approach was taken such that certain heterogeneities in the cancer biology were accounted for by linking relevant Irish data available from the NCRI. For instance, the model did not differentiate between cancer sites, such as the colon or rectum. Instead, where appropriate, the resource requirements were scaled based on the relative proportion of each cancer site, ensuring that the model reflects the distribution of colon and rectal cancers in the population. Similarly, the model accounted for cancer stages by linking the mode of detection (screening versus symptomatic) to Irish estimates of the expected number of cancers in each stage found through either screening or symptomatic presentation. Since these estimates were derived from a subset of the age range of interest (60–69 versus 50–74), there remains uncertainty about how well these estimates will apply to age groups that are not yet eligible for screening in Ireland.

The resource requirements for surveillance of CRC patients were based on those included in the 2009 HIQA HTA that preceded the introduction of BowelScreen.⁽¹²⁾ While there are no national guidelines for follow-up of CRC survivors in Ireland, a 2023 consensus statement on medical oncology surveillance of patients with gastrointestinal malignancies suggested that the National Comprehensive Cancer Network (NCCN) guidelines could be adopted for this purpose.^{(401, 402) (391)} The surveillance recommendations from the consensus group, which vary according to cancer stage and cancer site, are summarised in Table 8.9 in Chapter 8. As the model did not explicitly incorporate cancer sites or cancer stages, the surveillance

resource requirements included in the model may not capture the full complexity of CRC patient surveillance.

The model did not account for sex differences, which could lead to overlooking important disadvantages experienced by women in FIT-based screening. A 2023 review highlighted several sex-specific issues, including differences in FIT sensitivity, false positivity rates, cancer detection rates, and interval cancer rates.⁽²⁹⁷⁾ Although these sex differences are unlikely to significantly bias the overall population estimates for resource and budgetary requirements, ignoring these factors may lead to less precise estimates of CRC risk specific to each sex.

Like most economic models of CRC screening,⁽⁴⁰³⁾ the present analysis focused on the adenocarcinoma pathway of CRC development and did not explicitly consider the serrated pathway. Serrated polyps, which account for up to 15–40% of all CRCs, have distinct morphological and chemical characteristics.^(159, 160) For instance, recent studies have shown that FIT may be less sensitive in detecting serrated polyps.⁽²⁹⁴⁾ Additionally, colonoscopies are more likely to miss serrated lesions due to their flat or sessile shape and their tendency to be obscured by the surrounding epithelium and a mucus layer.^(159, 404) Failing to incorporate these distinct routes of carcinogenesis could lead to an overestimation of the effectiveness of CRC screening programmes in detecting CRC.⁽⁴⁰⁵⁾ In Ireland, 0.74% (2022–2023) of BowelScreen samples were found with sessile serrated lesions with dysplasia.⁽¹⁴⁹⁾

The present analysis does not account for routine and symptomatic colonoscopies performed for reasons unrelated to CRC, such as monitoring of inflammatory bowel disease (IBD) and other gastrointestinal conditions. In reality, colonoscopies performed for other reasons could be a source of incidental CRC detection, and ignoring these within the model could potentially lead to an overestimation of CRC risk by the present analysis.

Another factor not explicitly addressed in the present analysis is hereditary conditions such as Lynch syndrome and familial adenomatous polyposis. An Irish analysis of BowelScreen data found that 1.5% of CRC cases identified through screening would have warranted referral to genetic services.⁽⁶²⁾ Lowering the screening age may increase the likelihood that people with hereditary conditions (who are unaware they have the condition) are discovered through screening, which may increase the requirement for additional resources for genetic testing and counselling.

The cohort model was parameterised using recent Ireland-specific data where available. However, some parameters were based on international estimates due to the lack of specific information from the Irish context. Notably, estimates of adenoma and CRC prevalence (inclusive of undiagnosed cases) were derived from a 2021 English modelling study, which itself used German data for estimating

adenoma prevalence.^(366, 406) These quantities cannot be directly inferred from Irish registry data and Ireland-specific estimates would require a colonoscopy-based screening study, which does not currently exist in Ireland. While care was taken to select data from similar contexts (for example, from England) it is possible that differences exist that may impact the model's output.

CRC treatment costs were estimated using a costing study by Tilson et al.,⁽³⁷⁵⁾ which was based on 2008 data. For the purposes of the present analysis, these treatment costs were adjusted for inflation using the Consumer Price Index (CPI) for health. While the Tilson et al. study reflects treatment information from 2008, the CPI-adjusted figures from the study continue to be used in recent health economic evaluations published in 2024 and 2025.^(407, 408) However, the CRC treatment landscape has evolved considerably since this time.⁽⁴⁰⁹⁾ In Ireland, the most significant changes have occurred in the range of available chemotherapy regimens for treatment of stage IV CRC, while the use of chemotherapy and radiotherapy in stage II and III disease has also shifted to some extent. Health economic studies published since Tilson et al. were sought in an effort to identify more recent sources of cost data in the European setting. The most recent example identified was a 2024 cost-effectiveness study set in the Netherlands and based on 2018 cost data.⁽³⁶⁹⁾ Despite changes in the treatment regimens, CPI-adjusted costs from Tilson et al. broadly aligned with those used in the 2024 Netherlands study.⁽³⁶⁹⁾ By 2018, targeted therapies for stage IV CRC—such as bevacizumab and cetuximab—were already well established, and international guidelines for chemotherapy and radiotherapy had also been widely adopted. This concordance supports the continued relevance of the CPI-adjusted Tilson estimates,⁽³⁷⁵⁾ despite the evolution of treatment practices.

Producing a new, de novo estimate of treatment costs would be resource-intensive. Therefore, two sensitivity analyses were conducted to quantify the impact of the uncertainty in treatment costs. In the first analysis, all treatment costs were inflated from 2008 to 2024 based on the observed increase in the inpatient DRG costs for colon and rectal resection (Inpatient DRG G01 and G02) during this period: this is in contrast with the base-case where the costs were adjusted based on the CPI for health. The rationale for the alternative cost inflation approach is that the CPI for health does not explicitly account for and may not reflect the change in healthcare costs in the public healthcare setting. The DRG cost for colon and rectal resection reflects a large portion, but not all, of the treatment costs for early stages. Assuming this DRG-based cost inflation, the cumulative cost over 10 years was estimated to be 1.5% higher than the base-case where the treatment costs were inflated based on the CPI. This small impact of further inflating the treatment cost is consistent with the model finding that extending screening to those aged 50-54 would reduce the impact of treatments on the overall budget by decreasing the CRC cases requiring treatment.

The second sensitivity analysis focused on the uncertainty in the treatment costs of stage IV CRC. Estimating the full cost of stage IV chemotherapy in Ireland, without access to patient-level data on use of particular regimens and related expenditures, would be especially challenging. This sensitivity analysis, assuming a higher stage IV treatment cost (double the cost), estimated a 6% reduction in the overall incremental cost, as the screening intervention would prevent more advanced cases, leading to a greater offset in treatment costs. This sensitivity analysis suggests that even substantial uncertainty in stage IV costs would be unlikely to materially affect the key findings of the present analysis.

The present budget impact analysis covers the years 2031 to 2040. If trends in historical levels of inflation continue in the future, the budget impact will be higher. Some of the predicted increase is known. For example, public sector pay agreements are in place until June 2026, which include future salary increases,⁽⁴¹⁰⁾ and annual employer pay related social insurance (PRSI) increases are planned until 2028.⁽⁴¹¹⁾ However, as the costs of this analysis are presented in 2024/2025 euro, it would not be appropriate to incorporate future price increases into this analysis. If the results of this analysis are interpreted in future years, they should be adjusted for inflation.

The accuracy and long-term relevance of the findings of this chapter are additionally subject to uncertainties related to developments in diagnostic and treatment practices, which may result in substantial changes to future resource requirement. For example, an updated national clinical guideline published by the NCCP in December 2024 recommends the consideration of neoadjuvant therapy for all patients diagnosed with locally advanced operable rectal cancer, as there is strong clinical evidence for improved outcomes.⁽¹⁸⁰⁾ From a resource perspective, neoadjuvant therapy will be followed by pelvic MRI and colonoscopy to monitor response to treatment.⁽⁴¹²⁾ Therefore, the demand for radiology and endoscopy resources is anticipated to increase as a result of this recommendation. Furthermore, as advanced organ preservation approaches emerge in rectal cancer management (for example, transanal local excision), MRI will additionally be required for the identification of suitable patients and detection of cancer recurrence.⁽⁴¹³⁾ Therefore, it is likely that radiology estimates provided in the present analysis will be outdated and underestimated in the future.

Finally, the findings of the present work should also be considered in light of uncertainties surrounding the ongoing BowelScreen expansion to those aged 55–74, which was here assumed to be completed by 2030. Nonetheless, the ongoing expansion is subject to annual budgetary discretion and available capacity, and it is possible that the targeted expansion to those aged 50–54 could commence earlier or later than 2031 as modelled in this study. While a later starting year may result in a larger, older population and higher costs due to inflation, the interpretation of

findings from the present analysis is unlikely to be qualitatively affected by minor uncertainties in the starting year.

7.6.4 Conclusion

Expanding the BowelScreen programme to include those aged 50–54 is expected to yield population health benefits by reducing CRC cases and detecting cancers at earlier stages within the first 10 years of implementation. However, this expansion will inevitably place substantial demands on health service resources and budgets. Over the 10-year period, the model estimated the incremental budget impact associated with intermediate, 1-yearly and 2-yearly expansions as €66, €57, and €45 million respectively. However, given the limitations of the data used to inform the model, these estimates are inherently uncertain. The current analysis emphasises the critical need for preparedness in resource management at every level of the CRC health services pathway.

8 Organisational considerations

8.1 Key points

- This chapter considers the resource and organisational implications of extending BowelScreen to those aged 50–54 years. A successful colorectal cancer screening programme is contingent on timely access to high-quality endoscopy services for participants who receive a positive FIT result, histopathology to process samples taken during colonoscopy, and diagnostic radiology for suspected cancer cases. These services have experienced ongoing capacity challenges, including long waiting lists and deteriorating report turnaround times:
 - At the end of January 2025, over 27,000 patients (excluding children and screening participants) were waiting for gastrointestinal (GI) endoscopy appointments.
 - None of the laboratories in Ireland’s eight designated cancer centres met turnaround time targets for GI endoscopic biopsies or cancer resection cases in 2023 (the latest available data).
 - The recommended report turnaround time targets for MRI, CT, ultrasound and X-ray were not met by 22 of 41 radiology services in 2023.
- Lowering the starting age of BowelScreen from 55 to 50 would increase the eligible population by approximately 27%. Compared to offering screening to those aged 55 to 74 only, this age extension would require approximately 2,000, 2,400 and 2,300 additional colonoscopies (index, additional planned procedures and surveillance) as part of the BowelScreen programme in year one, year five and year ten, respectively, as well as increasing the demand on histopathology and diagnostic radiology services.
- BowelScreen operates within the general symptomatic services; colonoscopy and CT colonography procedures are performed in units that also provide services to symptomatic patients, while samples taken at colonoscopy are processed by laboratories that also process samples from symptomatic cases. As such, pressures on the general symptomatic services can impact the programme’s ability to deliver screening in line with its quality assurance standards and requirements.
 - Waiting times for BowelScreen colonoscopy and CT colonography appointments have to date not reached the minimum performance threshold specified in the programme quality assurance standards.

- Minimum experience levels and performance quality indicators for screening colonoscopies limit the number of endoscopists who meet the BowelScreen quality assurance criteria.
- Screening colonoscopies are generally performed by consultant gastroenterologists or general surgeons, while samples removed at colonoscopy are reported on by histopathologists. Workforce shortages have been highlighted across all three specialties.
 - The National Doctors Training and Planning unit estimated the number of consultants in gastroenterology and hepatology, general surgery and histopathology that will be required by 2038, outlining the required increase in the annual number of higher specialist training places to meet the projected demand.
 - Training for these roles typically spans a period of five to eight years, with constraints on a potential expansion of training programmes including the supply of trainees, sufficient training capacity, and availability of funding for training posts.
- The Programme for Government 2025 outlined a commitment to the building of four new elective treatment centres, which, once operational, could provide capacity for up to 128,100 additional endoscopy procedures annually. This additional endoscopy capacity could help meet existing unmet demand, the increased demand from future demographic changes, the planned BowelScreen expansion to those aged 55–74 years, and potentially support the extension to those aged 50–54 years.
 - According to Sláintecare 2025+, the two new elective treatment centres in Cork and Galway are expected to become operational in 2030. However, operational dates for the two new Dublin treatment centres have not been reported.
 - If endoscopy capacity were to remain constrained at the time of implementation of an age extension, one additional endoscopy room may be sufficient to support expansion of the programme to include those aged 50–54, assuming that up to 3,050 procedures may be conducted per room annually.
 - Delivering both the infrastructure and resourcing for the new facilities will be challenging. Given a finite number of endoscopists with the required level of experience and expertise to perform screening colonoscopies, as well as capacity constraints in histopathology and

radiology services, the potential additional capacity of the new elective treatment centres is unclear.

- Capacity may be impacted by a myriad of factors. Developments and advances in screening and diagnostic techniques and treatment, such as advanced endoscopic techniques, molecular testing and total neoadjuvant therapy, will continue to increase demands for endoscopy, histopathology and radiology resources. The estimates presented in this chapter are therefore likely to underestimate the future demand on these services that will result from an extension of CRC screening.
- The services required by BowelScreen are experiencing significant ongoing capacity challenges. Extending the programme without coordinated efforts to address the existing constraints is likely to negatively impact the ability of both BowelScreen and the symptomatic services to provide care in accordance with quality assurance standards and KPI targets; this could potentially lead to longer waiting lists and worsening turnaround times.

8.2 Introduction

In order for a screening programme to be effective, all parts of the screening pathway must be provided appropriately, from invitation of the target population to effective treatment for individuals diagnosed with the disease.^(3, 414) Population-based screening programmes require substantial investment in equipment, staff and infrastructure, which can strain a health system.⁽⁴¹⁴⁾ This may, in turn, negatively impact the delivery of other healthcare services and reduce the quality of care for people with symptomatic conditions.⁽⁴¹⁴⁾ Implementation of the proposed extension of Ireland's national colorectal cancer screening programme to include people aged 50 to 54 requires consideration of the core principles and elements of a screening programme,^(414, 415) including evidence that the complete screening programme can be implemented and presents an effective use of available resources.⁽³⁾

The aim of this chapter was to consider the resource and organisational implications of extending BowelScreen to those aged 50–54 years. The assessment of necessary organisational changes was carried out in accordance with guidance specified in the European Network for Health Technology Assessment (EUnetHTA) HTA Core Model®.⁽⁴¹⁶⁾ The analysis considered the impact of extending BowelScreen on human (that is, staff) and capital resources. The consequences that an age extension may have on the healthcare system as a whole were also considered.⁽⁴¹⁶⁾ As this HTA assessed the potential expansion of an existing programme, this chapter focuses on

the additional resources that would be required if BowelScreen were to be extended to include those aged 50–54. Based on the existing rate of expansion and consultation with the BowelScreen programme, it was assumed that the planned expansion to those aged 55–74 could be completed by 2030. Therefore, 2031 was chosen as the base year for extension to those aged 50–54, as outlined in Chapter 7.

The existing programme, and the proposed extension to include those aged 50–54, are outlined below (section 8.3). This is followed by a discussion of the capacity challenges experienced by endoscopy, histopathology and radiology services involved in the screening of BowelScreen participants, as well as services required for treatment of screen-detected cases (section 8.4). Potential challenges associated with meeting quality assurance and performance targets, in the context of existing capacity constraints within the healthcare system, are considered in section 8.5. Staffing and training requirements are discussed in section 8.6, with infrastructure and other resources considered in section 8.7. Potential implementation scenarios for an age extension are discussed in section 8.8.

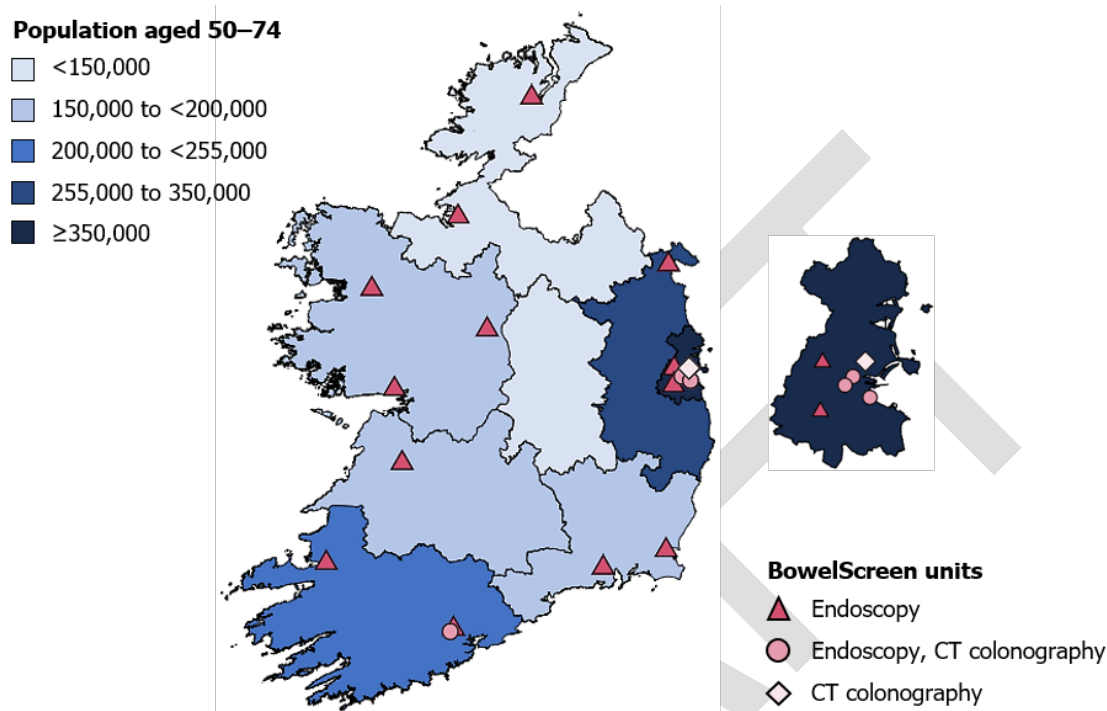
8.3 The BowelScreen programme

The BowelScreen programme commenced in Ireland in 2012, following the publication of two HIQA reports in 2009 and 2010 that examined colorectal cancer screening and resource use in cancer screening programmes.^(12, 13) BowelScreen is delivered operationally by the HSE National Screening Service (NSS). The programme uses a quantitative faecal immunochemical test (FIT) device ('OC-Sensor™') as its primary screening tool, with a decision threshold of 45µg of haemoglobin (Hb) per gram of faeces (45µg/g). Once an individual has agreed to participate, a test kit is sent to their home, which is then returned by post and sent to a contracted private laboratory for analysis. Results of the test are issued to both the individual and their general practitioner (GP). Participants with a faecal haemoglobin concentration of 45µg/g or higher are invited for a colonoscopy in one of 15 endoscopy units, as of January 2025.^(61, 62) Two additional endoscopy units, located in Cork University Hospital and Tallaght University Hospital, are expected to commence screening colonoscopies as part of BowelScreen in 2025 (Figure 8.1). Colonoscopy capacity is monitored by BowelScreen, and invitations to participate are issued with the aim of maximising the available capacity.⁽⁴¹⁷⁾ As such, screening participants may be required to attend an endoscopy unit that is further away in order to receive an appointment.

Computed tomography (CT) colonography may be conducted in the event of an incomplete colonoscopy, or if an individual refuses colonoscopy or is deemed unsuitable (for example, as a result of poor health or a higher risk of perforation). CT colonography is carried out in line with European Society of Gastrointestinal and

Abdominal Radiology practice guidelines in one of five CT colonography units (Figure 8.1).⁽⁶³⁾

Figure 8.1 Location of BowelScreen endoscopy and CT colonography units and projected population aged 50–74



Source: Central Statistics Office (CSO);⁽⁴¹⁸⁾ BowelScreen.
Population projections for the year 2031, based on the CSO 'moderate net migration' scenario.

All samples taken during colonoscopy are examined by BowelScreen histopathologists in one of eight designated adult cancer centre laboratories.⁽⁶¹⁾ One additional laboratory, located in Tallaght University Hospital, is expected to commence the processing of samples taken during colonoscopies performed in the hospital in 2025. Depending on colonoscopy findings, the individual is either returned to routine screening or is followed up in a surveillance programme (see Chapter 2, section 2.4.2), or, in cases where cancer is detected, referred for treatment (see Chapter 3, section 3.6). Figure 8.1 shows the location of endoscopy and CT colonography units that are expected to perform screening as part of BowelScreen in 2025. As the programme continues to expand, the participation of additional units will be required. Infrastructure and resource requirements are considered in more detail in section 8.7.

As of April 2025, BowelScreen invites adults aged 59–70 for screening every two years, with an expansion to those aged 55–74 committed to in the National Cancer Strategy 2017–2026 and 2020 Programme for Government.^(1, 2) The Programme for

Government 2025 again included a commitment to extend BowelScreen, although the target age range was not specified.⁽¹⁴⁾ The 2025 HSE National Service Plan outlined the expansion of the programme to include those aged 58–70 on an incremental basis by 2026 as a key area of focus,⁽¹⁵⁾ with €1.9 million announced as part of Budget 2025 to support this expansion.⁽⁴¹⁹⁾

Table 8.1 shows the number of invitations, satisfactory FITs, number of index and surveillance colonoscopies, and number of CT colonographies for each round of the programme. The number of BowelScreen index colonoscopies (that is, the initial colonoscopy following a positive FIT) per screening round has ranged from 3,727 in 2020–2021 to 7,333 in 2012–2015 (Table 8.1). In addition to index scopes, a number of additional planned procedures are performed, ranging from 742 in 2018–2019 to 915 in 2022–2023. Reasons for additional planned procedures include incomplete index colonoscopy due to poor bowel preparation, the participant's tolerance level for the first procedure, the requirement to have a second colonoscopy to check a site previously examined or resected, or a clinical decision to perform colonoscopy over two visits instead of surgery.⁽¹⁸⁾ Between 2012–2023, approximately 12,000 surveillance colonoscopies were performed as part of the BowelScreen surveillance pathway (described in Chapter 2, section 2.4.2). Adenoma detection rates have consistently exceeded 55%.

8.3.1 Proposed extension of the BowelScreen programme

With the planned expansion of BowelScreen to those aged 55–74 years, participating individuals will receive up to 10 rounds of screening. Under the additional proposed age extension, which would lower the starting age to 50, participating individuals would receive up to 13 rounds of screening if they were to participate in each screening round for which they are eligible (see Chapter 2, section 2.4.4). Lowering the starting age of BowelScreen from 55 to 50 would increase the eligible population by 27% by 2040 if fully implemented,⁽³⁸¹⁾ potentially more than doubling the size of the screening population compared to that eligible for screening in 2025.

Table 8.2 outlines the potential impact of extending the programme to those aged 50–54 in terms of the estimated annual number of BowelScreen index and surveillance colonoscopies and participants with screen-detected adenomas or cancers, based on the cohort model presented in Chapter 7 and an immediate implementation scenario. Table F.1 in Appendix F presents the corresponding estimates for a two-yearly implementation. The total number of cancers (screen-detected and symptomatic) and resources required for both screen-detected and symptomatic cancers is presented in Chapter 7.

It is important to note that while the model was parameterised using recent Ireland-specific data where available, estimates of adenoma prevalence (inclusive of undiagnosed cases) were derived from a 2021 English modelling study, which used

German data to estimate adenoma prevalence.^(366, 406) As adenoma detection rates vary substantially according to the experience and expertise of endoscopists (see section 8.5.2), estimates of adenoma prevalence are subject to a considerable degree of uncertainty. As such, the model estimates of the number of participants with adenomas detected, and the resultant adenoma detection rates, may be underestimated, and should be interpreted with caution.

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Table 8.1 Number of BowelScreen invitations, screening procedures and screening outcomes by programme round

	Programme round				
	2012–2015	2016–2017	2018–2019	2020–2021 ^{\$}	2022–2023
Age range	60–69	60–69	60–69	60–69	59–69
N eligible invited	450,452	544,149	533,118	290,750	606,275
N FIT satisfactory	182,741	225,359	223,636	135,383	278,711
N FIT positive	8,982	8,161	7,370	4,570	8,673
FIT positivity rate	4.9%	3.6%	3.3%	3.4%	3.1%
N index colonoscopy	7,333	6,385	5,771	3,727	6,683
% index colonoscopy within 30 days	63%	47%	69%	83%	75%
N additional planned procedures	NR	783	742	802	915
N surveillance colonoscopy	468	1,702	2,817	3,233	3,798
N CTC	265	204	163	72	173
% CTC within 30 days of referral*	80%	81%	77%	63%	64%
N participants with adenomas detected	4,052	3,585	3,183	2,159	4,069
N adenomas removed [‡]	18,293	13,794	5,365	6,403	12,661
Adenoma detection rate (on index colonoscopy)	55.2%	56.1%	55.2%	57.9%	58.6%
Number of cancers detected	474	389	303	199	433
Cancer detection rate (per 1,000 with satisfactory FIT)	2.59	1.73	1.35	1.47	1.55

Source: BowelScreen. Key: CTC – computed tomography colonography. FIT – faecal immunochemical test. N – number of. NR – not reported.

^{\$} The 2020–2021 programme round was significantly impacted by the COVID-19 pandemic, as both clinical and programme staff were redeployed and or working as part of the national response to the pandemic.

* This figure does not necessarily capture individuals offered appointments within the timeframe of 30 days but who deferred their appointment, for example due to travel distances or personal reasons.

[‡] Some participants have multiple adenomas.

Table 8.2 Estimated number of invitations and screening outcomes following BowelScreen extension: immediate expansion scenario

Parameter	Year 1 ^{\$}		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
Invitations distributed [¥] (N)	624,217	833,982	679,925	899,131	746,138	947,381
FIT kits distributed (N)	281,311	346,758	306,674	375,020	336,833	399,501
FIT uptake rate (%)	45.1%	41.6%	45.1%	41.7%	45.1%	42.2%
FIT positive (N)	10,453	12,616	11,483	13,665	12,697	14,619
FIT positivity rate (%)	3.7%	3.6%	3.7%	3.6%	3.8%	3.7%
Index colonoscopy (N)	8,249	9,955	9,061	10,783	10,019	11,536
CT colonography (N)	177	214	194	231	215	247
Participants with adenomas (total) (N)	3,630	4,292	4,039	4,688	4,508	5,053
Adenoma detection rate (%)	44.0%	43.1%	44.6%	43.5%	45.0%	43.8%
Participants with CRC (N)	707	788	786	852	879	925
Cancer detection rate per 1,000 screened	2.51	2.27	2.56	2.27	2.61	2.32

Key: CRC – colorectal cancer. CSO – Central Statistics Office. CT – computed tomography. FIT – faecal immunochemical test.

¥ Assuming 50% of the eligible population is invited each year in a biennial screening programme. Based on CSO population projections assuming moderate net migration.

\$ Base year: 2031.

Note: Adenoma detection rate excludes participants who also have CRC.

While the National Cancer Strategy 2017–2026 and the 2020 Programme for Government outlined a commitment to expand BowelScreen to those aged 55–74 as per the original aim of BowelScreen,^(1, 2) as of 2025, this has not been achieved. A successful colorectal cancer screening programme requires timely access to endoscopy, histopathology and radiology services, as well as access to treatment and surveillance for screen-detected cases. Lowering the colorectal cancer screening age will require significant healthcare resources, including financial resources, staffing, and endoscopy, histopathology and radiology services. As of 2025, the programme does not use dedicated, screening-only facilities, instead operating within the general symptomatic services. Colonoscopy and CT colonography procedures are performed in units that also provide services to symptomatic patients, while samples taken at colonoscopy are processed by laboratories that also process samples from symptomatic cases. As such, any expansion to the programme will be constrained by capacity challenges within the wider healthcare system. The next section outlines the ongoing capacity challenges experienced by these services in Ireland (section 8.4), followed by a discussion of quality assurance standards (section 8.5), staffing requirements (section 8.6), and infrastructure and resources (section 8.7). Potential implementation scenarios for an age extension are discussed in section 8.8, while section 8.9 outlines information resources and awareness campaigns that may require consideration if BowelScreen is extended to those aged 50–54.

8.4 Healthcare system context

8.4.1 Endoscopy capacity

Endoscopy capacity in Ireland is strained, with wait lists of over 18 months for some patients. The National Gastrointestinal Endoscopy Quality Improvement (NEQI) programme publishes annual reports on endoscopy data submitted by participating hospitals to support ongoing quality improvements. In 2023 (the year with the most recently reported data), 51 of 52 hospitals (all 36 public and voluntary hospitals and 15 private hospitals) submitted quality improvement data.⁽⁴²⁰⁾ In 2023, over 300,000 colonoscopies, flexible sigmoidoscopies (FSIGs) and oesophagogastroduodenoscopies (OGDs) were recorded by the NEQI programme as having taken place across the 51 participating hospitals in Ireland; these included a total of 145,978 colonoscopies.⁽⁴²⁰⁾ Four sites contributed data for the first time in 2023; when these were excluded, the number of colonoscopies had increased by 9.5% between 2022 and 2023, equivalent to an additional 11,594 procedures. The 2023 NEQI programme report further noted a consistent annual increase in the overall volume of procedures recorded by participating units between 2016 and 2023 (with the exception of 2020).⁽⁴²⁰⁾

At the end of January 2025, 27,679 adults (excluding screening participants) were waiting for a gastrointestinal (GI) endoscopy appointment, a fall from the 33,832 patients waiting in April 2021. While most were treated within the Sláintecare target

of 12 weeks, 12,283 patients (44%) were waiting longer, including 2,653 (9.6%) who were waiting between six and 12 months and 515 (1.9%) patients who were waiting over 12 months.⁽⁴²¹⁾ A further 9,214 patients had a scheduled appointment date but had not yet undergone the procedure.⁽⁴²¹⁾ These numbers do not include patients who are scheduled to receive care through the National Treatment Purchase Fund (NTPF) or through insourcing (that is, the provision of additional procedures performed by contracted endoscopists using the same facilities).⁽⁴²²⁾ While the NTPF does not specifically report on urgent endoscopies, HSE Performance Reports indicated that a cumulative total of 1,927 people (including children) were waiting over four weeks for an urgent colonoscopy appointment date between January and June 2024,^(417, 423) missing the HSE target that all patients should receive an appointment date within this time frame.

BowelScreen colonoscopies

The BowelScreen programme was introduced in 2012. At that time, BowelScreen commenced screening those aged 60–69 years on a phased basis, initially using a FIT threshold of 20µg/g. The resultant 8.6% positivity rate overwhelmed the existing colonoscopy capacity, and the threshold was subsequently increased to 45µg/g in 2014 to reduce the number of individuals being referred for colonoscopy.^(18, 37, 60)

BowelScreen colonoscopies are an important contributor to overall demand for endoscopy. In 2023, nearly 3,500 index colonoscopies were performed as part of the BowelScreen programme, with almost 2,000 surveillance colonoscopies and over 500 additional planned procedures. According to NEQI programme data, the 15 units that carried out colonoscopies on behalf of BowelScreen recorded a total of 45,721 colonoscopies in 2023, suggesting that BowelScreen procedures accounted for approximately 13% of the colonoscopy workload of participating endoscopy units, and represented around 4% of the total national colonoscopy workload (Table 8.3).

Table 8.3 Total number of colonoscopy procedures in 2023

	Number in 2023
BowelScreen index colonoscopies	3,499
BowelScreen surveillance colonoscopies	1,974
BowelScreen additional planned procedures	524
Total number of colonoscopies performed in BowelScreen endoscopy units (n=15)	45,721 ^{\$}
Total number of colonoscopies performed in all NEQI endoscopy units (n=51)	145,978 [¥]

Source: BowelScreen and National Gastrointestinal Endoscopy Quality Improvement Programme.

Key: NEQI – National Gastrointestinal Endoscopy Quality Improvement Programme.

¥ All colonoscopies performed in the 51 endoscopy units that contributed data to the NEQI programme, including BowelScreen procedures and colonoscopies performed for other reasons.

\$ All colonoscopies performed in the 15 endoscopy units that provide services to the BowelScreen programme, including BowelScreen procedures and colonoscopies performed for other reasons.

Surveillance colonoscopies comprise a large proportion of BowelScreen's endoscopy requirement, accounting for approximately one third of BowelScreen colonoscopies in 2022–2023. The number of surveillance procedures is expected to continue to increase as the programme continues to expand and mature.⁽¹⁸⁾ In December 2022, BowelScreen implemented the British Society of Gastroenterology, the Association of Coloproctology of Great Britain and Ireland and Public Health England (BSG/ACPGBI/PHE) guidelines for colorectal cancer surveillance (see Chapter 2, section 2.4.2).^(65, 66) A retrospective application of the BSG/ACPGBI/PHE guidelines in one BowelScreen centre suggested that up to 48% of patients who had been classified as intermediate or high risk could be de-escalated and potentially avoid colonoscopy surveillance according to the new guidelines, which could lead to a significant reduction in the requirement for surveillance procedures following the implementation of the guidelines.⁽⁴²⁴⁾ At the time of writing, the actual impact of the new guidelines on BowelScreen surveillance requirements was unknown, as several years of data are required in order to fully assess their effect.

As BowelScreen continues to expand, the colonoscopy capacity required by the programme will increase significantly. While those aged 50–54 may be less likely to require surveillance as a result of a lower incidence of high-risk findings, extending BowelScreen to this age group will result in an increase in the absolute number of people entering the surveillance pathway each year. Table 8.4 presents the estimated number of BowelScreen index and surveillance colonoscopies that would be required if the programme were to be extended. A full and immediate expansion of BowelScreen to those aged 50–74 would require approximately 10,000 index colonoscopies in year one, with a further approximately 1,400 additional planned procedures. These numbers increase in later years, with 10,800 index colonoscopies

required in year five and 11,500 needed in year 10 as well as similar increases in the number of additional planned procedures. The numbers of surveillance colonoscopies increase at a greater rate given surveillance requirements increase as a programme matures. Approximately 2,400, 3,900 and 4,700 surveillance colonoscopies are needed in year one, year five and year ten, respectively. Compared to offering screening to those aged 55 to 74 only, an age extension including those aged 50 to 54 requires approximately 2,000, 2,400 and 2,300 additional colonoscopies (index, additional planned procedures and surveillance) as part of the BowelScreen programme in year one, year five, and year ten, respectively. The estimated number of BowelScreen participants requiring colonoscopy based on a two-yearly expansion scenario, similar to the rate of rollout of the existing expansion, is presented in Table F.2 (Appendix F). The estimated total number of both screening and symptomatic colonoscopies for each expansion scenario is presented in Chapter 7 and Appendix E.

Table 8.4 Estimated BowelScreen colonoscopies required under expansion

Number of participants [‡]	Year 1		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
Index colonoscopy	8,249	9,955	9,061	10,783	10,019	11,536
Additional planned procedures	1,129	1,363	1,240	1,476	1,372	1,579
Surveillance colonoscopy	2,374	2,374	3,389	3,860	4,026	4,629

[‡] BIA estimates based on CSO population projections (moderate net migration scenario) and empirically-derived screening uptake rates. Base year: 2031.

Key: BIA – budget impact analysis. CSO – Central Statistics Office.

In order to maximise the available endoscopy capacity, a proportion of BowelScreen surveillance colonoscopies are delivered at weekends through insourcing funded by the programme. However, concerns have been raised over plans for initiatives to reduce waiting lists, such as endoscopists performing procedures at weekends, as these may not consider the downstream impact of the increased activity on histopathology services.⁽⁴²⁵⁾ Histopathology capacity is considered in more detail below. Endoscopy staffing and training are discussed in section 8.6.2.

8.4.2 Histopathology capacity

Pathology services play a key role in CRC screening, as the management of participants, including decisions related to the need for further resection and surveillance after screening, depends on the quality and accuracy of the diagnosis.⁽⁴²⁶⁾ Diagnostic histopathology involves a combination of scientific expertise along with histopathologic examination and interpretation by a medically qualified

consultant histopathologist.⁽⁴²⁷⁾ Laboratory capacity is impacted by many factors, including specimen volume and complexity, and staffing.⁽⁴²⁸⁾

Histopathology workloads have increased significantly in Ireland, as a result of an increasing prevalence of chronic diseases among an ageing population and improved screening programmes resulting in earlier detection.⁽⁴²⁵⁾ Increases in case volume and complexity have, in turn, led to deteriorating biopsy turnaround times.⁽⁴²⁸⁾ The 2023 National Histopathology Quality Improvement Programme (NHQI) data report indicated that the absolute number of cases processed between 2022 and 2023 increased by over 50,000.⁽⁴²⁸⁾ This represents an increase of almost 10%, substantially exceeding the anticipated 2.5% annual growth rate assumed in the 2023 *Medical Workforce Planning for the Specialties of Pathology*.^(425, 428)

Gastrointestinal (GI) endoscopic biopsy accounted for the second highest histology case numbers after 'non-biopsy other', with 183,919 cases in 2023. The NHQI data further indicated a 25.6% increase in IHC over the five-year period from 2019–2023.⁽⁴²⁸⁾ The eight cancer centres in particular have experienced significant ongoing histopathology capacity challenges, with an increase of 7.3% in case volume between 2022 and 2023.⁽⁴²⁸⁾ In 2023, none of the eight cancer centres achieved the NHQI turnaround time target of 80% of small biopsy cases completed in five days or less, nor the target of 80% of GI endoscopic biopsies completed in seven days or less.⁽⁴²⁸⁾

BowelScreen histopathology

Any expansion of the BowelScreen programme will increase demand for histopathology services, with significantly higher adenoma detection rates and high-risk findings from screening colonoscopies following a positive FIT result compared to symptomatic procedures.⁽⁴²⁹⁾ While the number of polyps and adenomas detected among those aged 50–54 is likely to be lower compared to older age groups, the absolute number of samples that will require processing as a result of an extension to the BowelScreen programme will increase with a larger screening-eligible population. Table 8.5 outlines the estimated annual number of BowelScreen participants that would require histopathology if the programme were to be extended to those aged 50–74, compared to the number of participants aged 55–74 (based on an immediate expansion scenario). The estimated number of participants requiring histopathology based on a two-yearly expansion scenario is presented in Table F.2 (Appendix F).

Table 8.5 Estimated number of BowelScreen participants requiring histopathology: immediate expansion scenario

Number [¥]	Year 1		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
N participants requiring histopathology ^{\$}	4,328	5,069	4,811	5,523	5,372	5,960

[¥] BIA estimates based on CSO population projections (moderate net migration scenario) and empirically-derived screening uptake rates. Base year: 2031.

^{\$} Participants may have multiple specimens requiring histopathology.

Key: BIA – budget impact analysis. CSO – Central Statistics Office.

It is important to note, however, that these estimates are based on participants with adenomas or CRC only, as non-adenomatous polyps and sessile serrated lesions were not included in the cohort model presented in Chapter 7. Therefore, the actual increase in demand on histopathology services is likely to be significantly higher. Further, many participants will have more than one specimen removed at colonoscopy. Data supplied by one of the participating laboratories indicated that 1,760 samples from 543 BowelScreen colonoscopy participants were processed by the laboratory in 2024, necessitating a total of 6,984 routine procedures (including haematoxylin and eosin [H&E] staining and IHC) (Table 8.6).

Table 8.6 BowelScreen histopathology workload for St. James’s Hospital in 2024

Parameter	Number
BowelScreen participants with samples taken at colonoscopy	543
Specimens	1,760
Blocks	2,119
Routine procedures (H&E, special histochemistry, IHC, FISH)	6,984

Source: Personal communication. Note: In 2024, people aged 59–69 were eligible to participate in BowelScreen.

Key: FISH – fluorescence in situ hybridisation. H&E – haematoxylin and eosin. IHC – immunohistochemistry. WTE – whole time equivalent.

8.4.3 Radiology capacity

Access to accurate, timely and high-quality diagnostic radiology services is critical for the diagnosis of patients suspected of having cancer, as well as the staging and evaluation of patients with documented disease.⁽¹⁾ Expansion of CRC screening will impact radiology services, both in terms of increased demand for CT colonography as part of the screening pathway, and diagnostic radiology for screen-detected cases.

The 2023 National Radiology Quality Improvement Programme (NRQI) data report highlighted the increasing demand for complex radiology imaging.⁽⁴³⁰⁾ The report noted a 5.5% increase in radiology cases across the 48 hospitals participating in the NRQI programme between 2022 and 2023, with an increase in CT, magnetic resonance imaging (MRI) and positron emission tomography (PET) cases of 9.7%, 13.6% and 6.6%, respectively.⁽⁴³⁰⁾ While a 13.4% increase in the number of cases available for reporting was recorded between 2019 and 2023, it was noted that this does not capture the true increase in radiology workloads resulting from the growing complexity of cases. Larger increases of 53% for MRI, 33% for CT and 20% for PET illustrate the increase in workload complexity, as these modalities include a higher number of more complex images that require a greater investment of time for reporting and review.⁽⁴³⁰⁾ The NRQI working group highlighted concerns regarding the challenging working environment faced by radiology departments, resulting from a 'capacity demand mismatch' due to growing and increasingly complex workloads coupled with inadequate resourcing, and raised concerns over the impact this may have on patient care.⁽⁴³⁰⁾ In 2023, less than half of the NRQI sites (19 of 41) met or exceeded the recommended target of 90% of cases reported within the specified turnaround times for MRI, CT, ultrasound and X-ray combined across four referral sources (emergency department, inpatient, outpatient and GP).⁽⁴³⁰⁾

In 2024, the National Treatment Purchase Fund formally launched the first National Radiology Diagnostic Waiting List Management Protocol, which was developed to support waiting list management in radiology diagnostic settings.⁽⁴³¹⁾ Preliminary data collected as part of a pilot project, which has not been fully validated and is subject to a number of simplifying assumptions,⁽⁴³²⁾ suggested that, nationally, approximately 290,000 patients were on waiting lists for CT, MRI, ultrasound or vascular ultrasound in the last three months of 2024 (excluding children awaiting treatment in Children's Health Ireland services), of whom approximately 44% were waiting for six months or longer.⁽⁴³³⁾ However, these figures included routine and planned or surveillance procedures, which are scheduled at regular intervals and may not have exceeded the planned procedure date. Collection, collation, validation and reporting of diagnostic radiology waiting lists will commence in early 2025, with identification and procurement of radiology diagnostic services expected to coincide with the first publication of the national radiology waiting list.⁽⁴³⁴⁾

BowelScreen CT colonography and diagnostic radiology

As noted above, extending BowelScreen to those aged 50–54 will impact radiology services in terms of increased demand for both screening CT colonography (CTC) and diagnostic radiology services for screen-detected cases. BowelScreen participants may be referred for CTC as part of the screening pathway in the event of an incomplete colonoscopy, if an individual refuses colonoscopy or is deemed unsuitable (for example, as a result of poor health or a higher risk of perforation).

Referral rates to CTC following a positive FIT result have ranged from 1.6% in 2020–2021 to 2.8% in 2012–2015, with a total of 877 CTCs performed between 2012 and 2023.^(18, 148, 149) Given that colonoscopy completion rates tend to be lower among older age groups,^(435–437) and that younger participants are at decreased risk of perforation, referral rates for CTC are likely to be lower in those aged 50–54. However, given the increase in the size of the population that would be eligible for screening if BowelScreen were to be extended to those aged 50–54, a small increase in the absolute number of CT colonographies may be expected.

Similarly, while CRC incidence rates are lower among younger age groups, lowering the screening age to 50 will increase the absolute number of cancers detected initially, which will in turn impact demand for diagnostic radiology services.

Toutlines the estimated number of BowelScreen participants who would require screening CTC, diagnostic CT, MRI or PET scans if the screening age were to be lowered to 50, based on an immediate implementation scenario. Table F.2 in Appendix F presents estimates for the two-yearly expansion scenario.

For diagnostic resources incurred following the confirmation of CRC, the cohort model presented in Chapter 7 suggested an offset from symptomatic services later in the time horizon following implementation of the age extension, as a result of the earlier detection of cases that would have presented symptomatically at a later stage. The offset was predicted to be comparable in magnitude to the increased demand generated by expanded screening. Thus, the overall demand on diagnostic radiology services from screen-detected and symptomatic CRC cases is not expected to increase significantly in the medium to longer term following implementation of a full expansion of screening to age 50–74. However, changes and developments in CRC treatment, such as the potential for non-operative management of locally advanced rectal cancer with total neoadjuvant therapy, are likely to increase the demand for rectal MRI as part of surveillance protocols.⁽¹⁸⁰⁾

Table 8.7 Estimated number of BowelScreen participants requiring CT colonography and diagnostic radiology: immediate expansion scenario

Modality		Year 1		Year 5		Year 10	
		55–74	50–74	55–74	50–74	55–74	50–74
		Number of participants ^y					
Screening	CT colonography	177	214	194	231	215	247
	CT scan	697	778	772	836	864	906
Diagnostic	MRI (pelvis)	233	261	259	280	289	304
	PET	105	117	116	125	130	136

[‡] BIA estimates based on CSO population projections (moderate net migration scenario) and empirically-derived screening uptake rates. Base year: 2031.

Key: BIA – budget impact analysis. CSO – Central Statistics Office.

8.4.4 Colorectal cancer treatment

Effective screening programmes encompass all aspects of the screening process, including treatment for individuals diagnosed with the disease.^(3, 414) The primary methods of CRC treatment are surgery, radiotherapy, and systemic anti-cancer therapy (SACT), which includes chemotherapy and immunotherapy (see Chapter 3, section 3.6).⁽¹⁵¹⁾ Colorectal surgery falls within the specialty of general surgery, which is the largest surgical specialty in Ireland and also includes upper GI, breast, endocrine, hepatobiliary and transplant surgery.⁽⁴³⁸⁾

Waiting lists are a key driver of demand for general surgery.⁽⁴³⁸⁾ Between 2017 and 2019, approximately 30% of surgeries within the general surgery specialty were emergency procedures, leading to cancellations of elective procedures as emergency care is prioritised.⁽⁴³⁸⁾ While the 2017 *Oireachtas Committee on the Future of Healthcare Sláintecare Report* recommended that no one should wait more than 12 weeks for an inpatient procedure,⁽⁴³⁹⁾ these targets are not consistently met. In January 2025, a total of 15,372 adult patients were on waiting lists to be scheduled for general or GI surgery nationally as an inpatient or day case.⁽⁴²²⁾ Of these, 34% were waiting longer than six months and 9% were waiting longer than 18 months (data for the 12-week target is not published for this outcome). Waiting times are also significant for outpatient general surgery and GI surgical appointments. In January 2025, a total of 31,144 patients were waiting for their first appointment, with 18.5% of patients waiting longer than six months and 2.3% waiting longer than 12 months.⁽⁴²²⁾ While service reconfiguration involving a networked system of acute surgical care and elective-only hospitals is expected to increase access to general surgery and help reduce waiting lists, it is unclear how the reconfiguration of acute and elective services will evolve.⁽⁴³⁸⁾ Infrastructure and resources, including plans for

new elective treatment centres and surgical hubs, will be considered in more detail in section 8.7.

Improved cancer survival rates have increased the demand for systemic anti-cancer therapy, with greater numbers of patients receiving long-term treatment. Increased demand for SACT has, in turn, resulted in significant capacity pressures on day wards,⁽⁴⁴⁰⁾ with 561 people waiting for outpatient oncology appointments at the end of January 2025.⁽⁴²²⁾ Capacity challenges have also been experienced by radiation oncology services. While performance targets state that 90% of patients (excluding palliative care) should commence radiotherapy within 15 working days of being deemed ready to treat, between January and March 2024, 63.8% of patients received radiotherapy treatment within this time frame.⁽⁴¹⁷⁾

Screen-detected cancers

Expansion of the BowelScreen programme will result in an initial increased demand for surgery, chemotherapy and radiotherapy as a result of an increase in the number of screen-detected CRC cases. As outlined in Chapter 7, the incremental number and rate of cases in those aged 50–54 are predicted to peak within a 10-year time horizon in both the immediate and one-yearly expansion scenarios, stabilising at around 40 to 60 incremental cases (10 to 15 cases per 100,000) per year by 2041. Table 8.8 outlines the estimated number of screen-detected cancer cases that would require surgery, chemotherapy and radiation therapy, as well as the estimated numbers requiring treatment for each cancer stage, following a full expansion of BowelScreen to those aged 50–74, compared to the number of participants aged 55–74, based on an immediate expansion scenario. An estimated 78 additional people would require surgery in year 1 of the full expansion, with 36 and 11 requiring chemotherapy and radiation therapy, respectively, compared to screening those aged 55–74.

Lowering the starting age to 50, however, is likely to reduce the overall cancer burden in the population over time, with a decline in CRC cases in those aged 55–59 and 60–64 expected as the newly-screened cohort matures (see Chapter 7). Additionally, as screening facilitates earlier cancer detection, lowering the starting age to 50 would shift the cancer stage distribution at detection to less advanced stages. As the detection of cancer at earlier stages reduces the need for more costly advanced-stage treatments, a decline in the overall incremental cost of the age extension would be expected over time (see Chapter 7). The estimated number of participants requiring each treatment based on a two-yearly expansion scenario is presented in Table F.2 (Appendix F).

Table 8.8 Estimated number of BowelScreen participants with screen-detected CRC requiring treatment: immediate expansion scenario

Number of participants requiring treatment [‡]	Year 1		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
Surgery	677	755	753	816	842	886
Chemotherapy	315	351	350	380	392	412
Radiotherapy	98	109	109	118	122	128
Stage I treatment	290	323	322	349	361	379
Stage II treatment	156	173	173	187	193	203
Stage III treatment	212	236	236	256	264	277
Stage IV treatment	49	55	55	60	62	65

[‡] BIA estimates based on CSO population projections (moderate net migration scenario) and empirically-derived screening uptake rates. Base year: 2031.

Key: BIA – budget impact analysis. CRC – colorectal cancer. CSO – Central Statistics Office.

8.4.5 Post-CRC survivorship and surveillance

Cancer survivorship is recognised as a distinct phase in the continuum of cancer care, requiring follow-up and surveillance.^(1, 185) Earlier detection of cancer through screening and improved diagnostics and cancer treatments have led to significant increases in the number of cancer survivors who require standardised, scheduled follow-up care and surveillance following the completion of acute treatment.⁽⁴⁴¹⁾ A 2019 report *Living With and Beyond Cancer in Ireland* highlighted the need for improved integration between primary care, community and acute hospital sectors in order to better meet the needs of cancer survivors.⁽⁴⁴¹⁾

The National Cancer Strategy 2017–2026 outlined several components of survivorship care, including prevention and detection of new cancers and surveillance for recurrent cancers; monitoring and interventions for long-term and late effects of cancer, cancer therapies, and psychological and social effects; as well as coordination between specialist and primary care services to ensure the needs of survivors are met.⁽¹⁾ However, there are no national guidelines for follow-up of CRC survivors in Ireland, with heterogeneous surveillance practices representing an unmet need.^(390, 391) A 2023 consensus statement on medical oncology surveillance of patients with gastrointestinal malignancies in Ireland suggested that the National Comprehensive Cancer Network (NCCN) guidelines^(401, 402) could be adopted for this purpose.⁽³⁹¹⁾ The consensus group noted, however, that the guidelines could be considered quite intensive, suggesting that they should be individualised to meet the

needs of patients.⁽³⁹¹⁾ Table 8.9 summarises the consensus group recommendations for CRC surveillance.

Table 8.9 Consensus group recommendations for CRC surveillance

Cancer	Surveillance recommendations
Colon cancer (stage I)	Colonoscopy: at 1 year. If AA, repeat in 1 year. If no AA, repeat in 3 years, then 5 years
Colon cancer (stage II or III)	History/physical and CEA Every 3–6 months for the first two years, then every 6 months for a total of 5 years. Colonoscopy: at 1 year, then at 4 years, then every 5 years. CT TAP: Every 6–12 months for 5 years. If high risk, every 3–6 months for 2 years, then every 6–12 months for a total of 5 years.
Rectal cancer (transanal local excision only)	Proctoscopy (with EUS or MRI with contrast) every 3–6 months for the first 2 years, then every 6 months for a total of 5 years.
Rectal cancer (stage I with full surgical staging)	Colonoscopy: at 1 year. If advanced adenoma, repeat in 1 year. If no advanced adenoma, repeat in 3 years, then every 5 years. History/physical and CEA: every 3–6 months for the first two years, then every 6 months for a total of 5 years.
Rectal cancer (stage II to IV)	Colonoscopy: at 1 year, except if no pre-op colonoscopy due to obstructing lesion, colonoscopy in 3–6 months. If AA, repeat in 1 year. If no AA, repeat in 3 years, then every 5 years. CT TAP: Stage II, III: every 6–12 months for a total of 5 years. Stage IV: every 3–6 months for 2 years, then every 6–12 months for a total of 5 years.

Source: Keane et al. 2023.⁽³⁹¹⁾ Key: AA – advanced adenoma; CEA – carcinoembryonic antigen; CRC – colorectal cancer; CT TAP – computed tomography of thorax, abdomen, pelvis; EUS – endoscopic ultrasound; MRI –magnetic resonance imaging.

While extending BowelScreen to those aged 50–54 will result in an initial increase in the number of CRC and high-risk adenoma cases detected, a decline in CRC cases in older cohorts is expected as the newly screened cohort matures. Table 8.2 outlines the estimated number of people with high-risk adenomas or CRC detected in the first, fifth and tenth year of an immediate expansion to those aged 50–74, compared to screening those aged 55–74. As outlined in Chapter 7, an immediate expansion is projected to result in an overall reduction in the absolute number of cases compared to screening those aged 55–74 by the seventh year of the expansion. While the two-yearly expansion scenario did not show a reduction in cases within the 10-year time frame (see Table F.1, Appendix F), a longer-term decrease is anticipated based on the declining incremental case numbers observed in the latter half of the period.

However, as highlighted above, lowering the screening age to 50 will increase the demand for screening resources, specifically colonoscopy, CTC, and histopathology. The increased demand is expected to outweigh any offset from reduced symptomatic cases, as the majority of participants in a population-based screening programme will not have CRC or high-risk lesions. Outpatient visits are similarly predicted to

increase, due to an increase in follow-up appointments for CRC patients detected through expanded screening.

An expansion of the age range for screening would bring more people into the health system than would otherwise present symptomatically in this age group (see Chapter 7). The following section examines the potential impact of existing capacity constraints on performance targets and quality assurance requirements and standards.

8.5 Quality assurance

Quality assurance (QA) is a key component of population-based screening programmes, as the quality and outcomes of screening depend on performance at each step of the screening process. Screening is performed on predominantly healthy people and has the potential to cause serious harms, including unnecessary anxiety for participants and exposure to the risk of invasive procedures for the detection and removal of lesions.⁽¹³³⁾ Assuring the quality of services is essential to achieving the intended benefits of screening, while minimising potential harms to those taking part. Quality standards, quality requirements and Key Performance Indicators (KPIs) for the BowelScreen programme are set by the BowelScreen Clinical Advisory Group, and are outlined in the *BowelScreen Standards for Quality Assurance in Colorectal Screening*.⁽³⁰⁵⁾ The programme's performance is monitored against the standards by a quality assurance committee. The standards are kept under review and revised as necessary, as further evidence or data become available.⁽³⁰⁵⁾

Pressures on symptomatic services can impact the programme's ability to deliver a screening service in line with its quality assurance requirements. This section considers the BowelScreen QA standards according to different elements of the screening pathway and in the context of the ongoing capacity challenges highlighted in section 8.4, with a focus on how these relate to the potential expansion of the programme.

8.5.1 FIT testing

BowelScreen uses a quantitative FIT device (OC-Sensor™) as its primary screening tool, with a decision threshold of 45µg Hb/g faeces (45µg/g). The processing of BowelScreen FIT samples is outsourced to a private laboratory under tender. The BowelScreen QA standards outline the quality assurance requirements and standards that must be met by the service provider. The medical laboratory that processes FIT samples must be accredited by the Irish National Accreditation Board (INAB) to the ISO15189 standard for requirements for quality and competence for medical laboratories.^(305, 442) The BowelScreen QA standards specify that the service must be led by a medically qualified consultant chemical pathologist and overseen by a designated registered senior medical scientist on a day-to-day basis. All medical

laboratory staff must receive relevant training in the processing of FIT kit samples.⁽³⁰⁵⁾ Equipment must be validated and test methods verified and accredited in accordance with ISO requirements. While the analysis of FIT samples is automated, a sufficient throughput is required to process the requisite number of BowelScreen samples within the agreed turnaround time. The laboratory must have a contingency plan in place at all times to ensure the turnaround time is met if an analytical machine is not available.⁽³⁰⁵⁾

Laboratory turnaround times

The BowelScreen QA standards require that a minimum of $\geq 95\%$ of FIT kits should be dispatched by the service provider within three working days when requested by participants, while all FIT results should be received by NSS within three working days of receipt of the sample in the laboratory.⁽³⁰⁵⁾ Extending BowelScreen to those aged 50–54 will increase the number of FIT kits to be dispatched and processed by approximately 30% compared to screening those aged 55–74. The increase in the number of samples to be processed will increase the laboratory's workload, and should be accounted for as part of future procurement processes.

FIT uptake rates

The BowelScreen QA standards define a minimum FIT uptake rate of 50%, with an achievable target of 60%.⁽³⁰⁵⁾ To date, this has not been achieved, with uptake rates ranging from 40.6% in 2012–2015 to 46.6% in 2020–2021. Preliminary data indicated that uptake for the third quarter of 2024 remained below the minimum standard at 41.1%.⁽⁴⁴³⁾ As uptake rates tend to be lower among younger age groups,^(135, 435, 444) additional efforts to increase uptake among those aged 50–54 may be required if BowelScreen is extended to this age group (see section 8.9).

8.5.2 Colonoscopy

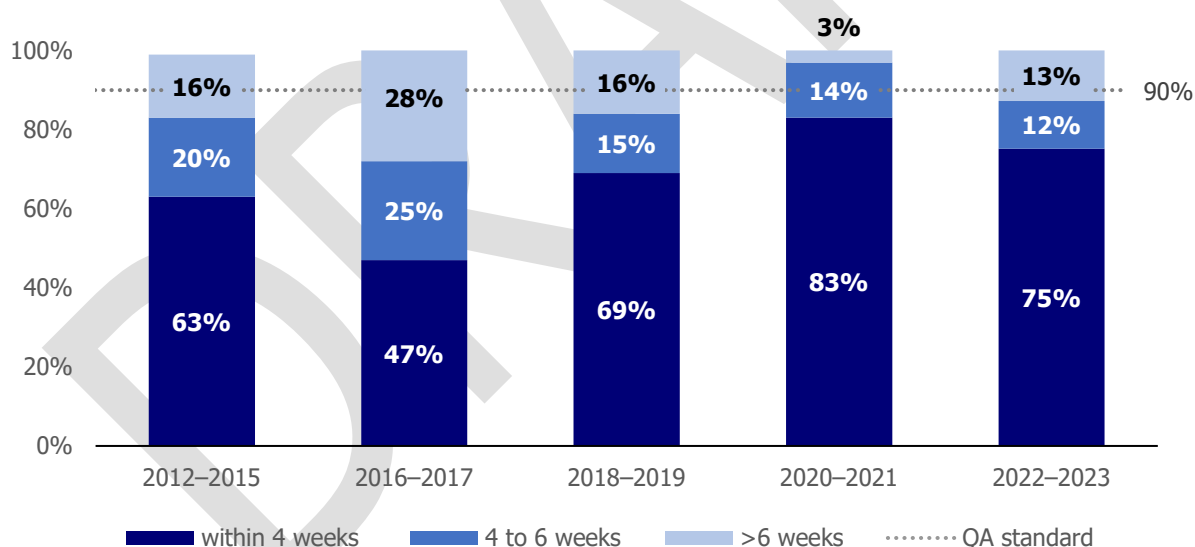
BowelScreen participants with a positive FIT result are invited for colonoscopy in one of 15 colonoscopy screening units, with two additional endoscopy units expected to commence BowelScreen colonoscopies in 2025 (Figure 8.1). The BowelScreen quality assurance standards require that all BowelScreen endoscopy units are accredited, or have plans to achieve accreditation, by the Joint Advisory Group on GI Endoscopy (JAG). The JAG programme, which is an initiative of the Royal College of Physicians, assesses endoscopy services in the UK and Ireland that are registered with JAG.^(305, 445) JAG standards cover all aspects of a high-quality clinical service and are organised into four domains, comprising clinical quality, patient experience, workforce, and training. In April 2025, four BowelScreen endoscopy units were fully JAG accredited, with a 'deferred' status for a further four units (that is, the service is close to being accredited and has some actions it must take to meet the standards).⁽⁴⁴⁶⁾ Given the ongoing capacity constraints experienced by endoscopy

services and the increased demand that will result from an extension to the BowelScreen programme (see section 8.4.1), the requirement for all screening units to maintain JAG accreditation may not be feasible.

Colonoscopy waiting times

The BowelScreen QA standards require that an index colonoscopy should be offered within four weeks (≤ 20 working days) from when a participant is deemed clinically suitable following pre-assessment in over 90% of cases.⁽³⁰⁵⁾ Pressures on symptomatic services can impact BowelScreen waiting times;⁽¹⁸⁾ the percentage of BowelScreen participants who were offered a colonoscopy appointment within four weeks ranged from 47% in 2016–2017 to 83% in 2021–2022 (Figure 8.2). In March 2024, just under 90% of appointments were scheduled within the target time of 20 working days, with 11 of the 15 BowelScreen colonoscopy centres meeting the expected target of 90% within 20 days.⁽⁴¹⁷⁾ With further expansion of the BowelScreen programme, it may become increasingly challenging for BowelScreen colonoscopy units to meet this QA standard.

Figure 8.2 BowelScreen colonoscopy waiting times by programme round



Colonoscopy performance indicators and quality assurance standards

Complete and thorough examination of the colon at index colonoscopy is vital to identify CRC and precursor lesions, while polypectomy (that is, the removal of polyps) and complete excision of detected lesions is essential to prevent early recurrence and interval CRC.⁽⁴⁴⁷⁾ A significant proportion of interval cancers are

estimated to result from inadequate excision or missed lesions at the time of index colonoscopy.⁽⁴⁴⁸⁻⁴⁵⁰⁾ As endoscopy is an operator-dependent test, key performance indicators (KPIs) and quality assurance standards aim to maximise safety and effectiveness, reduce practice variation, and improve patient experience.⁽⁴⁵¹⁾

Colonoscopy performance can be assessed using objective measures, including caecal intubation rate (CIR) and polyp or adenoma detection rate (PDR or ADR). CIR refers to the proportion of colonoscopies where the caecum – that is, the anatomical endpoint of the colon – is reached, with lower CIRs increasing the risk of interval cancer.⁽⁴⁵²⁾ ADR indicates the proportion of procedures during which at least one histologically-confirmed adenoma was detected, with higher ADRs associated with a reduced risk of post-colonoscopy CRC.^(449, 451, 453, 454) As endoscopy reporting systems do not generally incorporate histological assessments, PDR, which reflects the proportion of procedures during which polyps are detected, has been adopted as a surrogate marker for ADR.⁽⁴⁵⁵⁾ An analysis based on NEQI data of all colonoscopies recorded between 2016–2022 found that endoscopists with annual procedural volumes of 100 or more colonoscopies demonstrated significantly higher CIRs (93% versus 90.4%, $p<0.001$) and PDRs (32% versus 28.9%, $p<0.001$), with endoscopists completing ≥ 300 colonoscopies per year achieving the highest caecal intubation (94.5%) and polyp detection rates (34.2%).⁽⁴⁵⁶⁾

In order to perform screening colonoscopies as part of BowelScreen, endoscopists are required to have completed a minimum of 500 colonoscopies throughout their career, with at least 150 procedures in the last 12 months and a demonstrated PDR of $>20\%$. The BowelScreen QA standards further require a minimum CIR and ADR of $\geq 90\%$ and $\geq 45\%$, respectively, for BowelScreen index colonoscopies.⁽³⁰⁵⁾ The programme has previously highlighted that colonoscopy capacity in Ireland is constrained by a short supply of endoscopists with an appropriate skill level.⁽¹⁸⁾ Endoscopy staffing and training will be discussed in more detail in section 8.6.

While ADR varies according to endoscopist experience and expertise, adenoma prevalence decreases with age. Lowering the screening age to 50 may therefore impact the overall adenoma detection rate of the programme. Internationally, reported adenoma detection rates in those aged 50–54 have varied. A study of screening colonoscopies in the US reported an ADR of 31.1% (95% CI, 30.7%, 31.4%) in those aged 50–54, and an ADR of 35.6% (95% CI, 35.4%, 35.8%) in participants aged 50–75.⁽⁴⁵⁷⁾ However, as ADR depends on the endoscopist and indication for colonoscopy, as well as on the demographic characteristics of participants, it is difficult to directly compare ADRs across studies and settings. A 2022 analysis of colonoscopies performed following a positive FIT result in the French CRC screening programme, which screens people aged 50–74 using the OC-Sensor™ FIT device with a threshold of 30µg/g, reported an overall ADR of 57.6%.⁽⁴⁵⁸⁾ The analysis excluded colonoscopies where CRC was detected, as well as

those performed by endoscopists with <30 colonoscopies during the study period. ADRs increased significantly with age in multivariate analyses, although the ADRs for each age group were not reported. An analysis of colonoscopies performed as part of the Slovenian CRC screening programme, which commences screening at age 50, reported adenoma detection rates of between 51.3% and 52.1%.⁽⁴⁵⁹⁾ ADRs increased significantly with age, although age-stratified ADRs were not reported.

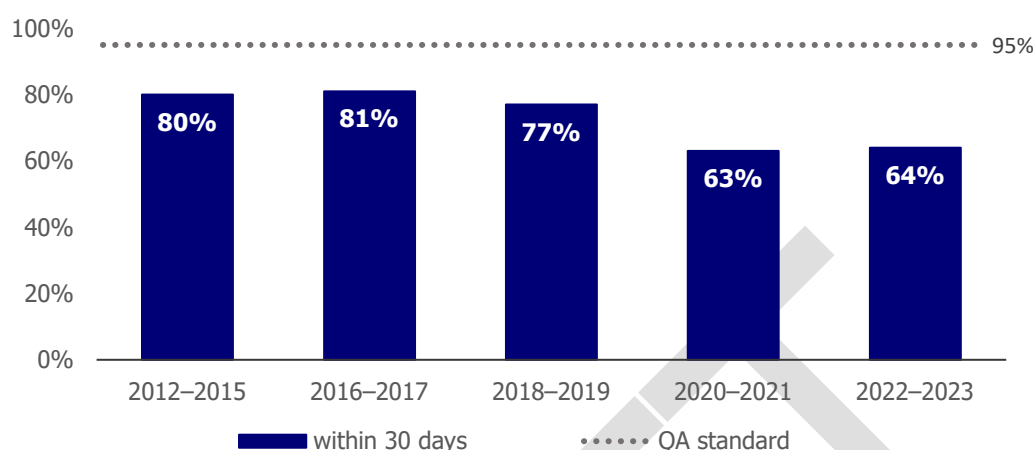
As outlined in Table 8.2, estimates from the cohort model presented in Chapter 7 suggested an ADR of approximately 43–44% if screening were expanded to include those aged 50–74, which would fall short of the minimum BowelScreen QA standard of $\geq 45\%$. However, it is important to note that estimates of adenoma prevalence were derived from a 2021 English modelling study.^(366, 406) As adenoma detection rates vary significantly depending on the experience and expertise of endoscopists, estimates of adenoma prevalence are subject to a considerable degree of uncertainty. As such, model estimates of the number of participants with adenomas detected, and the resultant adenoma detection rates, should be interpreted with caution. While ADRs are likely to be lower in those aged 50–54, the extent to which lowering the screening age to 50 may impact the overall BowelScreen adenoma detection rate is unclear.

8.5.3 CT colonography

CT colonography waiting times

The BowelScreen quality assurance standards state that 95% of participants should be offered a CT colonography appointment within 30 working days of the referral date, with a minimum of 90% of CTC reports signed off within 10 working days of completion of the examination.⁽³⁰⁵⁾ The percentage of participants who have been offered an appointment within this timeframe has ranged from 63% in 2020–2021 to 81% in 2016–2017 (Figure 8.3). While the number of participants who require CTC each year is small (Table 8.1) and may be expected to be lower in the younger age group, given the increase in the size of the population who would be eligible if screening were extended to those aged 50–54, the absolute number of individuals who might require CTC could increase by approximately 27 procedures per year (Table 8.2).

Figure 8.3 CT colonography appointment waiting time*



Source: BowelScreen. Key: CT – computed tomography. QA – quality assurance.

* This figure does not necessarily capture individuals offered appointments within the timeframe of 30 days but who deferred their appointment, for example due to travel distances or personal reasons.

8.5.4 Histopathology

All samples taken during BowelScreen colonoscopies are processed in one of eight designated cancer centres, with a ninth laboratory expected to come on stream in 2025. The BowelScreen QA standards require that histopathology laboratories must achieve and maintain INAB accreditation.⁽³⁰⁵⁾ Named BowelScreen histopathologists are required to report on lesions removed at endoscopy, with double reporting of all polyp cancers (stage pT1) to minimise overdiagnosis of adenocarcinoma and to ensure the accuracy of reporting of early-stage cancer.⁽³⁰⁵⁾

Histopathology turnaround times

Turnaround time (TAT) refers to the time interval between when a case⁴ is first received by a laboratory and approval of the final report by a consultant histopathologist.⁽⁴²⁸⁾ It represents a key measure of the overall function of a laboratory service and is considered an important key quality indicator due to its impact on the clinical management of patient cases.^(428, 460) In 2021, the NHQI TAT target for GI endoscopic biopsy was increased from 80% of cases completed by day five to 80% of cases completed by day seven.⁽⁴⁶⁰⁾ In 2023, none of the eight cancer centres achieved the NHQI target of 80% of small biopsy cases completed in five days or less, nor the target of 80% of GI endoscopic biopsies completed in seven

⁴ A case refers to a patient's pathological material, which may comprise a single sample or multiple samples (specimens) from a single procedure.

days or less.⁽⁴²⁸⁾ Similarly, none of the cancer centres met the target of 80% of cancer resection cases completed by day seven or less, reflecting a 'mismatch between demand and capacity'.⁽⁴²⁸⁾

While turnaround times for BowelScreen samples had not been reported at the time of writing, the QA standards require a turnaround time of ≤ 5 working days for a minimum of $\geq 90\%$ of samples.⁽³⁰⁵⁾ Given the existing pressures on laboratory services, this may not be achievable. A survey conducted as part of the 2024 *Review to Inform the Strategic Direction of Laboratory Medicine* indicated that 61% of laboratories reported an inability to meet local and or national turnaround times.⁽⁴²⁷⁾ The most pressing challenges reported by laboratories were inappropriate IT and automation (90%), staffing (87%) and space (43%).⁽⁴²⁷⁾ The report highlighted a 'critical and chronic shortage' of suitable candidates to fill medical scientist posts, underlining the need for training, education and professional development of laboratory staff to ensure the effective development of laboratory medicine services.⁽⁴²⁷⁾ The 2023 NHQI data report similarly stressed the urgent need for investment in laboratory medicine, including staffing and infrastructure, to meet the yearly increases in demand and maintain service quality.⁽⁴²⁸⁾ The following sections will consider staffing and training requirements (section 8.6) and infrastructure and resources (section 8.7) in more detail.

8.6 Staffing requirements

Screening programmes are resource-intensive. The NSAC *Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme* highlight that 'adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme'.⁽³⁾ This section will consider the potential implications of extending BowelScreen to those aged 50–54 on staffing and training requirements, in the context of the capacity challenges outlined in section 8.4 and existing workforce shortages. As the cohort model presented in Chapter 7 predicted a partial offset from symptomatic services for diagnostic and treatment resources required after the confirmation of CRC, including fewer resources required to treat advanced stage cancers, this section focuses on the services that would be expected to experience a sustained increase in workload as a result of an expansion of the screening age range.

8.6.1 Programme staff

As of April 2025, dedicated BowelScreen staff comprised a programme manager, deputy programme manager, programme coordinator, quality assurance coordinator, two clinical coordinators, two administrators and four assistant staff officers (Table

8.10). Approximately two BowelScreen nurses are funded per participating endoscopy unit to manage the pre-assessment process. Three additional nurses will support the expansion of the programme to new endoscopy units in 2025 and beyond. To support the planned expansion of the programme to those aged 55–74, BowelScreen anticipates that a head of service and additional programme staff will be required, including a second deputy programme manager and quality assurance coordinator, an additional administrator and two assistant staff officers (BowelScreen, personal communication). According to the programme, the implementation of a further age extension to include those aged 50–54 is expected to necessitate a third clinical coordinator and two additional assistant staff officers (Table 8.10). From an operational perspective, it is expected that the majority of the additional administrative workload associated with extending BowelScreen to those aged 50–54 could be absorbed by existing programme structures, assuming the programme will be resourced appropriately to manage the planned expansion to 55–74.

Table 8.10 BowelScreen programme staff requirements

Parameter	HSE staff grade	2025 WTE	Est. additional WTE for 55-74	Est. additional WTE for 50-54
Head of service			1.0	
Programme manager	General manager	1.0		
Deputy programme manager	Grade VIII (Clerical)	1.0	1.0	
Quality assurance coordinator	Grade VII (Clerical)	1.0	1.0	
Clinical coordinator	Grade VII (Clerical)	2.0		1.0
Programme Coordinator	Grade VII (Clerical)	1.0		
Administrators	Grade VI (Clerical)	2.0	1.0	
Assistant staff officer	Grade V or IV (Clerical)	4.0	2.0	2.0
Clinical lead		0.2		
BowelScreen nurses	Clinical nurse specialist		2.0 per endoscopy unit	
Other				
ICT developer (maintenance phase)	Assume staff costs covered by aggregate database cost.			
Software management company	Not quantifiable prior to tender. IT support may be outsourced.			

Source: BowelScreen.

Key: Est. – estimated. HSE – Health Service Executive. ICT – information and communication technology. WTE – whole time equivalent.

8.6.2 FIT sample processing

The analysis of FIT samples is automated. As of April 2025, the processing of BowelScreen FIT samples is outsourced to a private laboratory under tender. The BowelScreen quality assurance standards require that the medical laboratory service processing BowelScreen FIT samples must be led by a medically qualified consultant chemical pathologist and overseen by a designated senior medical scientist, who authorises the release of BowelScreen FIT results.⁽³⁰⁵⁾ Table 8.11 outlines the estimated minimum staffing requirements for a laboratory processing BowelScreen FIT samples.

Table 8.11 Estimated minimum staff required for a laboratory processing BowelScreen FIT samples

Grade	WTE
Consultant chemical pathologist	0.3
Senior medical scientist	2.0
Medical laboratory assistant	2.0

Source: Personal communication.

Key: FIT – faecal immunochemical test. WTE – whole time equivalent.

Acute hospital laboratory services are provided by medical scientists, clinical biochemists, clinical scientists, medically qualified pathologists, medical laboratory aides (MLAs) and clerical staff.⁽⁴²⁷⁾ A 2023 report on *Medical Workforce Planning for the Specialties of Pathology* highlighted consultant pathologist shortages, resulting in onerous on-call rotas, sub-optimal consultant cover in some sites, and long outpatient waiting lists in some specialties.⁽⁴²⁵⁾ In 2022, there were an estimated 11.5 whole time equivalent (WTE) consultant chemical pathologists working in the public sector in Ireland, with some consultants covering more than one site.⁽⁴²⁵⁾ The HSE National Doctors Training and Planning unit (NDTP) estimated that an additional 6.8 WTE consultant chemical pathologists were required to meet the unmet demand in 2023, with the gap between supply and demand projected to increase to 15.2 WTEs by 2035.⁽⁴²⁵⁾ A critical and chronic shortage of suitable medical scientist candidates to fill posts has also been reported.⁽⁴²⁷⁾

In the future, it is possible that the processing and analysis of BowelScreen FIT samples may be insourced as part of the reform of laboratory services.⁽⁴⁶¹⁾ The BowelScreen quality assurance standards require that all medical laboratory staff receive relevant training in the processing of FIT kit samples.⁽³⁰⁵⁾ However, current Higher Specialist Training in chemical pathology includes minimal training in FIT testing, as samples are currently processed in private facilities, limiting the exposure of trainees to FIT. To ensure the sustainability of the programme, it may be

necessary to consider the provision of training in FIT as part of chemical pathology training.

8.6.3 Endoscopy

Endoscopies are primarily performed or overseen by consultant gastroenterologists or general surgeons, depending on the site and type of endoscopy.⁽⁴⁶²⁾ In 2023, a total of 834 endoscopists performed colonoscopies across the 51 sites participating in the NEQI programme.⁽⁴²⁰⁾ Of these, 84% met the NEQI target PDR of >20%, while 75% achieved the minimum target CIR of $\geq 90\%$ and 40% reached the achievable target of $\geq 95\%$ of colonoscopies with the caecum intubated.⁽⁴²⁰⁾ Of the 834 endoscopists, 330 (40%) completed at least 150 colonoscopies,⁽⁴²⁰⁾ the minimum number of procedures per annum required for BowelScreen endoscopists. As BowelScreen participants are referred for colonoscopy following a positive FIT result, adenoma detection rates are significantly higher in BowelScreen colonoscopies compared to symptomatic procedures.⁽⁴²⁹⁾ As a result, screening colonoscopies are more complex and require a greater level of experience and expertise, with the programme highlighting that colonoscopy capacity in Ireland is constrained by a short supply of endoscopists with an appropriate skill level.⁽¹⁸⁾

Between 2016 and 2022, 66% of the national colonoscopy volume was completed by 36% of endoscopists.⁽⁴⁵⁶⁾ An expansion of the eligible age range for screening could therefore substantially impact the workload of consultant gastroenterologists and general surgeons performing BowelScreen colonoscopies.⁽⁴⁶²⁾ Strategies to redistribute endoscopy activity would require a significant overhaul of current practice, as the lower polyp detection rates among lower activity endoscopists would require intervention if their activity were to be expanded.⁽⁴⁵⁶⁾ Further, not all endoscopists will be interested in performing screening colonoscopies. According to a 2022 UK study, approximately one third of consultants who were not performing screening procedures reported that they would consider upskilling to perform colonoscopies as part of the UK CRC screening programme.⁽⁴⁶³⁾ A more recent UK study, published in 2025, reported that 7.5% of the consultant workforce expressed an intention to train in bowel cancer screening colonoscopies.⁽⁴⁶⁴⁾ The most frequently-cited activities that endoscopists would relinquish to support increased screening in both studies were outpatient clinics, acute general internal medicine or surgical on call and general internal medicine ward cover,^(463, 464) highlighting the potential opportunity cost associated with increasing the screening colonoscopy workload of existing BowelScreen endoscopists.

It is important to note that colonoscopies represent only one aspect of the workload of general surgery and gastroenterology specialties. General surgery is the largest surgical specialty in Ireland, comprising colorectal surgery, upper GI surgery, breast and endocrine surgery, and hepatobiliary and transplant surgery.⁽⁴³⁸⁾ Due to their

broad range of competence, general surgeons are essential for emergency departments, particularly in remote or rural settings.⁽⁴³⁸⁾ The NDTP noted that demand for general surgery staff was mainly a result of the acute undifferentiated work and large number of emergency rosters, suggesting that efforts should be made to decouple emergency and elective care.⁽⁴³⁸⁾ Consultant gastroenterologists provide expertise in the diagnosis, treatment and prevention of all forms of gastrointestinal diseases, and are almost exclusively dual-trained in General Internal Medicine (GIM).⁽⁴⁶²⁾ As a result, dual-trained gastroenterology consultants also staff acute medical units.⁽⁴⁶²⁾ In December 2023, there were an estimated 179 WTE consultants in general surgery working in the public and private sectors,⁽⁴³⁸⁾ with an estimated 130 WTE consultants in gastroenterology and hepatology.⁽⁴⁶²⁾ Projections by the NDTP indicated that an estimated 285 WTE consultants in general surgery and 237 WTE consultants in gastroenterology and hepatology will be required by 2038.^(438, 462) The NDTP further highlighted the importance of regular reviews of workforce requirements in light of ongoing service developments, including the new surgical hubs and planned elective treatment centres.⁽⁴³⁸⁾

Gastroenterology training

Consultants in gastroenterology and hepatology are almost exclusively dual-trained in GIM.⁽⁴⁶²⁾ Following internship, trainees progress to Basic Specialist Training (BST), a two-year hospital-based programme completed in senior house officer (SHO) posts.⁽⁴⁶²⁾ This is followed by Higher Specialist Training (HST), with supervised hospital-based training as well as attendance of courses and study days to acquire the non-clinical skills and general medical professional knowledge necessary.⁽⁴⁶²⁾ Following satisfactory completion of training, a Certificate of Satisfactory Completion of Specialist Training (CSCST) is awarded. While this confers eligibility to enter the Specialist Division of the Medical Council register and apply for a consultant post, many doctors will complete post-CSCST fellowship training before taking up consultant positions. As such, the HST training period typically spans five to eight years. In addition to the recognised training programmes, candidates can apply for entry into the Specialist Division of the Medical Council register based on their experience, which is assessed against the specialty curriculum.⁽⁴⁶²⁾ To meet the projected growth in demand, the NDTP estimated that the annual HST intake for gastroenterology and hepatology would need to increase from 11 trainees in 2023 to 18 by 2030.⁽⁴⁶²⁾

General surgery training

The National Surgical Training Programme (NSTP) provides training for medical graduates who intend to pursue a surgical career. Following internship, training consists of two years of Core Specialist Training (CST), followed by six years of Specialist Surgical Training. Whilst trainees are engaged in specialist training, they

are typically employed at specialist registrar (SpR) level.⁽⁴³⁸⁾ An alternative pathway for doctors at non-training grades is in development; subject to criteria and an assessment process, which will likely be introduced in July 2026.⁽⁴³⁸⁾ To meet the projected demand for general surgery, the NDTP suggested that the annual HST training intake would need to increase from 15 in 2023 to between 20 and 30 trainees between 2024 and 2030.⁽⁴³⁸⁾ However, the NDTP further highlighted that it would be 'very challenging' to recruit more than 20 HSTs for general surgery between now and 2030, and that the current cohort of trainees exiting general surgery training would not be sufficient to meet workforce demands in the short-term.⁽⁴³⁸⁾ The importance of regular reviews of workforce requirements in light of ongoing service developments, including the new surgical hubs and planned elective centres, was also noted.⁽⁴³⁸⁾

Endoscopy training

Training to perform and achieve competency in endoscopy is a key component of specialist training in both gastroenterology and general surgery.⁽⁴⁶⁵⁾ In 2021, the HSE Endoscopy Programme published a *Competency model for skills training in GI endoscopy in Ireland*, which outlines a common outcomes-based approach to endoscopy skills acquisition for adoption by both gastroenterology and surgical specialty training programmes in Ireland.⁽⁴⁶⁵⁾ The model proposes an initial training period during which trainees receive direct supervision in the relevant procedures by a competent endoscopist. A minimum of 200 procedures in upper and or lower gastrointestinal endoscopy with satisfactory KPIs is suggested prior to trainees receiving 'provisional approval'. Trainees then enter a second stage of training, during which support is received from a consultant trainer, with hands-on skills training focused on therapeutic endoscopy and more challenging or difficult procedures. A minimum of 100 additional procedures with satisfactory KPIs are suggested at this stage to demonstrate competency and to be eligible for final certification.⁽⁴⁶⁵⁾

While earlier endoscopy sub-specialisation during training may facilitate earlier skills acquisition and produce a larger cohort of highly skilled endoscopists,⁽⁴⁶³⁾ several constraints on a potential expansion of HST programmes have been highlighted. These include the supply of BST trainees, sufficient training capacity, and availability of funding for HST training posts.⁽⁴⁶²⁾ Given that trainees who commence HST in 2025 will not be available to enter the consultant workforce until approximately 2033,^(438, 462) it is likely that endoscopy capacity will continue to be constrained by a shortage of endoscopists with an appropriate skill level in the short to medium term.

It is important to note that endoscopy units are reliant on nurses and the wider endoscopy team, including administrative support.⁽⁴⁶⁴⁾ In addition to the endoscopist performing the colonoscopy, two staff-grade nurses are present during the

procedure, with additional nursing staff required to monitor patients in recovery. The knowledge and skills required for endoscopy nurses have expanded with the development and expansion of endoscopy procedures,⁽⁴⁶⁶⁾ with competency-based training for endoscopy nurses taking approximately one year. Each endoscopy room is estimated to require a minimum of five endoscopy nurses to manage patient admissions and pre-procedure checklists, the procedure room, recovery room, and discharge.⁽⁴⁶⁷⁾ In addition, decontamination staff are required for decontamination of endoscopes. While two BowelScreen nurses are funded per endoscopy unit to manage triage and pre-assessment of programme participants, patient check-in is managed by existing administrative staff in each unit.

8.6.4 Histopathology

Given advances in treatment options, increasingly complex histopathology interpretations are required to provide prognostic information and inform treatment decisions, necessitating consultant and medical scientist expertise, as well as equipment and space.⁽⁴²⁵⁾ As highlighted above, consultant pathologist shortages have resulted in onerous on-call rotas, sub-optimal consultant cover in some sites, and long outpatient waiting lists in some specialties.⁽⁴²⁵⁾ The *HSE Outline Strategic Plan for Laboratory Services (2026–2035)* acknowledged the training, recruitment and retention of medical and scientific staff with the skill mix required to deliver laboratory services as a key challenge.⁽⁴⁶¹⁾ In 2022, there were an estimated 127.2 WTE consultant histopathologists working across the public and private sector, with an estimated unmet demand for a further 25.5 WTEs.⁽⁴²⁵⁾ The *Review to Inform the Strategic Direction of Laboratory Medicine* noted a critical and chronic shortage of suitable medical scientist candidates to fill posts, owing to a combination of a lack of workforce planning and graduates pursuing alternative careers.⁽⁴²⁷⁾ The review suggested that an increase in the number of MLAs, in addition to an expansion of the MLA role, would be necessary in order to maintain current service levels.⁽⁴²⁷⁾

Expansion of the BowelScreen programme is likely to substantially increase the number of samples to be processed, leading to increased demands on histopathology services. Data supplied by one of the participating laboratories indicated that 1,760 samples from 543 BowelScreen colonoscopy participants were examined in 2024, necessitating a total of 6,984 routine procedures (including haematoxylin and eosin [H&E] staining and IHC). The estimated staffing requirements for this workload is shown in Table 8.12.

Table 8.12 BowelScreen histopathology workload and estimated staff requirement for St. James's Hospital in 2024

	Parameter	Number
BowelScreen workload	Participants with samples taken	543
	Specimens	1,760
	Blocks	2,119
	Routine procedures (H&E, special histochemistry, IHC, FISH)	6,984
	Grade	WTE
Estimated staff required	Consultant	0.4
	Senior scientist	0.8
	Medical laboratory assistant	0.5
	Grade IV clerical	0.5

Source: Personal communication. Key: FISH – fluorescence in situ hybridisation. H&E – haematoxylin and eosin. IHC – immunohistochemistry. WTE – whole time equivalent.

Note: In 2024, people aged 59–69 were eligible to participate in BowelScreen.

Compared to screening those aged 55–74, the cohort model presented in Chapter 7 indicated that screening those aged 50–74 could result in an estimated additional 743 participants with adenomas or CRC detected in year one of a full and immediate expansion, with 591 additional cases in year 10 (Table 8.2). However, as highlighted in section 8.3.1, the estimated number of participants with adenomas detected is likely to underestimate the actual histopathology workload that would result from an age extension, due to uncertainty regarding adenoma prevalence and the fact that non-adenomatous polyps and lesions were not explicitly modelled. Given increasing workloads and existing workforce shortages, significant investment in staffing and infrastructure will be needed to meet the increased demand and maintain service quality.⁽⁴²⁸⁾ The HSE Capital Plan 2025 outlined funding to support increased laboratory capacity nationally as part of wider support for diagnostic facilities.⁽⁴⁶⁸⁾ The Strategic Plan for Laboratory Services recommended that planning for service developments should consider access to and delivery of the laboratory services required to support any such developments, including the services required as a result of further investigation or follow up.⁽⁴⁶¹⁾

Training

Training in histopathology involves completion of a two-year BST programme in histopathology, followed by five years of Higher Specialist Training. In order to meet the projected growth in demand, the NDTP recommended a workforce of 224 WTE consultant histopathologists by 2035, proposing a staged increase in the annual intake of histopathology HST trainees from six in 2022 to 23 in 2031.⁽⁴²⁵⁾ In order to increase the histopathology medical workforce, sufficient training capacity and funding for BST and HST training posts, in addition to consultant posts, are required.

The NDTP further highlighted that the proposed increase in trainees would not be sufficient to fully address the projected demand, with an expected gap between supply and demand of 55.3 WTE consultant histopathologists by 2035.⁽⁴²⁵⁾ Given existing workforce shortages and the long lag between the intake of new trainees and their availability to enter the consultant workforce,⁽⁴²⁵⁾ it is unlikely that sufficient capacity will be available to absorb an expansion of the BowelScreen programme in the short to medium term without impacting target turnaround times for both screening and symptomatic services.

8.6.5 Radiology

CT colonography

Interpretation of CT colonography is complex, and may involve analysing between two to four times the number of images compared to a standard abdominal CT scan. CTC requires rectal intubation and insufflation, which is time-consuming and labour-intensive. *Guidelines for the Use of CT Colonography (CTC) as part of the National Colorectal Screening Programme in Ireland*, published in 2012, suggested that consultant radiologists involved in reading CTC studies as part of BowelScreen should have completed at least one accredited training course including the evaluation of 50 CTC cases with full colonoscopic correlation or mentored double-reading of 100 cases, with a further period of mentored supervision and double-reading of no less than 50 additional cases.⁽⁴⁶⁹⁾ The BowelScreen quality assurance standards require radiologists to perform a minimum of 100 CTC procedures per year.⁽³⁰⁵⁾ Reading the initial 150 cases and achieving adequate numbers to maintain competency may be challenging, particularly for lower volume units. Table 8.13 outlines the estimated staffing requirements for a centre receiving 200 BowelScreen CTC referrals a year. Based on the cohort model presented in Chapter 7, extending BowelScreen to those aged 50–54 is estimated to incur an additional 27 CTC procedures each year (

Table 8.7).

Table 8.13 Estimated annual staffing requirements for 200 CT colonography referrals

	Staffing	Estimated hours per week
Clinical	Consultant radiologists (n=2)	3 hours for 4-6 clients (1 session)
	Radiographers (n=3)	
	Nursing support (number not stated)	
Administrative	Local coordinator	11 hours
	Data manager	1–2 hours
	Clerical staff support	4 hours

Source: Guidelines for Use of CT Colonography (CTC) as part of the National Colorectal Screening Programme in Ireland (2012).⁽⁴⁶⁹⁾

Diagnostic radiology

Expansion of CRC screening will increase demand for diagnostic radiology, including CT, MRI and PET scans for screen-detected cases. As outlined in section 8.4.3, concerns have been raised regarding the challenging working environment faced by radiology departments due to growing and increasingly complex workloads coupled with inadequate resourcing.⁽⁴³⁰⁾ The Faculty of Radiologists and Radiation Oncologists published *Guidance on Radiologist Workload Figures* in 2024 to assist in workforce planning for radiology services.⁽⁴⁷⁰⁾ The guidance document provides indicative estimates of the reporting time required per study for each imaging modality, noting, however, that the hourly figures cannot be directly converted into annual activity periods without accounting for time spent in non-clinical work and in non-countable activities.⁽⁴⁷⁰⁾

In 2023, there were approximately 300 WTE radiology consultants employed in the public system, with 43 vacant posts.⁽⁴⁷¹⁾ Similar to training in other medical specialties, Higher Specialist Training in diagnostic radiology involves a five-year programme of structured, supervised clinical training in specialist registrar posts. Given existing challenges resulting from an increased demand for complex imaging coupled with a lack of resources and lack of protected time,⁽⁴³⁰⁾ further investment is likely to be required to ensure sufficient radiology capacity is available to meet increased demands from both screening and symptomatic services.

8.7 Infrastructure and resources

Healthcare infrastructure comprises the physical and organisational structures, facilities, and systems that support healthcare service delivery. Cancer screening is a complex public health strategy, which requires significant resources, infrastructure and coordination.⁽⁴¹⁴⁾ These will be considered in more detail below.

8.7.1 Screening units

In 2008, prior to the establishment of BowelScreen, the National Cancer Screening Service (NCSS) highlighted the significant organisational structures and systems required by colorectal cancer screening services, stressing that these should not interfere with the delivery of symptomatic services for people with gastrointestinal complaints.⁽¹⁶²⁾ The 2008 *Recommendations for a colorectal cancer screening programme in Ireland* recommended the establishment of four dedicated screening centres with two endoscopy suites each, geographically dispersed throughout the country and within close proximity of cancer centres, but operating discretely from the symptomatic service.⁽¹⁶²⁾ In order to address requirements for both screening and increased symptomatic capacity, the NCSS further suggested a model consisting of a total of eight colonoscopy centres (including four screening-only centres), with utilisation split evenly between screening and symptomatic services.⁽¹⁶²⁾ The screening colonoscopy centres were expected to require consultant medical staff (gastroenterologists, colorectal surgeons, anaesthetists, radiologists, pathologists), specialist nurses, radiographers, administrative and technical staff.

Since its inception in 2012, however, the BowelScreen programme has operated within the general symptomatic services. BowelScreen participants with a positive FIT result are invited for colonoscopy in one of 15 endoscopy units, with two additional units, located in Cork University Hospital and Tallaght University Hospital, expected to commence screening colonoscopies as part of BowelScreen in 2025 (Figure 8.1). As the programme continues to expand, the participation of additional units will be required, with each unit requiring approximately two years to become fully embedded within the programme. Requirements for BowelScreen endoscopy units are outlined in the programme quality assurance standards.⁽³⁰⁵⁾ These include JAG accreditation (see section 8.5.2) and demonstrable achievement of the programme requirement for photographic evidence of caecal intubation. Processes are also required to identify and manage underperformance of screening endoscopists against QA standards. Units performing advanced polypectomy procedures such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) must also have access to surgical backup.⁽³⁰⁵⁾ While BowelScreen provides a monetary contribution to participating endoscopy and CT colonography units to support service developments, sourcing capacity from additional units is challenging given the pressures from symptomatic waiting lists and the finite pool of endoscopists who meet the BowelScreen performance thresholds.

Capital investment and elective treatment centres

In 2021, the National Elective Ambulatory Care Strategy outlined a proposed increase in the HSE's capacity to provide elective procedures, including endoscopy, with the introduction of new elective hospitals across the country.^(472, 473) The 2025

Programme for Government committed to the building of four new elective treatment centres (previously referred to as elective hospitals) in Cork, Dublin (two sites), and Galway, in addition to the establishment of six surgical hubs in Cork, Dublin (two sites), Galway, Limerick and Waterford.^(14, 474) The HSE Capital Plan 2025 outlined the provision of €5 million in support of the design of these standalone centres in the Elective Hospitals Programme.⁽⁴⁶⁸⁾

The new elective treatment centres are expected to provide 42 additional endoscopy suites nationally, which are estimated to provide capacity for an additional 128,100 endoscopies annually.⁽⁴⁷²⁾ This is equivalent to approximately 3,050 procedures annually per room. Delivering both the infrastructure and resourcing of the new facilities is expected to be challenging.⁽⁴⁷²⁾ Regarding staffing for the proposed elective treatment centres, the Department of Health acknowledged that recruitment and training of staff would necessitate 'an appropriate lead time'.⁽⁴⁷²⁾ Potential role expansion for existing staff grades and the possibility that some staff 'may share work sessions across the acute hospital system' were also suggested.⁽⁴⁷²⁾ The *Path to Universal Healthcare: Sláintecare & Programme for Government 2025+* outlined an aim to initiate construction of the treatment centres in Cork and Galway in 2027, with a view to the centres becoming operational in 2030.⁽⁴⁷⁴⁾ While tender documents for the Dublin centres are expected to be issued alongside those for Cork and Galway in 2026, expected dates of operation for the two Dublin centres are not reported.⁽⁴⁷⁴⁾

Long waiting times for endoscopy procedures (section 8.4.1) illustrate a significant existing unmet demand. Much of the planned increase in endoscopy capacity may already be accounted for by the expected rise in demand from changing demographics.⁽⁴⁷²⁾ A significant increase in endoscopy capacity will be required to support the planned expansion of BowelScreen to those aged 55–74. To support a further extension of the programme to include those aged 50–54, approximately 2,000, 2,400 and 2,300 additional BowelScreen colonoscopies are estimated to be needed in year one, year five and year ten, respectively (section 8.4.1). If plans for the four new elective treatment centres are realised, there may be sufficient physical infrastructure to support the age extension by the time of implementation, if a decision is made to expand screening. If endoscopy capacity continues to be constrained, one additional endoscopy room may be sufficient to support an expansion of the programme to include those aged 50–54, assuming that up to 3,050 procedures may be conducted per room annually.⁽⁴⁷²⁾ However, as it may not be possible to achieve maximum efficiency from each room, and as screening colonoscopies can take longer than other endoscopy procedures, more than one room may be required in practice.

Given a finite number of endoscopists with the required level of experience and expertise to perform screening colonoscopies, as well as capacity constraints in histopathology and radiology services (see sections 8.4.2 and 8.4.3), the potential

impact of the new elective treatment centres, including the additional capacity that will be provided in practice, is unclear.

8.7.2 Medical laboratories

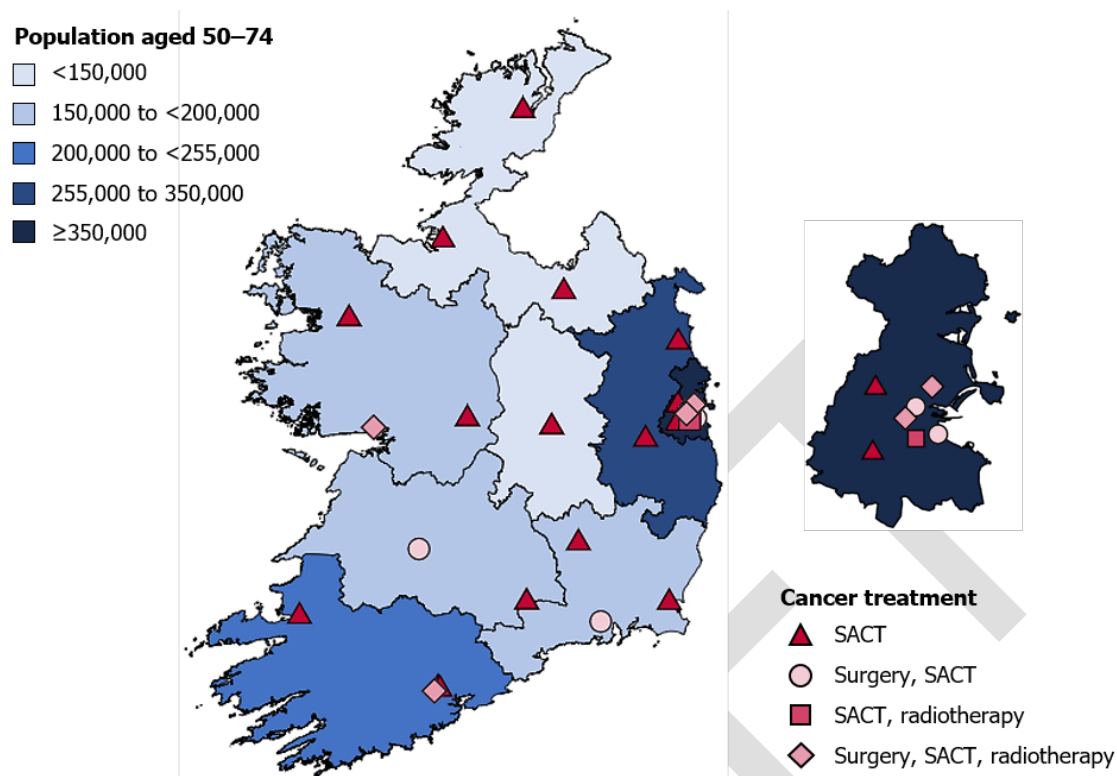
To support a national CRC screening programme, the 2008 NCSS recommendations included the development of a pathology reference centre to foster specific pathological expertise, standardised reporting criteria and reporting templates, and to ensure uniformity and consistency.⁽¹⁶²⁾ The *HSE Outline Strategic Plan for Laboratory Services (2026–2035)* recommended the development of a multidisciplinary HSE Central Laboratory Campus, to provide a base for the National Reference Laboratory Service, the National Genetics and Genomics services, and other key national services.⁽⁴⁶¹⁾ While the processing of BowelScreen FIT samples is, as of April 2025, outsourced to a private medical laboratory under tender, in future, this service may be delivered by chemical pathology laboratories in Model 4 hospitals, or by a central laboratory as part of the reform of laboratory services. However, what role, if any, a central laboratory might play in the delivery of screening services is not clear.

Pathology laboratory services play a key role in CRC screening, as the management of participants, including decisions related to the need for further resection and surveillance after screening, depends on the quality and accuracy of the diagnosis.⁽⁴²⁶⁾ All samples taken at BowelScreen colonoscopies are examined in one of eight designated adult cancer centres.⁽⁶¹⁾ A ninth laboratory, located in Tallaght University Hospital, is expected to commence the processing of samples taken at BowelScreen colonoscopies performed in the hospital in 2025. BowelScreen provides a monetary contribution to participating laboratories to support service developments. However, as highlighted in section 8.4.2, cancer centre laboratories are under significant pressure, which has impacted their ability to meet target turnaround times.

8.7.3 Treatment units

Surgery for colorectal cancer detected through BowelScreen is performed in one of eight designated adult cancer centres. Systemic anti-cancer therapy (SACT), which includes chemotherapy and immunotherapy, is provided in the eight cancer centres and 17 public hospitals. Public radiation oncology (radiotherapy) services are provided in five locations, with three centres in Dublin and one each in Cork and Galway (Figure 8.4).⁽⁴⁷⁵⁾ HSE service level arrangements are in place in Limerick and Waterford, where radiation therapy is provided with private sector partners. Some cancer drug treatment services are also available in private hospitals.

Figure 8.4 Location of public cancer treatment centres and projected population aged 50–74



Source: Central Statistics Office;⁽⁴¹⁸⁾ National Cancer Control Programme.⁽⁴⁷⁵⁾ Population projections for the year 2031, based on moderate net migration.
Key: SACT – systemic anti-cancer therapy.

Surgical hubs

The 2018 Health Service Capacity Review identified the need for greater separation between scheduled and unscheduled care.⁽⁴⁷⁶⁾ The 2025 Programme for Government committed to the establishment of six new surgical hubs,⁽¹⁴⁾ which are expected to deliver over 150,000 day cases, minor operations and outpatient consultations each year once fully operational.⁽⁴⁷²⁾ The first of these, the HSE Surgical Hub South Dublin, opened in February 2025, with the North Dublin Surgical Hub expected to become operational in Q4 2025.⁽⁴³⁴⁾ Funding for a surgical hub at Merlin Park University Hospital in Galway was provided as part of Budget 2025,⁽⁴¹⁹⁾ with the HSE Capital Plan 2025 outlining the provision of €173.3 million to continue the expansion of the Surgical Hub Programme.⁽⁴⁶⁸⁾ It is anticipated that the remaining hubs in Cork, Waterford and Limerick will be delivered on a phased basis in 2026.⁽⁴³⁴⁾ The primary purpose of the surgical hubs is to enhance capacity for day case surgery and ambulatory care, in order to address pressures on waiting lists.⁽⁴⁷⁷⁾ The increased protected capacity for elective procedures is expected to free up capacity for emergency and more complex care.⁽⁴⁷⁸⁾ However, the activity targets of the new

surgical hubs will depend on recruitment and staffing (see section 8.6).⁽⁴³⁴⁾ At the time of writing, the potential impact of the surgical hubs, including the additional capacity that will be provided in practice, is unclear.

8.7.4 Information and communication technology systems

BowelScreen programme database

Health information systems are essential to the operation of effective screening programmes.⁽⁴¹⁴⁾ As such, BowelScreen maintains a database of individuals eligible for screening, which includes data on screening results and further assessments. Expansion of the programme will increase the administrative workload associated with management of the register and data reporting. The *National Screening Service Strategic Plan 2023–2027* highlighted data and information as key strategic enablers, outlining a commitment to use advances in information technology and data to inform and strengthen service delivery, support evidence-based decision-making and improve efficiency.⁽⁴⁷⁹⁾ Developments to date include the introduction of individual health identifiers (IHIs), which reduce administrative burden and minimise duplication.⁽⁴⁸⁰⁾ In 2024, printed and postal communication with GPs was replaced with electronic messaging through Healthlink, improving the speed, reliability and accuracy of communication from the programme.⁽⁴⁸⁰⁾ A modernised patient database system was introduced to the BreastCheck programme in 2024;⁽⁴⁸⁰⁾ a similar system is likely to be required to support the planned expansion of BowelScreen to those aged 55–74. It is therefore assumed that any required database upgrades will be in place in advance of an additional extension of the programme.

8.7.5 Reform of healthcare service delivery in Ireland

In 2017, the *Oireachtas Committee on the Future of Healthcare Sláintecare Report* recommended the establishment of regional bodies accountable for implementing integrated care at sub-national level.⁽⁴³⁹⁾ In line with this recommendation, six new Health Regions have been established, with the aim of facilitating comprehensive integrated, person-led, community-first health and social care through the alignment of acute and community-based services.⁽⁴⁸¹⁾ Each Health Region is responsible for providing both hospital and community care for people living in the region, with its own budget, leadership team and responsibility for local decision-making.⁽⁴⁸²⁾ As of 2024, the relationship and interaction between the NCCP and the Health Regions for the organisation, delivery, and reporting of cancer services at regional level was reported to be in development.⁽⁴⁸³⁾ In 2025, the NSS outlined a commitment to support the work of the Regional Executive Officers of the new Health Regions to ensure the standardised delivery of screening services across the country, including access to the appropriate screening pathways for all eligible screening participants.⁽⁴⁸⁰⁾ The extent to which the new Health Regions may impact the funding, operation or delivery of national screening programmes is unclear.

8.8 Implementation

Successful screening programmes require adequate staffing and facilities for testing, diagnosis, treatment and programme management, which should be in place prior to implementation. While BowelScreen was introduced in 2012 with the aim of offering free screening to people aged 55–74,⁽¹⁴⁸⁾ implementation has progressed on a phased basis, commencing with those aged 60–69. In October 2023, the programme was expanded to include those aged 59. As of April 2025, screening is available to people aged 59–70, with plans to lower the screening age to 58 by 2026. The National Screening Service has outlined the gradual expansion of the age range in ‘carefully managed stages, to ensure everyone we offer screening to has access to onward testing and treatment, if needed’.⁽⁴⁸⁴⁾ In 2024, NSS developed a five-year plan for programme funding, including capital and revenue, to support the future financial requirements for its screening programmes and corporate services.⁽⁴⁸⁰⁾ Based on the current rate of expansion and in consultation with the programme, the cohort model presented in Chapter 7 assumed that expansion to those aged 55–74 would be completed by 2030, with implementation of the proposed extension to those aged 50–54 commencing in 2031.

Three implementation scenarios were considered as part of the budget impact analysis presented in Chapter 7: immediate expansion to all individuals aged 50–54, one-yearly expansion (that is, increasing the screening age range by one year each calendar year) and two-yearly expansion (increasing the screening age range by one year every two years). The analysis indicated that the increased demand on endoscopy, histopathology and diagnostic radiology resources associated with an expansion of the programme to those aged 50–54 is expected to outweigh any offset from reduced symptomatic presentations. While all three scenarios showed similar trends, slower implementation is expected to incur smaller initial requirements at the expense of achieving the full effect of the intervention at a later time.

Considering the significant capacity challenges faced by endoscopy, histopathology and radiology services, coupled with the length of time required to train the relevant specialties, it is unlikely that the planned expansion to age 55–74 could progress at a more rapid pace. Further, at existing levels of capacity, the requirement for additional procedures and cases could impact both BowelScreen quality assurance standards and KPI targets for symptomatic services, including longer waiting lists and worsening turnaround times. While it may be possible to relieve demand on endoscopy services from symptomatic procedures (see section 8.10.1), this may not result in a proportionate decrease in demand for histopathology or radiology services, given the greater yield from colonoscopies following a positive FIT result.

Significant investment and planning would be required to support both the planned expansion, as well as any potential future extension of the programme. As

BowelScreen operates within general symptomatic services, it is difficult to estimate the precise staffing requirements for each stage of the screening pathway. Funding to support the new elective treatment centres and surgical hubs was outlined in the 2025 HSE Capital Plan,⁽⁴⁶⁸⁾ with funding of €1.9 million included as part of Health Budget 2025 to support the expansion of BowelScreen to ages 58–70.⁽⁴¹⁹⁾ As the planned expansion progresses, the additional demand placed on services should be carefully monitored. It will be crucial for any plans for an additional extension of the screening age range to consider existing infrastructure and staffing deficits, and in particular the time and financial resources required to address such shortfalls.

8.9 Education, information and awareness

Participation in screening is key to the overall success of a screening programme. The World Health Organization states that 'cancer screening programmes will only make a substantial difference to population health if a sufficient proportion of the eligible population uses them'.⁽⁴¹⁴⁾ As a result, it is vital that all screening programmes aim to achieve and maintain a minimum level of uptake. Knowledge, education, health literacy, stigma, and anxiety can act as barriers to participation in screening. Screening programmes should endeavour to provide sufficient and appropriate information to eligible individuals to ensure that they can make informed decisions about screening.⁽⁴¹⁴⁾ This section provides an overview of strategies to increase uptake, as well as information resources and awareness campaigns that may require consideration for a BowelScreen age extension.

8.9.1 Uptake rates

Low uptake of colorectal cancer screening is a recognised issue. While the minimum BowelScreen target uptake rate is $\geq 50\%$, with an achievable standard of $\geq 60\%$,⁽³⁰⁵⁾ FIT uptake rates have ranged from 40.6% in 2012–2015 to 46.6% in 2020–2021, with preliminary data indicating an uptake rate of 41.1% in the third quarter of 2024.⁽⁴⁴³⁾ Participation rates have consistently been lower in those aged 60–64 than among those aged 65–69 (see Table 2.2, Chapter 2). Internationally, lower uptake rates have also been observed in those aged 50–54 compared to older age groups.^(435, 485)

Strategies to increase uptake rates

To increase uptake, BowelScreen has trialled the use of 'FIT-Direct', in which a FIT kit is sent directly to eligible individuals rather than requiring the acceptance of an invitation.⁽⁴⁸⁶⁾ FIT-Direct significantly increased uptake; however, the initiative also resulted in a significant increase in the number of unsatisfactory samples (that is, samples deemed unacceptable for testing).⁽⁴⁸⁶⁾ A similar initiative, targeting only first-time invitees, found that FIT-Direct resulted in significantly higher likelihood of

uptake in those who had not responded to their initial invitation, over and above the uptake of the usual reminder letter or a modified reminder letter.⁽⁴⁸⁷⁾

In 2024, the National Screening Service, in conjunction with the Department of Health, commenced work on the 'Better Letters' initiative for BowelScreen.⁽⁴⁸⁰⁾ This initiative aims to increase uptake through the incorporation of behavioural science insights into screening invitation letters.⁽⁴⁸⁰⁾ Other more targeted initiatives have also been employed by NSS and BowelScreen. This includes engaging with Pavee Point to develop literature and infographics to encourage individuals from the Traveller community to participate in national population-based screening programmes.⁽⁴⁸⁸⁾

Other countries and screening programmes have similarly employed initiatives to help to improve overall participation in screening. In the Netherlands, the use of advanced notification letters (that is, a letter issued to eligible participants preceding the screening invitation) resulted in a significant increase in screening uptake across all age groups.⁽⁴⁸⁹⁾ Similarly, an Australian study that investigated the use of a modified advanced notification letter to improve screening uptake specifically in males (among other strategies), found that those who received the letter were 12% more likely to participate in screening than those who received the standard invitation ($p=0.001$).⁽⁴⁹⁰⁾ Regarding initiatives to increase screening in those aged 50–54 specifically, the authors of one 2020 study, which examined the feasibility of social network use to encourage participation, suggested that the use of a specific targeted message or video on the Facebook platform may be an effective way to mobilise this age group to participate in screening.⁽⁴⁹¹⁾

While successful initiatives have been trialled in the Irish context, these may need to be modified to consider the expansion of the programme to a younger cohort. It would be important to consider the effectiveness of initiatives by age group rather than the entire eligible cohort so as not to overestimate the potential impact on the target group. As outlined in Chapter 7, higher uptake rates magnify the impact of screening, resulting in a higher initial increase in CRC cases detected and greater resource requirements and costs, as well as a larger reduction in CRC cases over time. The additional demands placed on endoscopy, histopathology and radiology services therefore warrant consideration as part of any efforts to increase uptake rates.

Colonoscopy acceptance rates

Colonoscopy acceptance rate, that is, the percentage of participants with positive FIT results who undergo colonoscopy,⁽³⁰⁵⁾ is an important predictor of outcomes. Findings from a study based on a regional FIT-based CRC screening programme in Italy indicated that the risk of CRC death was over 100% higher in those who did not complete a colonoscopy following a positive result on a stool-based test, compared

to those who did.⁽⁴⁹²⁾ BowelScreen colonoscopy acceptance rates among those aged 60–69 have ranged from 78.8% in 2018–2019 to 82.4% in 2012–2015, with no clear or consistent trend by age.^(18, 148, 149) For each round of the programme, colonoscopy acceptance rates have fallen below the programme’s minimum quality assurance standard of $\geq 85\%$.⁽³⁰⁵⁾ An earlier FIT pilot programme in Ireland, which screened people aged 50–74, reported a colonoscopy uptake rate of 87% across both screening rounds.⁽⁴⁹³⁾ Internationally, colonoscopy rates following positive FIT results are similar across age groups.^(435, 494) Data from the first three years of the Danish National Colorectal Cancer Screening Programme suggested little difference in the acceptance rates of follow-up procedures following a positive FIT result across different age groups.⁽⁴³⁵⁾ As BowelScreen continues to expand to those aged 55–74, it will be possible to monitor colonoscopy acceptance rates across a broader age range.

8.9.2 Information and awareness campaigns

Awareness of CRC and of BowelScreen are likely to contribute to the uptake of the programme. Research carried out on behalf of the programme in 2021, which included 320 people aged 60–69, indicated a high level of awareness of the programme, with 94% of those surveyed being aware of BowelScreen, and 91% aware that CRC screening is a good way to identify individuals who are at risk of developing cancer.⁽⁴⁹⁵⁾ However, 42% reported knowing nothing or very little about CRC; 59% reported that they would not be confident in spotting CRC symptoms; 36% reported knowing very little or nothing about CRC screening; and 42% did not know why it is important to participate in CRC screening.⁽⁴⁹⁵⁾ Awareness of CRC symptoms and screening may be lower among those aged 50–54, who may not have the same level of familiarity with BowelScreen or CRC as their older counterparts who may have had direct or indirect experiences with the programme.

Marketing plays an important role in the realisation of screening programmes, with advertising campaigns used by BowelScreen showing success in increasing the uptake of the programme. For example, a 2023 BowelScreen social media campaign, which highlighted the lowering of the screening age to 59, resulted in a 279% increase in registrations to the programme when compared to the non-campaign period.⁽⁴⁸⁴⁾ Given the success of this form of marketing, it is likely that similar campaigns would encourage registrations in the 50–54 age group should the proposed extension be implemented. There may also be benefits to targeting elements of a campaign to appeal to a younger audience. For example, by casting younger actors in television or social media campaigns to better reflect the age of the newly-eligible cohort, or different background settings and dialogues that may help those aged 50–54 to resonate more with the message being delivered.

BowelScreen has developed multiple leaflets to help educate and inform people about the programme, with useful information about the programme itself, the screening test, and colonoscopy.⁽⁴⁹⁶⁾ The programme also provides information in audio and video format on its website, as well as information presented in multiple languages. While many of these resources will be applicable to the cohort under consideration for extension, it may be necessary for the programme to adapt these resources to both update the information provided and to help to appeal to a younger audience.

The overall awareness and understanding of the BowelScreen programme and of CRC in general requires the production of both physical and online materials. As noted above, the programme has produced multiple leaflets and online resources. Based on the cohort model presented in Chapter 7 of this report, the expansion of the programme to include those aged 50–54 would constitute up to 219,000 additional invitations being sent each year (Table 8.2). In addition to the workload associated with the processing of additional invitations, an expansion of the age range will increase the burden of other administrative tasks associated with the operation of the programme, including database management and maintenance (see section 8.6). As outlined in the National Screening Service 2024 end of year report, the NSS is also developing a self-registration portal for the programme, which will allow eligible individuals to give consent to participate and be sent a FIT kit.⁽⁴⁸⁰⁾ Benefits of this may include a reduction in call centre enquiries and the more accurate delivery of the test kit.⁽⁴⁸⁰⁾ Additionally, the online portal may appeal more to a younger cohort than the current consent methods, as it provides additional flexibility in responding to the screening invitation, and in future might help to reduce the amount of physical documentation sent to participants.

8.10 Discussion

Population-based CRC screening is resource-intensive, requiring timely access to high-quality endoscopy services for participants who receive a positive FIT result, histopathology to process samples taken during colonoscopy, and diagnostic radiology for suspected cancer cases. Extending BowelScreen to those aged 50–54 would increase the size of the eligible population invited for screening each year by approximately 27%. Compared to offering screening to those aged 55 to 74 only, this age extension would require approximately 2,000, 2,400 and 2,300 additional colonoscopies (index, additional planned procedures and surveillance) as part of the BowelScreen programme in year one, year five and year ten, respectively. These numbers are in addition to the estimated 10,000 procedures that will be required once the expansion to 55–74 has been completed. The number of cases requiring histopathology is also likely to increase significantly. As outlined in Chapter 7, the expected increased demand for screening resources, including colonoscopy, CTC and histopathology, outweighs any offsets from reduced symptomatic cases, as screening

those aged 50–54 would bring more people into the health system than would otherwise present symptomatically in this age group. For diagnostic resources incurred following the confirmation of CRC, including molecular testing, CT, MRI, PET and rigid sigmoidoscopy, a partial offset from symptomatic services is expected later in the time horizon following full implementation, which is predicted to be comparable in magnitude to the increased demand generated by expanded screening.

According to the NSAC *Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme*, adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of a screening programme.⁽³⁾ At the time of writing, however, endoscopy, histopathology and radiology services continue to experience significant capacity challenges, with long waiting lists and deteriorating turnaround times falling below quality targets. Additional challenges relating to facilities and infrastructure, including IT, have also been highlighted. Screening programmes can inadvertently result in the reallocation of healthcare resources, which can negatively affect other areas and potentially reduce the quality of care for people with symptomatic conditions.⁽⁴⁹⁷⁾ As BowelScreen operates within general symptomatic services that are experiencing significant ongoing capacity challenges, extending the programme without addressing the existing constraints may in some cases result in neither BowelScreen participants, nor patients presenting symptomatically, receiving care in accordance with recommended targets for appointments and report turnaround times. The four new elective treatment centres are expected to provide capacity for over 125,000 additional endoscopies annually. As of May 2025, it is not clear when the Dublin facilities are expected to be operational,⁽⁴⁷⁴⁾ nor how much additional capacity will be provided in practice (see section 8.7.1). The following section considers other potential initiatives to relieve demand on endoscopy services and maximise capacity, including waiting list management and triaging of symptomatic or surveillance cases.

8.10.1 Initiatives to relieve demand and maximise capacity

When BowelScreen commenced in 2012, the FIT threshold was initially set at 20µg/g. In 2014, this was increased to 45µg/g to ease pressure on endoscopy capacity within the programme.^(18, 60) While higher FIT thresholds result in lower positivity rates and fewer colonoscopy referrals, cancer detection rates are also reduced.^(61, 132) This section discusses other initiatives that may relieve demand on endoscopy services or maximise the available capacity.

FIT for symptomatic colonoscopy triage and post-polypectomy surveillance

Faecal immunochemical tests with low thresholds (10µg/g) may be used as part of the symptomatic referral pathway, to facilitate the prioritisation of symptomatic

patients for investigation for colorectal cancer, high-risk adenomatous polyps or inflammatory bowel disease.^(37, 38) In November 2024, the HSE Endoscopy Programme published two position papers on the use of FIT in primary care and acute hospital GI endoscopy services.^(37, 38) The programme endorsed the use of FIT in primary care prior to considering referral for colonoscopy in people presenting with signs or symptoms suspicious of colorectal cancer,⁽³⁸⁾ as well as for triage of colonoscopy referrals, where appropriate.⁽³⁷⁾ The programme advised that FIT should be offered to newly referred patients even if they have previously had a negative FIT result through BowelScreen.⁽³⁷⁾ The requirement for effective follow up of patients who do not return a sample or who have a negative FIT with persistent or worrying symptoms was highlighted, as the use of FIT alone cannot rule out colorectal cancer. The HSE Endoscopy Programme further endorsed the use of FIT as part of the validation of routine colonoscopy waiting lists for patients who have not had a FIT prior to being placed on the list.⁽³⁷⁾

The use of FIT in post-polypectomy surveillance has also been investigated, with a 2025 modelling study suggesting that FIT-based surveillance strategies could be safe and cost-effective, with the potential to reduce the number of surveillance colonoscopies by up to 15%–41%.⁽⁴⁰⁷⁾ A study of over 5,000 participants categorised as intermediate risk following polypectomy in the English CRC screening programme similarly found that annual low-threshold FIT surveillance would be cost-saving compared with 3-yearly colonoscopy.⁽⁴⁹⁸⁾ The estimated programme sensitivity for colorectal cancer over three rounds of yearly FITs at a threshold of 10µg/g was 84.6% (95% CI: 65.1%, 95.6%), with a specificity of 70.8% (95% CI: 69.6%, 72.1%). Positivity rates ranged from 14% for the first completed FIT to 9% for the third.⁽⁴⁹⁸⁾ The HSE Endoscopy Programme suggested that FIT could be considered to prioritise patients who are on waiting lists for polyp surveillance, post-CRC screening and moderate-risk familial CRC history screening (excluding suspected or confirmed hereditary colorectal cancer syndromes) for investigation, if the waiting times for these procedures are excessive.⁽³⁷⁾

Colon capsule endoscopy

Colon capsule endoscopy (CCE) is a method of visualisation of the colon involving a small camera contained within a capsule, which captures images of the internal structures of the colon and rectum when swallowed.⁽⁴⁹⁾ Two systematic reviews published in 2021 and 2022 suggested that CCE appeared to be a safe and effective alternative for the detection of colorectal polyps and cancer in a screening setting, although concerns were raised over low completion rates.^(499, 500) A single-centre pilot study of 66 symptomatic patients in Ireland similarly suggested that CCE may be a safe and effective alternative to colonoscopy in symptomatic average-risk patients, although the capsule excretion rate was low at 76%.⁽⁵⁰¹⁾ Reading of colon capsules is time-consuming and reinvestigation rates, due to incomplete examination or the

need for polypectomy or biopsy, are high.⁽⁵⁰²⁾ In 2023, the HSE Endoscopy Programme published *Clinical Guidance for Colon Capsule Endoscopy Services*, which suggested that CCE should be considered for non-urgent symptomatic patients, patients who have undergone an incomplete colonoscopy or who have declined a colonoscopy, high-risk patients where diagnostic delay due to colonoscopy capacity may be an issue, and as an alternative for polyp surveillance where access to surveillance colonoscopy is prolonged.⁽⁵⁰⁾ At the time of writing, CCE is not used by the BowelScreen programme.

Waiting List Action Plan

The 2025 National Waiting List Action Plan (WLAP) aims to maximise the efficient use of available resources in order to deliver capacity, enhance reform and support scheduled care services to improve access to care for patients.⁽⁴³⁴⁾ According to the plan, no one should be waiting over four weeks for access to urgent colonoscopy, with a target of 50% of patients waiting less than 12 weeks for a GI endoscopy appointment by the end of 2025.⁽⁴³⁴⁾ A number of initiatives were outlined, including deploying additional weekend, evening and out-of-hours activity to reduce waiting lists, and supporting diagnostic capacity where required for additional OPD activity. It is anticipated that the NTPF will extend the range of specialties and procedures tendered in 2025 to better support the longest-waiting patients nationally, with this additional capacity expected to yield an additional 1,500 endoscopies.⁽⁴³⁴⁾ However, it is important to note that initiatives such as increasing weekend and out-of-hours activity and sourcing additional capacity from private hospitals will draw on the same finite staffing pool. As such, the WLAP 2025 acknowledges that 'competition for scarce capacity within the health service – in the context of the HSE and the NTPF seeking to secure additional activity from the public and private services – may impact the ability to achieve the projected level of activity'.⁽⁴³⁴⁾ Further increases in preventative and screening services, in addition to new service developments, could increase additions to the waiting list above anticipated levels, which may impede achievement of the targets set out in WLAP 2025.⁽⁴³⁴⁾

Health service capacity review

As of May 2025, a health service capacity review is underway to inform long-term capacity planning under Sláintecare.⁽⁴⁷⁴⁾ The results of the exercise may be helpful in determining the capacity of the healthcare system to absorb the change in healthcare demand associated with a BowelScreen age extension. It is envisaged that the review will not be a standalone piece of work and that the underlying model informing the review will be further developed over time to allow for the inclusion of additional data and policy considerations as required. If a decision is made to extend BowelScreen to those aged 50 to 54, model updates should account for this policy change if possible.

Staffing

Strategic workforce planning

Sláintecare 2025+ outlines a strategic workforce planning programme.⁽⁴⁷⁴⁾ The programme is designed to build a sustainable health and social care workforce to meet future population demand for health services, by ensuring there are enough qualified healthcare workers, at the right skill mix, and at the right time. It includes long-term strategic health and social care workforce planning across many stages of staff development, from increasing the number of third level places across healthcare disciplines (including nursing and medicine) to increasing specialist medical postgraduate training places. A total of 221 additional postgraduate speciality training posts are planned for 2025, including five new additional radiology specialist training posts.

The ability of these additional training posts to address skills gaps relevant to this HTA will depend on the availability of doctors who wish to take up these posts and the competing healthcare system demand for their skills once qualified. If a decision is made to extend screening to those aged 50 to 54 years, the potential mismatch between the length of the higher specialist training required (minimum four to six years with additional years required for fellowship and statutory leave), the potential timeline for implementation, and the evolving demand for healthcare resources as a BowelScreen age extension programme matures should be considered.

Insourcing and weekend working

In order to meet rising demands for endoscopy, insourced and weekend working are increasingly used. However, these strategies may adversely affect quality indicators, including polyp detection. A UK study of almost 100,000 colonoscopies performed by almost 2,500 endoscopists found that both the mean number of polyps (MNP) and PDR were statistically significantly lower for procedures performed at weekends compared to weekdays, as well as for insourced procedures, when adjusting for case mix.⁽⁵⁰³⁾ A post-hoc analysis limited to colonoscopies performed as part of the UK Bowel Cancer Screening Programme demonstrated similar effects, with significantly lower MNP (IRR 0.80, 95% CI 0.71, 0.90) and PDR (OR 0.69, 95% CI 0.55, 0.86) at weekends compared to weekdays. The authors highlighted the importance of considering potentially unintended consequences of initiatives to maximise colonoscopy capacity.⁽⁵⁰³⁾

Nurse endoscopists

In addition to consultant gastroenterologists and general surgeons, endoscopies may be performed by advanced nurse practitioners (ANPs) with the requisite levels of training and experience. However, non-medical endoscopists represent less than 3% of the endoscopy workforce in Ireland.⁽⁴⁵⁶⁾ In contrast, 23% of endoscopies in the UK are performed by clinical (that is, nurse or other non-medical) endoscopists.⁽⁵⁰⁴⁾ Clinical endoscopists account for 12% of the UK endoscopy workforce,⁽⁵⁰⁴⁾ but deliver more endoscopy sessions per head than consultants (mean 4.0 vs 2.3, $p < 0.001$).⁽⁴⁶⁴⁾ The expanded use of clinical nurse specialists (CNS) and ANPs in endoscopy could reduce the demand for consultant gastroenterologists.⁽⁴⁶²⁾

In 2021, 17 ANPs in gastroenterology nursing and six candidate ANPs were reported to be practicing within the public health service in Ireland.⁽⁵⁰⁵⁾ A 2023 survey of 141 endoscopy nurses reported that 24% were interested in pursuing a career in an advanced role as nurse endoscopist, to include performing endoscopy procedures.⁽⁴⁶⁶⁾ There are two pathways leading to ANP registration in Ireland, involving the completion of either an approved Master of Science in Advanced Practice Nursing programme, or through a development pathway following completion of a number of courses that collectively fulfil the Advanced Practice (Nursing) Standards and Requirements.⁽⁵⁰⁶⁾ Graduate Certificate and Master of Science Nursing programmes in Advanced Practice (Gastroenterology), which included advanced practice modules specific to endoscopy, were previously available;^(507, 508) however, as of 2025, there is no formal nationally accredited specialised training programme for nurse endoscopists in Ireland. While an expanded use of nurse endoscopists could decrease the endoscopy workload of consultant gastroenterologists and general surgeons, a formal national training pathway for advanced nursing practice in gastroenterology would be desirable. However,

expanded training for nurse endoscopists may further constrain endoscopy training capacity for medical Higher Specialist Training programmes.

It is important to note that initiatives to increase endoscopy capacity will also place further demands on histopathology and radiology services. The use of FIT triage, while potentially decreasing the total number of colonoscopies, may not result in a proportionate decrease in histopathology activity, as procedures following a positive FIT would be expected to yield a greater number of samples. Any strategies to increase endoscopy activity should be matched by initiatives to increase downstream histopathology and radiology capacity to prevent delays in accessing diagnostic services for people with abnormal screening results, as well as for those presenting symptomatically.⁽⁴⁹⁷⁾

8.10.2 Other capacity considerations

It is important to note that capacity may be impacted by a myriad of factors, including developments and advances in screening and diagnostic techniques and treatment. Some of these will be considered below.

Developments in colorectal cancer treatment

Advanced endoscopic techniques

While the majority of polyps are small and suitable for polypectomy at the time of screening colonoscopy, large non-pedunculated colorectal polyps (LNPCPs) $\geq 20\text{mm}$ previously required surgical resection to ensure safe removal. As a result of developments in advanced endoscopic techniques such as endoscopic mucosal resection (EMR), however, it is possible to safely resect LNPCPs as day case procedures.⁽⁵⁰⁹⁾ A retrospective analysis of BowelScreen EMRs in one centre reported that 52 EMR procedures were completed in 50 BowelScreen participants with LNPCPs between 2019 and 2023, with 71% of EMRs completed on the date of the index colonoscopy.⁽⁵⁰⁹⁾ All EMRs were completed by three consultant gastroenterologists. Adenocarcinoma was identified in four of the 51 specimens with available histology (7.8%), with all four patients referred for surgical management. In the remaining 92% of participants, endoscopic resection was successful in avoiding surgical intervention, with acceptably low recurrence and complication rates.⁽⁵⁰⁹⁾ While advanced endoscopic techniques such as EMR can reduce the demand for inpatient admissions and operating theatre time for surgical resections,⁽⁵⁰⁹⁾ complex colonoscopies require more time and must be performed by endoscopists with the required level of competence and experience.

Total neoadjuvant therapy (TNT)

The introduction of total neoadjuvant therapy (that is, the combination of neoadjuvant radiotherapy and systemic chemotherapy; see Chapter 3) has increased

the potential for non-operative management of locally advanced rectal cancers with organ preservation, known as the watch-and-wait (W&W) approach.⁽⁵¹⁰⁾ This approach will, in turn, increase demands for rectal MRI, which plays a critical role in non-operative management surveillance protocols for rectal cancer patients.⁽⁵¹⁰⁾ As part of the 2024 updated NCCP guideline on neoadjuvant treatment of patients with locally advanced rectal cancer, the guideline development group acknowledged the implications of total neoadjuvant and neoadjuvant chemotherapy on down-stream radiology and endoscopy resources, as a result of an increase in the number of patients undergoing surveillance.⁽¹⁸⁰⁾

Molecular testing

In addition to the initial histological examination of samples, molecular testing may be required to classify tumours according to clinical risk or biological subtypes.⁽⁵¹¹⁾ As genomic alterations can have distinct prognostic implications and may predict therapeutic responses,⁽⁵¹²⁾ molecular profiling has the potential to improve outcomes by 'delivering the right drug to the right patient'.⁽⁵¹¹⁾ The Cancer Molecular Diagnostics Advisory Group, which was established by the NCCP in 2017, defines molecular pathology in cancer as 'the use of molecular biomarkers in the diagnosis, prognosis, disease monitoring and treatment stratification of human cancers'.⁽⁵¹³⁾ Testing for genetic mutations can range from small-scale single-gene tests to disease-focused gene panels and whole exome sequencing, depending on the clinical purpose and cost.⁽⁵¹⁴⁾ However, data on the rate of molecular diagnostic use in Ireland is not centrally recorded or publicly available,⁽⁵¹⁴⁾ with the National Cancer Strategy highlighting the poor organisation and fragmentation of molecular cancer diagnostic services.⁽¹⁾ Increases in the number of samples to be processed and cancers diagnosed as a result of an expansion to the BowelScreen programme, in addition to ongoing developments in novel and targeted treatment regimens, will continue to increase the requirement for molecular pathology, placing further demands on histopathology services.

As colorectal cancer treatments continue to evolve, demands for endoscopy, histopathology and radiology resources are likely to continue to increase. The estimates presented in this chapter are therefore likely to underestimate the future demand on these services that will result from an extension of CRC screening.

Genetic testing and hereditary cancer services

Extending BowelScreen to those aged 50 to 54 may increase the possibility that some individuals who are unaware of a genetic predisposition to CRC could be discovered and diagnosed as a result of screening (see Chapter 9, section 9.4.1). This could in turn increase the requirement for cascade testing in order to identify relatives with an inherited cancer predisposition and who may benefit from risk

reduction and early detection measures.⁽⁵¹⁵⁾ However, the *Hereditary Cancer Model of Care*, published in 2023, highlighted that services for hereditary cancer in Ireland were 'underdeveloped and under-resourced', with a lack of capacity in genetic assessment, testing and counselling; surveillance imaging and endoscopy; risk-reducing surgery; related health needs such as fertility and reproductive care; and follow-up care.⁽⁵¹⁵⁾ A 2021 report on *The Unmet Need in Cancer Genetic Services* indicated substantial variation in the waiting times for an initial consultation with a genetics service for those who may have a genetic risk for cancer, ranging from one month to over two years.⁽⁵¹⁶⁾

As of October 2024, there were no standardised national guidelines in Ireland for universal testing for Lynch Syndrome, the most common cause of hereditary CRC, with testing of CRCs diagnosed through BowelScreen at the discretion of each screening site.⁽⁶²⁾ An analysis of 184 CRCs diagnosed at two BowelScreen sites between 2015 and 2020 found that 8% (n=14) had abnormal staining of mismatch repair (MMR) proteins by IHC, of whom 1.5% (n=3) would have warranted referral to genetic services.⁽⁶²⁾ The authors noted that if universal testing were to be implemented by all screening sites, a similar prevalence of MMR deficiency would generate a significant workload, both through the initial IHC and further downstream testing.⁽⁶²⁾

Service developments

Any decision to implement screening should also consider future developments that will impact services and which could affect their ability to absorb an increased workload arising from an expansion of screening. For example, the HSE Outline Strategic Plan for Laboratory Services (2026–2035) describes how digitalisation of imaging has the potential to transform services and is progressing rapidly within the histopathology discipline.⁽⁴⁶¹⁾ While such developments have the potential to release staff time in the long-term, substantial changes to work practices can have significant up-front resource requirements with regard to service redesign and training. The In Vitro Diagnostics Medical Devices Regulation (EU) 2017/746 involves more onerous regulatory requirements,⁽⁵¹⁷⁾ which must be navigated by pathology services. The prevalence of inflammatory bowel disease (IBD) has also been increasing rapidly in westernised countries,⁽⁵¹⁸⁾ increasing demand for endoscopy procedures and care from specialist gastroenterology services. These examples illustrate some of the competing resource demands on the services required to support screening.

Private screening

FIT kits can be purchased privately from a number of providers, with prices ranging from €45 to €89 according to the websites of four private providers consulted for this

assessment (accessed in October 2024). While it is unclear to what extent these services are available in Ireland, increased media attention on CRC screening, including as a result of this HTA, could lead to a greater interest among individuals who may be outside of the age range being screened by BowelScreen, and who may turn to private testing. This may pose challenges for GPs determining whether to refer a patient for colonoscopy based on the results of a private FIT, as well as potentially increasing demand for colonoscopy. The extent of private CRC screening in Ireland is unclear. However, it is important to consider that an expansion of the programme to a wider age group may increase awareness of CRC and screening, which could in turn lead to an increased demand for private testing and further strain colonoscopy, histopathology and radiology capacity.

Incidental diagnoses

Screening for colorectal cancer can result in incidental diagnoses of other conditions, including incidental discovery of inflammatory bowel disease.^(519, 520) Incidental diagnosis of colitis has been reported in 3% of FIT-positive BowelScreen participants, with new diagnoses of IBD including ulcerative colitis, Crohn's disease and segmental colitis associated with diverticulosis requiring treatment.⁽⁵²¹⁾ While this represents an unintended benefit of screening, individuals with previously undiagnosed IBD may require further treatment and or surveillance, placing increased demands on these services.

8.10.3 Implementing an age extension amidst capacity constraints

BowelScreen commenced in 2012 with the aim of offering free screening to people aged 55–74.⁽¹⁴⁸⁾ Endoscopy capacity has impacted the programme since its inception, resulting in an increase of the FIT threshold in 2014. As of April 2025, screening is available to people aged 59–70, with plans to lower the screening age to 58 by 2026. Based on the current rate of expansion and consultation with the programme, the cohort model presented in Chapter 7 assumed that expansion to those aged 55–74 would be completed by 2030, with implementation of the proposed extension to those aged 50–54 commencing in 2031. Given the significant capacity challenges faced by endoscopy, histopathology and radiology services, coupled with the length of time required to train the relevant specialities and limited funding and capacity for HST training posts, it is unlikely that the planned expansion to age 55–74 could progress at a more rapid pace. Further, at existing levels of capacity, the requirement for additional procedures and cases could impact both BowelScreen quality assurance standards and KPI targets for symptomatic services, including longer waiting lists and worsening turnaround times. Efforts to maximise endoscopy capacity may have deleterious consequences for downstream histopathology and radiology services, while relieving demand from symptomatic procedures may not result in a proportionate decrease in demand for histopathology

or radiology. Significant investment and planning is therefore required to ensure the necessary resources are in place to support both the planned expansion, as well as any potential future extension of the programme.

If a decision is made to lower the screening age to 50, alternative implementation options could also be considered. These could include prioritising the expansion of the age range downwards, and delaying expansion to those aged over 70 until after the extension to those aged 50–54 has been completed. However, given that CRC incidence increases with age and that the maximum benefit of FIT-based screening derives from participation in multiple screening rounds, the potential benefits and harms of this approach would warrant careful consideration. A 2022 evaluation of the Dutch CRC screening programme assessed whether improvements of the programme could be achieved by expanding the age range from 55–75 to 50–80, calibrating the FIT threshold, amending the screening interval, or applying risk stratification.⁽⁵²²⁾ Based on this evaluation, the Health Council of the Netherlands recommended that no modifications be made to the programme at that time. However, the Council also recommended a regional pilot study of once-off FIT screening of people aged 50, following which participants with a negative FIT result would enter the regular screening programme at age 55, with the aim of determining the potential health gains and disadvantages of such an approach, as well as providing data on feasibility and uptake rates.⁽⁵²²⁾ A similar pilot could be considered in Ireland, and may help to address some of the uncertainties regarding uptake rates, FIT positivity rates, adenoma and cancer detection rates in this age group.

8.10.4 Limitations

The consideration of the potential organisational implications of extending BowelScreen to those aged 50–54 presented in this chapter is subject to several limitations and uncertainties. As highlighted in Chapter 7, estimates of the resources required for an expansion to the screening age range were based on the adenoma-carcinoma pathway. As a result, resources incurred for the resection, testing and surveillance of serrated lesions or non-adenomatous polyps were not included. As BowelScreen operates within the general symptomatic services, it is difficult to estimate the discrete staffing requirements for each stage of the screening pathway, as, with the exception of the BowelScreen nurses managing the pre-assessment and triage of participants, all staff involved in screening will carry both screening and symptomatic workloads.

Resource estimates presented in this chapter are based on uptake rate estimates derived from empirical data observed in Ireland and Canada (for age groups not currently screened in Ireland). As highlighted in Chapter 7, the BowelScreen QA standard target uptake rate of 60% was associated with additional resource requirements for screening those aged 50–74 of approximately 170,000 FIT kits,

6,500 colonoscopies, and 2,100 participants requiring histopathology, compared to the empirically-estimated uptake rate. However, preliminary data for 2024 indicated that uptake rates ranged from 34% to 41% in the first three quarters of the year.⁽⁴⁴³⁾ As uptake rates tend to be lower among younger age groups, the empirically-derived uptake rates are likely to provide a more realistic estimate of the resources required for a potential age extension of the programme. As highlighted in Chapter 7, limited data were available to inform many of the other parameters. As a result, the resource estimates presented in this chapter are subject to uncertainty, and the true numbers required could be higher or lower in practice.

Finally, it is important to note that the aim of the model presented in Chapter 7 was not to predict the clinical effectiveness associated with lowering the screening age from 55 to 50. Chapter 5 (review of clinical effectiveness) and Chapter 6 (review of cost-effectiveness) include more detailed information on the expected clinical benefits of extending screening to those aged 50–54.

8.10.5 Conclusion

Given existing workforce shortages, increasing workloads and deteriorating turnaround times, further investment in staffing and training will be required to meet the increased demand on endoscopy, histopathology and diagnostic radiology services resulting from an expansion of the BowelScreen age range. Furthermore, in light of the time lag between the intake of new higher specialist trainees and their availability to enter the consultant workforce, forward planning is required to ensure sufficient staffing would be in place to absorb the increased workloads. As the programme operates within general symptomatic services that are experiencing significant ongoing capacity challenges, extending the screening age range without addressing the existing constraints is likely to negatively impact the ability of both BowelScreen and symptomatic services to provide care in accordance with quality assurance standards and KPI targets, potentially leading to longer waiting lists and worsening turnaround times.

9 Ethical, patient, and social considerations

9.1 Key points

- This chapter outlines the ethical, patient, and social implications that the proposed age extension of the BowelScreen programme to those aged 50 to 54 years may have for patients, families, the general public and the healthcare system in Ireland.
- Compared to those aged 55 to 74, the benefit of screening may be lower in those aged 50 to 54 due to lower incidence and mortality rates in this age group. This reduced benefit, however, should be considered in the context of reduced harms from screening.
- Lowering the screening starting age from 55 to 50 is likely to be cost-effective, and may therefore be considered good value for money and an efficient use of healthcare resources.
- Considering autonomy, it is important that individuals are aware of the benefits and harms of screening, to ensure that they can make informed decisions at each stage of the screening process.
- In terms of justice and equity, underserved groups, for example those from a lower socioeconomic background and persons with disabilities, are the least likely to benefit from screening as a result of reduced uptake, but are often the most vulnerable to colorectal cancer in terms of both incidence and outcomes.
 - To ensure equity within the programme, uptake in underserved groups should continue to be considered if the expansion to age 50 is implemented.
- While a commitment is in place to screen those aged 55 to 74 as part of BowelScreen, this has not yet been fully implemented. Lowering the screening age is likely to strain healthcare resources, including financial resources, staffing, endoscopy, histopathology and radiology services and screening infrastructure. It is important to consider the ethical implications of the potential diversion of resources from symptomatic services, and to ensure that the benefits of expanded screening justify the additional costs and resources.
- There were limited data available to address specific elements of the HTA, such as clinical and cost effectiveness, as well as test accuracy. As a result, the benefits and harms of extending BowelScreen to those aged 50 to 54 are

subject to a degree of uncertainty, as data relating to the 50 to 54 age group specifically was limited.

9.2 Introduction

In line with the scope of this HTA, the purpose of this chapter was to consider any ethical, patient, or social implications that the proposed age extension of the BowelScreen programme to those aged 50 to 54 years may have for patients, families, the general public or the healthcare system in Ireland. This chapter was developed broadly in line with the structure described in the European Network for Health Technology Assessment (EUnetHTA) HTA Core Model[®] and incorporates two assessment domains: ethical analysis, and patient and social aspects. Generally, the ethical considerations relating to a technology should be assessed with reference to the prevalent social and moral norms relevant to the technology, as well as with respect to the HTA itself (for example, the time at which a HTA is conducted).

An ethics workshop was undertaken, at which members of HIQA's HTA and Health Information and Standards Directorates discussed these issues. The findings of this workshop served to supplement a review of relevant literature that was undertaken. While systematic review literature was available,⁽⁵²³⁾ no systematic review specifically addressing the age group in question was identified. The main topics described in this chapter fall under five pillars of the ethical analysis domain of the EUnetHTA HTA Core Model[®], with patient and social perspectives discussed under these topic headings, where appropriate:

- benefit-harm balance (that is, providing benefits and balancing benefits against risks and costs)
- autonomy (that is, respecting the decision-making capacities of an autonomous person)
- respect for persons (that is, an individual's privacy, integrity and dignity)
- justice and equity (that is, fairness in the distribution of benefits, risks, and costs)
- ethical consequences of the HTA (that is, the considerations relating directly to conducting the assessment at this time).

A sixth pillar of the ethical analysis domain, 'legislation', was considered, but no specific concerns were identified for this pillar beyond those considered under the above five topics.

This chapter focuses on the ethical, patient and social implications of extending the BowelScreen programme to people aged 50 to 54 years, rather than examining the ethical and social consequences of colorectal cancer screening more broadly.

9.3 Benefit-harm balance of screening

Lowering the screening age increases the number of individuals undergoing screening, which may lead to earlier detection and potentially improved outcomes.⁽⁵²⁴⁾ However, it also raises concerns about potential harms, such as false positives and unnecessary procedures, including colonoscopies.⁽⁵²⁴⁾ Striking the right balance between potential benefits and harms is crucial, especially for younger individuals who may have a lower risk of developing colorectal cancer.⁽⁵²⁴⁾

9.3.1 Benefits of colorectal cancer screening in people aged 50 to 54

Earlier detection of colorectal cancer and pre-cancerous lesions

The primary benefit of a colorectal cancer (CRC) screening programme is the earlier detection of CRC. Screening can also facilitate the detection and removal of pre-cancerous lesions, which may otherwise progress to cancers (see Chapter 3).⁽¹⁰⁾ When cancer is detected at an earlier stage, the likelihood of the need for aggressive treatments is reduced. Cases of CRC detected by BowelScreen are more likely to be diagnosed at earlier stages, and less likely to be diagnosed at advanced stages compared to symptomatically detected cases (see Chapter 3, Epidemiology, section 3.9.3). Among those aged 50 to 54, approximately 140 cases of CRC are diagnosed each year, 67% of which are detected at advanced stages (Stage III or IV; see Chapter 3, section 3.9.3). Based on the evidence presented in Chapter 5 (Clinical Effectiveness), the extension of BowelScreen to those aged 50 to 54 would result in the earlier detection of CRC in this age group. The detection and removal of pre-cancerous lesions could also reduce the incidence and overall mortality of CRC in this age group. Early-stage cancers can often be treated with minimally invasive procedures, reducing the physical and emotional burden on patients. This leads to quicker recovery times and fewer complications, enhancing the overall patient experience.

Screening for colorectal cancer can also result in incidental diagnoses of other conditions, such as the endoscopic diagnosis of colitis at the time of colonoscopy. Incidental diagnosis of colitis has been reported in 3% of FIT-positive BowelScreen participants, representing an unintended benefit of the programme.⁽⁵²¹⁾

Cost effectiveness of screening those aged 50 to 54

Cost-effectiveness is important in the context of the ethical implications of a population-based screening programme, as it means that there is a better likelihood

of a healthcare budget being used effectively and efficiently. Inefficient use of the healthcare budget may be considered unethical, as resources could be used elsewhere. Screening for CRC using faecal immunochemical tests (FIT) has been shown to be cost-effective when compared to other screening methods, as well as compared to no screening.^(365, 367, 369) In the context of Ireland, the overall evidence presented in Chapter 6 suggested that screening all adults from age 50 to 74 is likely cost-effective compared with screening all adults from age 55 to 74, based on a willingness-to-pay threshold of €20,000 per QALY gained. This suggests that screening in those aged 50 to 74 would be a good use of the healthcare budget in the Irish context, representing good value for money and an efficient use of healthcare resources.

9.3.2 Harms of colorectal cancer screening in people aged 50 to 54

Psychological impact of screening

Screening for CRC may be associated with stress and anxiety for participants. A 2021 study examining the characteristics and attitudes of 1,545 first-round invitees to the BowelScreen programme (aged 60 to 70+ years) found that 22% (n=249) of study participants found the programme to be stressful.⁽³³⁶⁾ Participants noted sources of stress associated with screening included: waiting for results; feelings of embarrassment; completing the stool test itself; and the concern of a cancer diagnosis.⁽³³⁶⁾ Those receiving positive FIT results were significantly more likely to express stress surrounding the programme than those who received a negative FIT result (OR 7.7, 95% CI 5.3 to 11.3).⁽³³⁶⁾ This stress may be considered a harm of the programme, and is particularly relevant for those receiving false positive results, who may not experience any health benefit as a result of screening. While this study was limited to the age range of participants included in the first BowelScreen screening round, age did not appear to be associated with the likelihood of experiencing stress; there was no statistical difference in participants aged over 68 in terms of stress levels when compared to younger participants (age >68 years versus younger: OR 1.0, 95% CI 0.7 to 1.5).⁽³³⁶⁾

As part of the review of clinical effectiveness described in Chapter 5, three studies of the psychological harms of screening were identified. Of these, one study included participants aged 50 to 54, but did not present age-stratified results.⁽³²¹⁾ A 2020 study in the Netherlands explored associations between various demographic characteristics, including age, and psychological functioning among participants aged 55 to 75 referred for colonoscopy following a positive FIT.⁽³²⁴⁾ Age did not appear to be associated with the experience of psychological consequences (adjusted OR 0.97, 95% CI 0.94 to 1.00, $p=.075$) following colonoscopy. Worry about developing cancer, however, appeared to decrease with increasing age (adjusted OR 0.97 per year, 95% CI 0.95 to 1.00, $p=.037$).⁽³²⁴⁾

The potential for screening to cause anxiety is one of the factors informing BowelScreen's quality assurance standards.⁽³⁰⁵⁾ Ten standards specifically relate to timelines and turnaround times associated with the programme, including appointment wait times for colonoscopy and CT colonography, FIT result turnaround times, and colonoscopy and CT colonography result turnaround times. The primary rationale for these target turnaround times is to reduce anxiety and uncertainty for screening participants.

False negatives

A false negative in the context of CRC screening is typically defined as a negative result on a stool-based test such as FIT, despite the presence of a clinically relevant pathology. While less likely, false negatives can also occur at colonoscopy if lesions are not detected. False negatives can be harmful as they can result in colorectal cancer being missed, or being diagnosed at a later stage. The receipt of a false negative result may also give a participant a false sense of security and potentially result in a propensity to ignore or delay acting on symptoms that may be indicative of colorectal cancer in the time following a negative test result, as has been seen in breast cancer screening.⁽⁵²⁵⁾ This has the potential to delay treatment, resulting in more severe outcomes, including death.

Interval cancer, defined as 'a colorectal cancer diagnosed after a screening or surveillance exam in which no cancer is detected, and before the date of the next recommended exam',⁽⁵²⁶⁾ is a potential harm associated with CRC screening, and is common to all screening programmes.⁽⁵²⁷⁾ A 2014 meta-analysis of interval cancers reported across 13 population-based studies found that approximately one in 27 CRCs were interval cancers (defined as CRC occurring after an index colonoscopy).⁽⁵²⁸⁾ A 2024 Spanish study, which examined CRC diagnosed after a negative colonoscopy, reported CRC diagnosis rates between 0.4 and 4.1% between one and ten years following the procedure.⁽⁵²⁹⁾ Information on the occurrence of interval cancers, included as part of the information material provided to participants, can help to ensure that individuals are aware of the risks and to encourage interaction with a healthcare professional should symptoms occur. The current (as of January 2025) BowelScreen participant information leaflet, available online, provides information on the limitations of colorectal cancer screening, including the development of interval cancers and their rate of occurrence within the programme overall (stated as 'around two' in every 1,000 people screened).⁽⁵³⁰⁾

False positives

A false positive in the context of CRC screening is defined as a positive result on a stool-based test such as FIT, followed by a 'negative' colonoscopy. Estimates of the false positive rate (FPR) of FIT, that is the proportion of people without the condition

who will receive a positive FIT result, vary across studies and settings. FPR is a function of both the threshold used to denote FIT positivity, as well as what is considered a 'positive' finding on colonoscopy – that is, whether or not the presence of non-advanced adenomas or serrated polyps constitutes a 'positive' or 'negative' colonoscopy.⁽⁵³¹⁾ Studies included in the review of FIT test accuracy conducted as part of this HTA (see Chapter 4) mainly reported findings for colorectal cancer and advanced neoplasia (CRC and advanced adenomas); as such, a false positive FIT would represent an absence of CRC or advanced adenomas detected on colonoscopy (but not the absence of non-advanced adenomas or other lesions). The FPR for FIT thresholds between 40 and 45µg/g, calculated from data extracted from studies with colonoscopy as the reference standard and advanced neoplasia as target condition, ranged from 1.4% to 3.7%.

The extent to which FPR may vary by age is uncertain. As noted in Chapter 4, the review of FIT test accuracy identified limited age-stratified data on the clinical performance of FIT at thresholds similar to that used in Ireland, with no clear or consistent evidence to suggest that FIT test accuracy varies significantly by age for the detection of CRC at a threshold of 45µg/g. A 2018 meta-analysis found no evidence of a systematic effect of age on false positive FIT results, although the majority of included studies used a FIT threshold of ≤20µg/g.⁽²⁸⁵⁾ Based on data extracted from a report of the German colonoscopy screening 'BLITZ' study,⁽²⁷²⁾ the FPR in those aged 50 to 59 (at a FIT threshold of 45µg/g) was calculated as 2.6%, compared to 3.1% in those aged 60 to 79.

Colonoscopy harms

While individuals receiving false positive FIT results may not be at immediate risk of colorectal cancer, they will still undergo a colonoscopy, an invasive procedure with associated health risks. These adverse events can be broadly categorised into gastrointestinal and non-gastrointestinal events, as shown in Table 9.1.

Table 9.1 Adverse events associated with colonoscopy

Gastrointestinal adverse events	Non-gastrointestinal adverse events
Perforation - One of the most severe complications associated with colonoscopy - Often requires surgical intervention and can lead to significant morbidity.	Cardiopulmonary complications - including arrhythmias, myocardial infarction, and respiratory distress - The risk is higher in patients with pre-existing cardiopulmonary conditions.
Post-polypectomy bleeding - Most bleeding episodes are minor and can be managed endoscopically - Severe cases may require hospitalisation.	Sedation-related complications Hypotension and hypoxia are relatively common, particularly in older adults and those with comorbidities.
Infection Although rare, infections can occur, particularly if there is a failure in sterilisation or if the patient is immunocompromised.	

A 2020 Danish retrospective cohort study of adverse events relating to colonoscopy found that, of the 49,445 colonoscopies performed, 9.9% were associated with adverse events.⁽²⁵³⁾ These events were categorised as follows: bleeding (3.07%), pain (2.00%), instrumental including perforations (0.99%), infection (0.87%), cardiovascular (0.65%), pulmonary (0.36%), damage to skin/bones (0.34%), thromboembolic (0.1%), drug reactions (0.04%), and 'other' (1.62%).⁽²⁵³⁾ Ten of these events were fatal (0.20%).⁽²⁵³⁾

Adverse events of colonoscopies performed as part of the BowelScreen programme, including colonic perforation, post-polypectomy perforation and post-polypectomy bleeding requiring transfusion, are rare, affecting less than 0.1% of index colonoscopies performed between 2012 and 2023, and are detailed in Chapter 5 of this report. While screening participants receiving a colonoscopy following a false positive FIT are at risk of experiencing harms, adverse events including bleeding and perforation are more likely following polypectomy,⁽⁵³²⁾ and therefore will be less likely to impact individuals with a false positive FIT result (that is, where a colonoscopy takes place but adenomas or CRC are not identified). The BowelScreen quality assurance standards provide performance thresholds for each of these potential harms, as outlined in Table 9.2 below.⁽³⁰⁵⁾

Table 9.2 BowelScreen quality assurance standards for colonoscopy harms

Harm	Minimum performance threshold
Perforation	<1 per 1,000 colonoscopies
Post-polypectomy perforation	<2 per 1,000 colonoscopies where polypectomy is performed
Post-polypectomy bleeding requiring transfusion	<1% colonoscopies where polypectomy is performed

Source: BowelScreen quality assurance standards.⁽³⁰⁵⁾

Data modelled as part of the budget impact analysis (Chapter 7) estimated that there would likely be a small increase (zero to two cases per year) in complications associated with colonoscopies due to an increase in the number of procedures being carried out.

While data relating to harms in the 50 to 54 age group were limited, results from the review of clinical effectiveness conducted as part of this assessment (Chapter 5) indicated an increased rate of serious adverse events in those aged over 60 years, compared to those aged 59 years and under. For example, one study reported a serious adverse event rate of 198 per 100,000 in those aged 59 or younger, compared to a serious adverse event rate of 302 per 100,000 colonoscopies in those aged 60 or older. This suggests that physical harms in the 50 to 54 age group may be less likely than in the age group currently screened as part of the BowelScreen programme.⁽³³⁰⁾

Overtreatment and overdiagnosis

Overtreatment refers to medical interventions that may not provide a significant benefit to the patient and could potentially cause harm. In the context of CRC screening, this could involve the removal of polyps that might never have caused symptoms or developed into cancer. This can lead to unnecessary procedures, which carry their own risks. Overdiagnosis occurs when screening identifies lesions that would not have caused symptoms or death during a patient's lifetime. Treating these lesions, therefore, constitutes overtreatment.

Future screening participation following a false positive FIT

A 2019 retrospective cohort study of the impact of false positive FIT results (that is, faecal haemoglobin concentration above the screening threshold with no evidence of CRC or adenomas requiring surveillance) in the first BowelScreen round (2012–2015) found a significant reduction in re-attendance rates for individuals with false positive

FIT results.⁽⁵³³⁾ The re-attendance rate among screening participants with a false positive FIT was 73.1%, compared to 87.5% among those with a negative FIT. There was a significant association between older age and re-attendance; those aged 65 and older were less likely to re-attend for screening following a false positive result than those aged 60 to 64 (71.0% versus 77.6% respectively).⁽⁵³³⁾

Lower attendance rates among people with a previous false positive FIT may result from numerous factors. One reason could be the 'health certificate effect', whereby an individual receives a result indicating the absence of a disease or condition and feels that this has certified them as healthy and no longer in need of medical care or advice.^(534, 535) This may have longer term implications, as CRC tends to develop gradually. Cancerous or pre-cancerous lesions may not have been detected during the screening process, while CRC that was not present at the time of screening could develop subsequently. As a result, failure to attend for future screening may result in a missed or later diagnosis of CRC, which could have been identified in a subsequent screening round. With the proposed extension of the programme to the younger cohort, a decision to not attend for future screening may occur at an earlier age and impact future detection at an age when the individual may be more likely to experience CRC. Market research carried out on behalf of the BowelScreen programme suggested that additional information on symptoms to look out for between screenings is required.⁽⁴⁹⁵⁾ Targeting younger age groups through avenues such as social media and tailoring information specifically to these age groups may facilitate the dissemination of information and help to raise awareness.

9.3.3 Benefit-harm balance of colorectal cancer screening in those aged 50 to 54

Considering the balance of the benefits and harms outlined above, lowering the age for CRC screening to 50 could lead to earlier detection of cancers and pre-cancerous lesions in this age group. This earlier detection could reduce the need for more aggressive treatments, and enhance patient quality of life. The proportion of CRC detected at more advanced stages in older age groups may also decrease over time, as a result of the earlier detection and treatment of cancer and pre-cancerous lesions in the younger age group. Lowering the screening starting age from 55 to 50 is expected to be cost-effective, and may lead to healthcare savings by reducing the need for expensive treatments of more advanced cancers.

Screening for CRC can cause stress and anxiety for participants. This stress often stems from waiting for results, feelings of embarrassment, completing the stool test itself, and the fear of a cancer diagnosis. Targeted information campaigns on television and social media may help to reduce stigma and potential fears and anxieties associated with participating in the programme.

While many of the benefits and harms of CRC screening in those aged 50–54 may be similar to those in older age cohorts, the degree to which these benefits and harms are experienced vary. For example, given that the prevalence of CRC and advanced neoplasia is lower in those aged 50–54 compared to those aged 55–74, the positive predictive value of FIT in those aged 50–54 is also likely to be lower. This means that the proportion of colonoscopies at which no lesions will be detected may be higher among those aged 50–54 compared to older age groups. Positive predictive values and negative predictive values are discussed in more detail in Chapter 4 of this report. While screening for colorectal cancer may be less effective in those aged 50–54 than in older age groups due to an overall lower CRC incidence, the harms of screening may also be lower. Further, the potential harms of not screening those aged 50–54 requires consideration, as the benefits of earlier detection, treatment, and improved outcomes would not be realised in this age group. By balancing the benefits of early detection with the potential risks of screening, extending the screening programme to those aged 50–54 is likely to be an effective and efficient use of healthcare resources in Ireland.

9.4 Autonomy and respect for persons

9.4.1 Autonomy

The principle of autonomy emphasises the importance of respecting an individual's right to make informed decisions about their care, support or treatment.⁽⁵³⁶⁾ Individuals considering screening should be fully informed about the potential benefits, risks, and limitations of screening, especially in the context of the lower screening age.⁽⁴¹⁵⁾ One qualitative study of informed decision-making in the context of CRC screening found that those interviewed considered a 'good' screening decision to be one made through reasoning and intuition.⁽⁵³⁷⁾ However, CRC screening non-participants expressed feeling social pressure to participate.⁽⁵³⁷⁾ This highlights the need to ensure informed consent, including providing information about the potential for over-diagnosis and unnecessary procedures.⁽⁵³⁸⁾ For those aged 50 to 54, there may be a barrier in terms of knowledge and awareness of the programme, as their peers may be less likely to have participated in CRC screening, as well as potentially not being as aware of the risks of CRC compared to older age groups.⁽⁵³⁹⁾ As mentioned above, the use of tailored information and targeted social media campaigns may help to spread awareness of CRC in younger age groups.

Population screening programmes require a certain level of participation before a significant public health benefit can be realised.⁽⁵⁴⁰⁾ There is a need and benefit to promoting the BowelScreen programme to improve the uptake rate. In 2022–2023, the uptake rate was 46.4%.⁽¹⁴⁹⁾ The minimum quality assurance standard for uptake as set by the programme is $\geq 50\%$, with an achievable standard of $\geq 60\%$.⁽³⁰⁵⁾ Low uptake can result in health inequalities, as vulnerable groups are often less likely to

participate.⁽⁵⁴¹⁾ Despite this, it is also important that the promotion of high uptake rates be balanced against respect for individual preferences, and ensuring that individuals are making a fully informed choice before agreeing to participate. The BowelScreen quality assurance standards highlight that those offered screening should be given enough information to enable an informed choice about screening to be made, and that this information should include both the benefits as well as the limitations of screening.⁽³⁰⁵⁾ The National Screening Service (NSS) has outlined the reduction of healthcare inequalities through the improvement of equity and participation in its screening programmes as a strategic objective.⁽⁴⁷⁹⁾ This may be of particular importance for those aged 50 to 54, given that the incidence of CRC in this group is lower than in older age groups, which may impact the potential benefit of screening in these individuals.

While participation in national screening programmes is encouraged, it is also important that a person should be given the choice not to participate. The BowelScreen quality assurance standards recommend that an opt-out process be in place for those who do not wish to take part in the programme, and that these people should not be contacted further should they make this decision.⁽³⁰⁵⁾

Genetic testing

Individuals with a possible genetic predisposition for CRC may be identified either due to a family history, or as a result of a CRC diagnosis that raises suspicion of an inherited component due to certain patient or tumour-related features.⁽⁵⁴²⁾ While people with hereditary conditions such as Lynch Syndrome (LS) or attenuated familial adenomatous polyposis (AFAP) will, on average, develop CRC at a younger age than that which is currently screened,^(188, 190, 192, 194) extending BowelScreen to those aged 50 to 54 years increases the possibility that some individuals who are unaware of their genetic predisposition could be discovered and diagnosed as a result of screening. Those aged 50 to 54 may also be more likely to have a greater number of younger first-degree relatives who could be unaware of their genetic predisposition. An Irish review of clinical outcomes of high-risk familial CRC screening found that the median age for first diagnosis of those tested as a result of familial identification was 47.2 years.⁽⁵⁴³⁾ As a result, in the context of an age extension, the requirement for cascade testing could increase, in order to identify relatives with an inherited cancer predisposition and who may benefit from risk reduction and early detection measures.⁽⁵¹⁵⁾

In the context of cascade testing of relatives, obtaining informed consent is crucial. Individuals must be fully informed about the potential benefits and risks of genetic testing, as well as the implications of test results for their health and the health of their relatives.^(544, 545) Cascade testing can impact family dynamics, as it involves testing the family of individuals diagnosed with colorectal cancer. In Ireland, the

individual receiving the positive result is often the person who advises their family that they may be eligible for cascade testing. While this responsibility may be given to a healthcare practitioner to relay information, it requires the consent of the individual in the first instance.⁽⁵⁴⁵⁾ This can raise ethical issues related to family communication and the sharing of genetic information. A 2021 report on *The Unmet Need in Cancer Genetic Services* noted concerns regarding privacy and confidentiality, as well as the longer-term management of genetic data and samples in Ireland.⁽⁵¹⁶⁾ The programme will need to continue to navigate these complex dynamics sensitively and ethically, ensuring that individuals have the support they need to communicate genetic risks to their relatives.

9.4.2 Respect for persons

Respect may be defined as the 'objective, unbiased consideration and regard for the rights, values, beliefs and property of other people'.⁽⁵³⁶⁾ The EUnetHTA HTA Core Model® suggests that the impact of a health technology on respect should be considered in terms of effects on human dignity, moral, religious or cultural integrity, and the privacy of the participants. Cultural or religious considerations may impact an individual's ability or willingness to participate in the BowelScreen programme. Those from specific cultural and or religious backgrounds may refuse to participate for reasons such as associated stigma, and where colonoscopy is concerned, the potential for an invasive medical procedure that may conflict with a person's religious convictions. Cultural or religious factors may be more likely to impact uptake among those aged 50 to 54, due to an increased level of cultural and religious diversity in this age group compared to the older cohorts.^(546, 547)

9.5 Justice and equity

Expanding screening to younger individuals may exacerbate existing disparities in access to healthcare.^(416, 524) It is important to ensure equitable access to screening for all individuals, regardless of socioeconomic status, race, ethnicity, or geographic location.^(524, 548) This section describes the considerations for justice and equity of the potential extension of the BowelScreen programme to those aged 50 to 54.

9.5.1 Distributive justice

Distributive justice concerns the fair allocation of resources within a society. In the context of healthcare, this principle demands that all individuals have equitable access to medical services, including preventive measures like cancer screening. The NSS outlines the reduction of inequality in screening as a strategic objective in its 2023–2027 strategic plan.⁽⁴⁷⁹⁾ A strategic framework aimed at understanding and improving equity in NSS screening programmes was also developed using a co-production approach, including consultations with community, voluntary and statutory sectors, patient representatives, and NSS staff.⁽⁵⁴⁹⁾ The 2024–2025 Action

Plan outlined priority areas for development, which includes the creation and delivery of an education, learning and development plan for NSS staff and screening providers regarding equity in screening, as well as the timeframe for completion of discrete objectives.⁽⁵⁵⁰⁾

Expanding CRC screening to those aged 50 to 54 aligns with the principle of distributive justice by addressing the needs of a population that may be at an increased risk but currently lacks access to screening. Globally, both CRC incidence and mortality are higher in those aged 50 years and above, compared to younger adults, with the incidence of colorectal cancer rising significantly after the age of 50.⁽²¹⁸⁾ By including individuals aged 50 to 54 in the screening programme, cancer may be detected at an earlier, more treatable stage, thereby improving outcomes and reducing healthcare costs associated with advanced cancer treatment in this age group.⁽⁵⁵¹⁾ This proactive approach may help to ensure that resources are allocated in a manner that maximises public health benefits and minimises disparities in cancer outcomes. Participation in the BowelScreen programme is free for eligible individuals, which helps to maintain a level of equity in CRC screening in Ireland. However, it is important to note that other indirect expenses, such as travel to and from endoscopy or CT colonography units, time off work to attend follow-up appointments, and childcare still apply. These indirect costs may also disproportionately affect certain groups, such as those from lower socioeconomic backgrounds or those with less familial or social support.

Lowering the starting age of screening from 55 to 50 is likely to be cost-effective (see Chapter 6). Other potential benefits to lowering the screening age could include a reduced need for chemotherapy as a result of earlier detection, which could alleviate day ward and outpatient capacity.⁽⁵⁵²⁾ Another potential benefit is that cases may be diverted from the symptomatic service in the longer term, as people are identified through screening rather than presenting symptomatically (see Chapter 7). This may in turn reduce the strain on symptomatic services.

Screening programmes should not exacerbate health inequalities,⁽⁵⁵³⁾ and expansion of the programme should not infringe on the age groups currently being screened. As colorectal cancer incidence increases with age, and a diagnosis of CRC is more likely in older age groups, it could be argued that investment in the programme to target uptake in the existing age groups may be more equitable than an expansion of the age range to include younger individuals. Extending the programme to those aged 50 to 54 may not minimise disparities if the same group of individuals is screened repeatedly, while those who may be at higher risk may be less likely to take up screening. Efforts should be made to reach underserved populations, as well as those with existing conditions (such as those with mental health conditions, or other restrictive diseases or illnesses), and those with lower incomes, to provide equitable access to screening services. This is particularly important, as these people may

benefit the most from screening, despite the fact that they are less likely to participate in the programme.^(46, 554, 555) For example, a 2023 review of Irish studies suggested that lower socioeconomic position, as well as being a member of the Traveller community, were negatively associated with participation in colorectal cancer screening.⁽⁵⁵⁴⁾ The Traveller community, in particular, may benefit from an extension of BowelScreen to those aged 50 to 54 in terms of distributive justice, as the proportion of those in the Traveller community who would be eligible for screening would increase significantly.⁽⁵⁵⁶⁾

It is also important that an expansion of screening does not adversely impact the provision of symptomatic services. Lowering the screening age is likely to strain healthcare resources, including financial resources, staffing, endoscopy, histopathology, and radiology services and screening infrastructure (see Chapter 8). For example, at the end of January 2025, 12,283 patients in the symptomatic setting were experiencing a wait time of over 12 weeks for a gastrointestinal (GI) endoscopy appointment, including 2,653 who were waiting between six and 12 months and 515 patients who were waiting over 12 months.⁽⁴²¹⁾ Similarly, histopathology workloads have increased significantly, with deteriorating biopsy turnaround times.⁽⁴²⁸⁾ A 'capacity demand mismatch' has also been highlighted within radiology services, due to growing and increasingly complex workloads coupled with inadequate resourcing.⁽⁴³⁰⁾ As BowelScreen operates within the general symptomatic services, the ethical implications of increasing screening workloads in the context of ongoing capacity challenges should be considered. Significant investment is likely to be required to ensure sufficient capacity to meet demand from both screening and symptomatic services. It is important to ensure that the benefits of expanded screening justify the resources required.

9.5.2 Uptake of colorectal cancer screening

Uptake of CRC screening tends to be poor when compared to other Irish screening programmes. Between 2022 and 2023, the uptake of BowelScreen was 46.4%.⁽¹⁴⁹⁾ In contrast, the uptake rate of the BreastCheck screening programme exceeded 70% in 2022.⁽⁵⁵⁷⁾ Reported reasons for lower uptake of CRC screening include 'embarrassment' and 'disgust' surrounding the initial test, the invasiveness of colonoscopy, lack of knowledge (based on health literacy and knowledge of others with CRC or cancer in general), and perception of risk.⁽⁵⁵⁸⁻⁵⁶⁰⁾ A 2015 qualitative study examining reasons for non-participation in the Northern Ireland Bowel Cancer Screening Programme identified themes such as fear of cancer, the test procedure, social norms, past experience of cancer and screening, and lack of knowledge or understanding about bowel cancer screening as potential reasons for non-participation.⁽⁵⁶¹⁾ A survey of people who had been invited to participate in a FIT-based screening programme in Dublin (prior to the commencement of BowelScreen) found that negative cancer and screening-related beliefs and or emotions were

negatively associated with participation.⁽⁵⁵⁹⁾ For uptake of colonoscopy following a positive FIT result specifically, reasons for non-participation reported in the 2022–2023 BowelScreen programme report included the person opting to attend privately (35%), not wishing to attend (33%), being seen elsewhere (15%), finding it too far to travel (5%) or having no transport (1%).⁽¹⁴⁹⁾

A range of factors may affect participation in CRC screening programmes. In addition to age, factors including gender, socioeconomic status, ethnicity, geographic location, and vulnerability may affect screening uptake. While the extent to which these interact with age is unclear, it may be important to consider variations in screening uptake across different groups when considering the ethical implications of extending the programme. The following section considers the potential impact of age, gender, socioeconomic status, ethnicity, geographic location, and vulnerability on the uptake of CRC screening.

Age

Screening participation has been shown to vary by age. In Ireland, BowelScreen uptake rates have ranged from 38.1% in those aged 60 to 64 years to 49.9% in those aged 65 to 69. In the first round of a FIT pilot study targeting those aged 50 to 74, which took place in a large Dublin hospital, uptake in those aged under 60 was lower than in those aged 60 to 64, 65 to 69, and 70 to 74, with participation rates of 57%, 61%, 66%, and 62%, respectively.⁽⁴⁴⁴⁾ A second study, based on two screening rounds from the same pilot, similarly found that age was associated with a higher rate of participation: the mean age of participants was 62.1 years, compared to a mean age of non-responders of 60.2 years ($p < 0.0001$, 95% CI 1.14, 1.24).⁽⁴⁹³⁾

Lower screening participation rates in the 50 to 54 age group, compared to those aged 55 and older, have also been demonstrated internationally. For example, in the United States in 2018, approximately 50% of adults aged 50 to 54 were up to date with CRC screening, compared to 79% of adults aged 65 to 75.⁽⁵⁶²⁾ Those aged 50 to 54 are more likely to be in full-time employment and to have caring responsibilities compared to their older peers.⁽⁵⁶³⁾ These factors may impact a person's ability to attend for colonoscopy, and as a result may impact their willingness and or ability to participate in the programme.

Gender

As discussed in Chapter 2 of this HTA, uptake in the BowelScreen programme has consistently been higher in women than men. Men and women often exhibit different health-seeking behaviours, which can impact their participation in colorectal cancer screening. Women are generally more proactive in seeking preventive healthcare services compared to men.⁽⁵⁶⁴⁾ This difference may be due to women's increased contact and experience with reproductive health services,⁽⁵⁶⁵⁾ as well as social norms

that encourage women to be more health conscious and to engage in regular health check-ups, including cancer screenings.⁽⁵⁶⁶⁾ For example, in the 2019 Irish Health Survey carried out by the Central Statistics Office, 82% of women reported that they visited a GP in the 12 months prior to the survey, compared to 68% of men.^(567, 568) Women may also perceive themselves to be at a higher risk of developing CRC due to a greater awareness of cancer risks as a result of interactions with breast and cervical cancer screening programmes. The 2010 French Health, Healthcare and Insurance Survey found that, among women, participation in breast and cervical cancer screening increased participation in CRC screening.⁽¹³⁶⁾ In contrast, men may underestimate their risk of colorectal cancer, leading to lower screening uptake. Reduced awareness among men was reflected in a 2020 publication, which found that more men than women (57% versus 44%) did not consider themselves to be at high risk of developing CRC.⁽³³⁶⁾ Further, market research carried out on behalf of the BowelScreen programme (eligible age 60 to 69 at the time of the survey) found that among those surveyed (n=320), 94% were aware of BowelScreen to some extent (the level of knowledge regarding colorectal cancer and the programme itself varied), with women being more aware than men (98% vs 91%).⁽⁴⁹⁵⁾ Addressing knowledge and perceptions through targeted education and awareness campaigns may help to reduce gender disparities in screening uptake.

Socioeconomic status, geographic location, and ethnicity

Socioeconomic status (SES) has been shown to impact participation in multiple screening programmes. A 2016 study examining the effects of sex and deprivation on participation in CRC screening in Dublin found that area-level deprivation was a stronger predictor for screening uptake than age or gender.⁽⁴⁴⁴⁾ The study authors also acknowledged that, given that their study population was based in a deprived area of a large city, deprivation at a national level may demonstrate even larger disparities in screening uptake.⁽⁴⁴⁴⁾ Targeted educational campaigns in low-income and underserved communities may raise awareness and encourage screening, particularly for younger age groups who may not yet see the immediate need for screening.

Ethnicity may also impact CRC screening uptake. A 2021 study examining ethnic disparities in CRC screening uptake (using gFOBT) in London found that white British individuals had the highest level of uptake (52.4%), followed by Irish (50.9%) and Chinese (50.8%).⁽¹³⁷⁾ All other ethnicities were found to have lower uptake rates, ranging from 29.4% to 49.2%.⁽¹³⁷⁾ Similarly, uptake of CRC screening in Scotland between 2007 and 2013 was highest amongst white British and Chinese individuals, with lower uptake rates in all other ethnic groups.⁽¹³⁸⁾

While FIT could be considered a test without geographic constraints, as the test kit is posted to participants and returned by mail, limitations and difficulties may arise at

the point of a screen-positive FIT result, when a participant is referred for colonoscopy. A 2021 systematic review exploring the influence of rural residence on the uptake of cancer screening found that there was a significant difference in the uptake of rural compared with urban residents.⁽¹³⁹⁾ The results of the four studies examining colorectal cancer specifically indicated that those in rural areas are approximately two thirds as likely to participate in CRC screening compared to their urban counterparts (pooled odds ratio 0.66, 95% CI: 0.50, 0.87), regardless of the screening modality (stool based or visual).⁽¹³⁹⁾ In Ireland, those living in rural areas, in particular those in the midlands, may experience difficulties in accessing endoscopy services within a reasonable travel distance from their home. This may be compounded in the 50 to 54 age group, who are more likely to be in full-time employment and have additional caring responsibilities compared to older age groups.⁽⁵⁶³⁾

Individuals with other conditions and vulnerable persons

Individuals with conditions such as intellectual disabilities, mental health difficulties or dementia may face unique barriers to screening not faced by members of the wider population. These barriers could include difficulties with comprehending information around the screening programme, decision-making capacity, as well as logistical issues. In 2023, the NSS published a report exploring the needs of disabled people in accessing national screening services.⁽⁵⁶⁹⁾ This report found that four out of eight people with an intellectual disability reported never having received a screening invitation despite being eligible; absence from the register or failure of a gatekeeper to pass on the invitation were highlighted as potential reasons for this.⁽⁵⁶⁹⁾ Themes such as inaccessible communications, dependency on others for assistance, and logistical issues in terms of travel were all raised as barriers to participation.⁽⁵⁶⁹⁾ A Canadian study found that individuals with an intellectual disability were about half as likely to be up to date with colorectal cancer testing than their peers without an intellectual disability (OR 0.53, 95% CI: 0.51, 0.54).⁽⁵⁷⁰⁾ In Denmark, people with mental health conditions have been reported to be less likely to participate in screening.⁽⁵⁷¹⁾ Recommendations to facilitate participation of disabled people in population-based screening programmes include the inclusion of people with disabilities in all aspects of the service design, the provision of accessible communications, and the provision of in-service disability awareness training to all staff involved in screening.⁽⁵⁶⁹⁾

Other vulnerable groups, such as people seeking international protection, people who are homeless, or individuals from the Traveller community may also experience difficulties in participating in the BowelScreen programme. Given that the FIT kit is sent via mail, individuals who do not have a permanent or long-term address on record may have difficulty in receiving the test. As eligible individuals are primarily identified through the Department of Social Protection database, those who have not

interacted with this service may be missed. The NSS and National Cancer Control Programme have worked with the Traveller community to increase participation in BowelScreen since 2022.⁽⁴⁸⁸⁾ The initiative has reported success in addressing barriers including challenges with literacy, sending and receiving post, and fear of the screening process.⁽⁴⁸⁸⁾

9.5.3 Targeted versus universal screening

Targeted screening focuses on specific populations known to be at a higher risk for colorectal cancer. One example of targeted screening is providing differential screening according to sex. Targeted screening by sex can be approached differently depending on the goal of the disparity being addressed. For example, in Germany, CRC screening is offered to men at an earlier age than women in order to address the fact that CRC is more common in men.⁽¹⁰⁵⁾ In contrast, Sweden uses a lower FIT threshold for positivity in women than men, to address the fact that women have lower FIT positive rates and tend to benefit less from colorectal cancer screening generally.^(103, 104, 296) However, it has also been suggested that the use of sex-specific thresholds could introduce sex differences in positive and negative predictive values and may disadvantage men.⁽²⁹⁶⁾ Any consideration of risk-based screening strategies, including the use of sex-specific thresholds, would warrant careful deliberation to avoid unintended consequences.

9.5.4 Private screening

FIT kits can be purchased privately from a number of providers in Ireland, with prices ranging from €45 to €89 according to the websites of four private providers consulted for this HTA (accessed in October 2024). Quality standards, performance characteristics and follow-up of people with positive results may vary across providers. One website suggested that a FIT result above 50ng/mL may require further investigation; while the FIT device was not specified, this threshold is considerably lower than that used by BowelScreen. Regarding follow-up for positive test results, the websites either recommended that the person seek further medical advice from their GP,^(572, 573) suggested that the provider could offer guidance on next steps⁽⁵⁷⁴⁾ or help the person to schedule a private consultation.⁽⁵⁷⁵⁾ While it is unclear to what extent these services are available in Ireland, increased media attention on CRC screening, including as a result of this HTA, could lead to a greater interest among individuals who may be outside of the eligible age range for BowelScreen, and who may turn to private testing. This may pose challenges for GPs determining whether to refer a patient for colonoscopy based on the results of a private FIT, as well as potentially increasing inequity in CRC screening.

There are numerous private endoscopy clinics in Ireland, and individuals may opt to attend privately following a private FIT, or to reduce waiting time following a FIT test within the BowelScreen programme. In the 2022–2023 BowelScreen programme

report, 35% of those who did not attend for colonoscopy through the programme reported having attended privately instead. The extent of private CRC screening (FIT or colonoscopy) in Ireland is unclear. However, it is important to consider that this avenue of testing may bring inequities into colorectal cancer screening in Ireland, as those with the means to pay for private testing may gain easier access to services such as colonoscopy than their counterparts accessing services through the public system or through BowelScreen.

9.5.5 Financial burden of colorectal cancer for patients and families

Financial toxicity (that is, the financial distress caused by cancer treatment), is a challenge for all age groups. One 2017 Irish study found that 90% of colorectal cancer survivors experienced an out-of-pocket cost of, on average, €1,589 in the year following diagnosis.⁽⁵⁷⁶⁾ More recently, a 2022 paper on CRC survivorship found that the financial impact of the disease persisted for many participants, some of whom remained on long-term leave from employment.⁽⁵⁷⁷⁾ Those aged 50 to 54 may be more likely to be affected by indirect costs, such as lost income and reduced productivity or ability to work.^(577, 578) Family members and carers may also experience financial burden throughout the diagnostic and treatment pathway.⁽⁵⁷⁹⁾ One Irish study found that 99% of carers surveyed had incurred weekly direct and indirect hospital costs of an average of €393 (IQR €131–€541) during the diagnosis and treatment phase.⁽⁵⁷⁹⁾ While not specific to those aged 50 to 54, the 2017 study found that, when modelled, stage at diagnosis (specifically stage III), as well as age below 70, were associated with higher out-of-pocket costs.⁽⁵⁷⁶⁾ Extending BowelScreen to those aged 50 to 54 would likely result in the earlier detection of CRC in this age group, which may help to reduce financial toxicity associated with advanced cancer treatment.

9.6 Ethical consequences of the HTA

This section will consider the ethical consequences of the HTA itself, namely the scope of the HTA, availability of evidence and the timing of the assessment.

9.6.1 Scope of the HTA

This HTA considers the expansion of the BowelScreen programme to those aged 50 to 54. Factors other than age, such as the FIT positivity threshold, screening intervals, screening methods and risk-based strategies could also be considered in future, as they may have an impact on the clinical and cost effectiveness of the programme, as well as on capacity requirements and the equitable allocation of resources. Future consideration of these factors could help to ensure the ongoing effectiveness, safety, and equitability of the programme and allow for the determination of the optimal strategy within the resources available.

9.6.2 Timing of the HTA and availability of data

Any expansion of the BowelScreen programme will need to consider capacity particularly in relation to the provision of colonoscopy, histopathology and radiology services. The BowelScreen FIT positivity threshold was originally set at 20µg Hb/g; however, in 2014, in response to endoscopy capacity challenges, the programme increased this threshold to 45µg Hb/g. The increased threshold resulted in lower positivity rates (from 8.6% to 4.1%) and fewer overall colonoscopy referrals.⁽⁶¹⁾ However, endoscopy capacity in Ireland remains strained, with wait times of over 18 months for some patients outside of the BowelScreen programme. At the end of January 2025, over 27,000 patients (excluding children and screening participants) were waiting for gastrointestinal (GI) endoscopy appointments.⁽⁴²¹⁾ This may have negative implications for BowelScreen if the programme were to expand. Specifically, it may be increasingly difficult for the programme to maintain quality assurance standards for waiting times should more colonoscopies be required as a result of an increased number of people being screened.

While the National Cancer Strategy 2017–2026 and the 2020 Programme for Government outlined a commitment to expand BowelScreen to those aged 55 to 74 as per the original aim of BowelScreen,^(1, 2) as of April 2025, this has not yet been achieved. The National Elective Ambulatory Care Strategy (2021) outlined a proposed increase in the HSE's capacity to provide elective procedures, including endoscopy, with the introduction of new elective treatment centres (previously referred to as elective hospitals) across the country.^(472, 473) The new elective treatment centres are expected to provide 42 additional endoscopy suites nationally, which are estimated to provide capacity for an additional 128,100 endoscopies annually.⁽⁴⁷²⁾ While this increase in capacity could improve the ability of BowelScreen to deliver additional screening and surveillance colonoscopies, the impact of these hospitals and the actual additional capacity they will provide is uncertain. Similarly, histopathology workloads have increased significantly, with deteriorating biopsy turnaround times.⁽⁴²⁸⁾ Lowering the screening age is likely to further strain healthcare resources and may adversely impact symptomatic services. Capacity is discussed further in Chapter 8 of this report.

At the time of writing, the BowelScreen programme screened those aged 59 to 70 years, with an anticipated expansion to those aged 58 to 70 in 2026.^(15, 580) While this HTA considered a potential extension to those aged 50 to 54, some of the assumptions and calculations carried out in areas such as the budget impact analysis, organisational considerations, and cost-effectiveness chapters were based on comparison with the expected scenario of screening those aged 55 to 74 years, as this was the age range previously committed to. As a result, in some instances projections and modelled effects were used instead of programme data that may become available in future when BowelScreen extends to encompass the 55 to 74

age group. The full extent of the investment or organisational changes that will be required as the programme continues to expand may not have been captured by the modelled programme.

Importantly, limited data were available specific to the expansion of an existing programme to those aged 50 to 54. Evidence for the clinical effectiveness of screening has generally considered alternative screening modalities or no screening as the comparator, rather than comparing the clinical effectiveness of screening at a starting age of 50 to the effectiveness of screening from age 55. Consideration of cost effectiveness involved a critical appraisal of published international models rather than the generation of a bespoke model specific to the Irish setting. Age-stratified data on the test accuracy of FIT at positivity thresholds similar to that used by BowelScreen were also limited. Overall, there was a dearth of disaggregated data relating specifically to those aged 50 to 54, and a lack of literature specifically comparing screening in this age group with older age groups. In future, as evidence for different age groups emerges, elements of the HTA such as the budget impact analysis and clinical effectiveness of screening may be subject to a lesser degree of uncertainty overall.

9.7 Discussion

9.7.1 Benefit-harm balance of screening those aged 50 to 54

It is important to consider both benefits and harms when introducing or amending a population-based screening programme. Earlier diagnosis and treatment, reduction of CRC incidence and mortality, as well as the risks of colonoscopy, have been documented as a result of the introduction of CRC screening programmes. What is less certain is the benefit of screening in those aged 50 to 54, compared to commencing screening at age 55. While those aged 50 to 54 are likely to benefit from earlier detection and treatment, the benefit when compared to screening from age 55 would likely be reduced as a result of lower incidence rates in this age group compared to older age groups. However, while the benefit may not be as high in this age group, harms relating to colonoscopy also appear to be reduced.

Screening in those aged 50 to 54 may also have a longer term impact on the older age groups as the extension is implemented and established. Starting screening earlier may reduce the number of people in older age groups undergoing procedures such as polypectomy at the time of colonoscopy and cancer treatments (following CRC diagnosis), as they are more likely to have been identified and treated at an earlier age where outcomes such as survival may be improved, and where harms are less likely.

9.7.2 Inequities in colorectal cancer screening

The aim of screening is to reduce the morbidity and mortality of an illness or disease in the population. As a publicly-funded programme, BowelScreen aims to ensure equity in colorectal cancer screening, which is reflected in the NSS 2023–2027 strategic plan objectives.⁽⁴⁷⁹⁾ While this may be the aim of the programme, aspects of inequity in screening still persist. For example, while women participate in BowelScreen at a higher rate than their male counterparts, FIT-based screening programmes are generally associated with a lower reduction in CRC incidence and mortality in women than in men.^(103, 104, 296, 297) Also, underserved groups, such as those from lower socioeconomic backgrounds, those from the Traveller community, and individuals with intellectual disabilities are less likely to access CRC screening, but are often at a higher risk. For example, in Ireland, men in the most deprived population quintile had a significantly higher incidence rate (8%) from 2014 to 2018, compared to those in the least deprived quintile.⁽⁵⁸¹⁾ These individuals may experience health inequalities at a wider level across the healthcare service. The NSS has committed to ensuring that all eligible people can access NSS screening services, highlighting health equity as a key priority.^(549, 550) One initiative to reduce disparities in the BowelScreen programme has been the introduction of easy-to-read and culturally appropriate information for those in the Traveller community.⁽⁵⁸²⁾ Other initiatives to improve equity in screening include improving health literacy through various methods, such as the development of accessible materials, engaging with local communities, and staff training.^(583, 584)

9.7.3 Implications of screening in those aged 50 to 54 for families, the general public and the healthcare system

While the age expansion of the programme considered by this HTA focuses on those aged 50 to 54, the implications of this expansion would not be limited to a single group. The families of those receiving a CRC diagnosis may be referred for cascade testing, which may have ethical implications. Referred family members will need to make a decision about whether or not to undergo testing, which could cause anxiety and stress. This is compounded by the fact that the results of the genetic testing may be negative, in which case these harms may have been unwarranted. Genetic testing is likely to be offered to family members younger than the screening participant who triggered the testing, and the ethical issues discussed in this chapter may have a similar or even more profound impact on family members who are younger still.

The expansion of the programme would constitute an increase in healthcare spending. Depending on how the programme is rolled out, screening those aged 50 to 54 could cost an extra €45 million to €66 million over ten years (versus just screening people aged 55 to 74). The HSE is a publicly-funded system (receiving funding from tax-payers), and has a limited budget. Because the tax-payer is paying

both directly and indirectly for the services provided by the HSE, it is important that these are a cost-effective and beneficial use of funds. As discussed in Chapter 6 of this report, screening for colorectal cancer with FIT in this age group is likely cost-effective compared to no screening. However, as outlined in Chapter 7 and Chapter 8, it will require significant investment and organisation to implement an expansion. In essence, there is a need to consider both the cost effectiveness of the programme expansion and what is feasible for the programme to deliver in both the short and long term.

As previously discussed, private avenues for CRC screening are available. The expansion of the programme to a wider age group may increase awareness of CRC and screening, which could in turn lead to an increased demand for private testing. An increase in private CRC screening may increase inequity, as those with the means to pay for private stool testing may gain easier access to services such as colonoscopy than their counterparts accessing services through the public system or through BowelScreen. An increase in private FIT testing could also further strain colonoscopy, histopathology and radiology capacity.

9.7.4 Conclusion

The expansion of the BowelScreen programme to include those aged 50 to 54 raises a variety of ethical issues. While the benefit of screening may be lower in those aged 50 to 54 due to lower incidence and mortality rates in this group compared to those aged 55 to 74, the harms of screening are also reduced. Extending BowelScreen to those aged 50 to 54 will increase demand on colonoscopy, histopathology and radiology resources, directly impacting an already strained healthcare system. It is important to consider the ethical implications of the potential diversion of resources from symptomatic services, and to ensure that the benefits of expanded screening justify the additional costs and resources. Should the decision be made to lower the screening age, the benefits and harms of screening in this age group, autonomy, equity for underserved groups, and overall participation, should also be carefully considered at the implementation stage of the programme, and mitigated where possible through careful planning and programme monitoring.

10 Discussion

10.1 Introduction

The purpose of this HTA is to systematically synthesise the evidence in relation to extending the BowelScreen colorectal cancer screening programme to those aged 50 to 54 years, in order to support the National Screening Advisory Committee (NSAC) in its recommendation to the Minister for Health on this topic. The HTA examined the clinical, economic, resource and ethical considerations associated with extending BowelScreen to include those aged 50–54. This chapter considers the totality of the evidence presented in the previous chapters, with respect to the NSAC *Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme*.⁽³⁾ Section 10.2 summarises the epidemiology and treatment of colorectal cancer. Section 10.3 considers the screening method, including the acceptability and uptake of FIT (section 10.3.2) and developments in alternative screening methods (section 10.3.3). Section 10.4 outlines the key findings regarding the clinical and cost effectiveness of lowering the screening age, while Section 10.5 considers the organisational and resource implications.

10.2 The condition and intervention

Considering the NSAC criteria, CRC presents an important public health problem, with a well-documented natural history. In Ireland, CRC is the second-most common cancer in men and the third-most common cancer in women, with approximately 2,750 new cases each year. CRC is the third leading cause of cancer death in Ireland, with approximately 1,000 CRC-related deaths annually.⁽⁷⁾ While the number of CRC cases has increased in the last two decades in Ireland, the crude incidence rate per 100,000 people peaked in 2015 and has remained stable since (see Chapter 3). Incidence has increased in those younger than 50, although the absolute incidence in this age group remains low. Colorectal cancer mortality in age groups older than 60 in Ireland has declined over time, but has remained stable in younger age groups.

Colorectal cancer typically develops slowly. Symptoms are often subtle, absent, or lack specificity at the earlier stages of cancer development. As survival is better if detected at earlier stages, the disease is a suitable target for a population-based screening programme. In Ireland, most screen-detected cancers are found at early stages (stages I or II, 62%; see Chapter 3). Treatment plans vary according to cancer stage, and may include a combination of surgery, chemotherapy, and or radiotherapy. As well as facilitating early detection, screening may also lead to a reduction in CRC incidence over time, through the detection and removal of pre-cancerous lesions. However, the natural history of pre-cancerous lesions is more uncertain. As these lesions are usually asymptomatic, their natural history is interrupted by polypectomy once detected.⁽⁵⁸⁵⁾ The clinical effectiveness of CRC

screening with regard to reductions in mortality and incidence are discussed in further detail in section 10.4.1.

10.3 The screening method

As outlined in the NSAC criteria, the screening method should be simple, safe, reliable and validated to ensure effective detection of the target condition.⁽³⁾ While colonoscopy is considered the reference standard for the detection of colorectal cancer and pre-cancerous lesions, it is an invasive procedure that is associated with a risk of complications, including bleeding and perforation.^(49, 253) Colonoscopy is also resource-intensive and requires access to specialist endoscopy facilities and trained endoscopists. As a result, most population-based screening programmes use a two-step strategy, in which a non-invasive screening test is used to identify individuals for further diagnostic testing.

In 2003, the European Council recommended 'screening with faecal occult blood test in men and women aged 50–74 years'.⁽¹⁶⁾ The 2022 updated European Council Recommendation outlined faecal immunochemical tests (FIT) as the preferred screening test for referring individuals aged 50–74 for follow-up colonoscopy.⁽⁶⁸⁾ FIT devices can be qualitative or quantitative. Analysis of quantitative FIT samples is automated, making the interpretation of results less subjective. Since its inception in 2012, BowelScreen has used a quantitative FIT device as its primary screening test, with follow-up colonoscopy or CT colonography for individuals with a positive FIT result. Compared to older guaiac-based faecal occult blood tests (gFOBT), FIT is superior in detecting advanced adenomas and colorectal cancer, with higher sensitivity and specificity for lower gastrointestinal bleeding and improved uptake.⁽³¹⁾ Invitation to two-yearly FIT-based screening, compared to invitation to once-off colonoscopy, has also been reported to be non-inferior for the outcome of CRC mortality at 10 years (RR 0.92; 95% CI 0.64, 1.32), with higher participation rates among those randomised to invitation to FIT-based screening compared to those randomised to invitation to colonoscopy screening.⁽⁵⁸⁶⁾ The processing of BowelScreen FIT samples is outsourced to a private laboratory under tender. The BowelScreen QA standards outline the quality assurance requirements and standards that must be met by the service provider (see Chapter 8, section 8.4.1).

10.3.1 FIT thresholds

Quantitative FITs estimate the concentration of haemoglobin (Hb) in stool. The concentration of Hb at or above which an individual is considered to have a positive screening test result is referred to as the FIT threshold. FIT thresholds are not fixed, and may be adjusted based on the positivity rate, sensitivity for CRC, or colonoscopy capacity.^(256, 257) The likelihood of neoplasia detection is related to both the test accuracy of FIT and the underlying prevalence of disease. The threshold chosen for

positivity will impact positivity rates and colonoscopy requirements, as well as the mortality and incidence benefits and cost effectiveness of a programme.⁽⁵⁸⁵⁾

Adjustment of the threshold can therefore facilitate the management of resource requirements, including colonoscopy, workforce availability, and treatment costs.⁽⁵⁸⁵⁾

Internationally, the threshold used to determine a positive FIT result was found to range from 15µg/g to 120µg/g, based on countries included in a review of international practice (see Chapter 2). These thresholds are likely determined by a number of factors, including epidemiological considerations such as local cancer incidence and prevalence, as well as organisational factors such as budget and endoscopy capacity.

As noted in Chapter 4, the reported sensitivity and specificity of FIT for the detection of CRC and pre-cancerous lesions have varied widely according to the FIT device used and threshold applied to denote test positivity.^(40, 73, 259) Generally, sensitivity increases at lower FIT thresholds, while specificity increases at higher thresholds.^(40, 73) As a result, lower thresholds result in higher cancer and adenoma detection rates, as well as higher false positive rates. In Ireland, BowelScreen originally commenced screening using a threshold of 20µg/g, which was subsequently increased to 45µg/g to relieve pressure on endoscopy services. The increased threshold resulted in lower positivity rates (from 8.6% to 4.1%) and fewer overall colonoscopy referrals, while the CRC detection rate per 1,000 people screened decreased from 3.8 at a FIT threshold of 20µg Hb/g to 2.3 at a threshold of 45µg Hb/g.⁽⁶¹⁾

As colonoscopy is a resource-intensive and invasive procedure with a risk of serious adverse events, it is important to consider the risks and benefits when setting or adjusting the FIT threshold. A 2024 study based on data from a Norwegian CRC screening trial, which included participants aged 50–74 and used a FIT threshold of >15µg/g, estimated the impact of higher thresholds on neoplasia detection rates, colonoscopy demands and severe adverse events.⁽⁵⁸⁷⁾ At a threshold of 15µg/g, 8.5% of participants (n=4,004) tested positive, with CRC detected in 0.4% (n=203) and advanced adenomas in 2.4% (n=1,119). At a threshold of 47µg/g, the positivity rate decreased to 4.2%, halving the number of participants referred to colonoscopy. At this threshold, it was estimated that 154 of the 203 CRCs would be detected, with a decrease in the proportion of stage I CRCs from 51.7% to 48.1%.⁽⁵⁸⁷⁾ Compared to the 15µg/g threshold, the positive predictive value (PPV, based on participants who attended follow-up colonoscopy) for CRC and AA was estimated to increase from 5.5% to 8.4% and from 32.0% to 42.0%, respectively. The rate of significant bleeding at colonoscopy was found to increase with increasing faecal haemoglobin concentration, as a result of the higher PPV and risk of post-polypectomy bleeding.⁽⁵⁸⁷⁾

To inform decision-making by the National Screening Advisory Committee, the review of test accuracy reported in Chapter 4 aimed to assess whether the test accuracy of FIT for the detection of CRC at a threshold of 45µg/g (that is, the threshold currently used by the BowelScreen programme), varies by age. While few studies have reported age-stratified results for FIT thresholds similar to that used by BowelScreen, there was no clear or consistent evidence identified to suggest that the test accuracy of FIT for the detection of CRC at a threshold of 45µg/g varies significantly by age.

FIT thresholds based on sex

While women tend to be more likely than men to participate in CRC screening, FIT-based screening programmes are associated with a lower reduction in CRC incidence and mortality in women than in men.^(296, 297) FIT positivity is lower in women than men,^(296, 297) and as a result, a lower proportion of women are invited for further investigation. The proportion of women diagnosed with an interval cancer following a negative FIT result is higher, despite there being no significant difference in the development of interval cancers between genders.⁽⁵⁸⁸⁾ Strategies such as varying the FIT threshold by sex have been implemented in Sweden, where a higher threshold is used for men, based on a higher faecal haemoglobin concentration compared to women. According to the programme, the use of a higher positivity threshold for men has provided a reasonable balance in outcomes between the sexes, without overburdening colonoscopy resources.⁽¹⁰³⁾ However, the use of sex-specific thresholds could introduce sex differences in positive and negative predictive values,^(271, 278) and may disadvantage men.⁽²⁹⁶⁾ Any consideration of risk-based screening strategies, including the use of sex-specific thresholds, warrants careful deliberation to avoid unintended consequences.

10.3.2 Acceptability and uptake

The success of a screening programme depends on uptake among the eligible population. The uptake or participation rate demonstrates the acceptability of a screening test, and is an important performance indicator for population-based screening programmes.⁽⁵⁸⁵⁾ A 2010 European Commission guideline document outlined a desirable CRC screening uptake rate of 65%, with an acceptable rate of 45%.⁽¹³³⁾ The BowelScreen target uptake rate is ≥50%, with an achievable standard of ≥60%.⁽¹⁸⁾ However, FIT uptake rates in Ireland remain sub-optimal, ranging from 40.6% in 2012–2015 to 46.6% in 2020–2021, with preliminary data indicating an uptake rate of 41.1% in the third quarter of 2024.⁽⁴⁴³⁾ Participation rates have consistently been lower in those aged 60–64 than among those aged 65–69 (see Table 2.2, Chapter 2). Internationally, uptake has also tended to be lower among younger age groups.^(113, 134, 135)

Population-based screening programmes require a certain level of participation before a significant public health benefit can be realised.⁽⁵⁴⁰⁾ Further, low uptake can

result in health inequalities, as vulnerable groups are often less likely to participate.⁽⁵⁴¹⁾ Reported reasons for lower uptake of CRC screening include 'embarrassment' and 'disgust' surrounding the initial test, the invasiveness of colonoscopy, lack of knowledge (based on health literacy and knowledge of others with CRC or cancer in general), and perception of risk.⁽⁵⁵⁸⁻⁵⁶⁰⁾ A survey of people who had been invited to participate in a FIT-based screening programme in Dublin (prior to the introduction of BowelScreen) found that negative cancer- and screening-related beliefs and or emotions were negatively associated with participation.⁽⁵⁵⁹⁾ As discussed in Chapter 9, people aged 50 to 54 may experience barriers in terms of knowledge and awareness of the programme, as their peers may be less likely to have participated in CRC screening, as well as potentially not being as aware of the risks of CRC compared to older age groups.⁽⁵³⁹⁾

To improve the public health benefits of screening, various strategies may be used to increase uptake. In Ireland, sending a FIT kit directly to individuals who have not responded to the original screening invitation has been shown to result in improved FIT uptake.⁽⁴⁸⁷⁾ In 2024, the National Screening Service, in conjunction with the Department of Health, commenced work on the 'Better Letters' initiative, which aims to increase uptake through the incorporation of behavioural science insights into screening invitation letters.⁽⁴⁸⁰⁾ However, as outlined in Chapters 7 and 8, higher uptake rates result in greater resource requirements and costs. The additional demands placed on endoscopy, histopathology and radiology services therefore warrant careful consideration as part of any efforts to increase uptake rates.

10.3.3 Alternative screening methods

As the scope of this HTA was limited to consideration of extending BowelScreen to people aged 50–54, alternative testing modalities were not considered. However, ongoing developments in novel, non-invasive screening tests may lead to changes in the screening pathway prior to or in tandem with the planned expansion of the programme to those aged 55–74. This section briefly outlines a number of alternative screening methods.

Risk-based screening

The 2022 updated European Council Recommendation noted the potential for implementation of risk-tailored strategies, such as introducing thresholds defined according to sex, age, or results of earlier screening rounds.⁽⁶⁸⁾ Risk-based screening strategies are based on the premise that individuals at higher risk of CRC are likely to derive greater benefit from screening. Risk-based screening involves the combination of several risk factors and or biomarkers into a risk prediction score, model or algorithm,⁽⁵⁴⁾ with the aim of tailoring screening strategies according to an individual's risk of CRC.⁽⁵⁵⁾

Risk-based strategies have the potential to improve the diagnostic yield of screening and reduce unnecessary procedures, which could improve the balance of benefits and harms at the individual level, as well as improving cost-effectiveness and presenting a more efficient use of resources.^(55, 589) However, risk-based screening increases the complexity of a screening programme, and may affect participation rates.⁽⁵⁵⁾ Identifying and quantifying risk in the target population and offering risk-based tailored screening would substantially impact the organisation of a screening programme, introducing new demands on staff, IT infrastructure and organisational systems, as well as raising additional patient and ethical considerations.⁽⁵⁹⁰⁾ A 2022 scoping review of risk-stratified CRC screening concluded that while a broad range of CRC risk prediction models have been examined, many lack acceptable discriminatory power or have not been externally validated.⁽⁵⁹⁰⁾ The authors further highlighted mixed findings regarding the efficacy of risk-based strategies in combination with or in comparison to FIT, making it difficult to draw definitive conclusions.⁽⁵⁹⁰⁾ Concerns have also been raised regarding the cost effectiveness of risk-based screening, with a 2020 modelling study indicating that screening based on polygenic risk with current discriminatory performance was unlikely to be cost-effective compared to uniform screening.⁽⁵⁹¹⁾ More research is needed on the feasibility, cost-effectiveness and impact on outcomes of risk-based screening tools in the context of established screening programmes.^(54, 55)

Screening based on faecal haemoglobin concentration

A number of studies have suggested that faecal haemoglobin (f-Hb) concentration among FIT negative screening participants may be associated with an increased likelihood of CRC or advanced adenoma (AA) detection in subsequent screening rounds.^(256, 592, 593) Among BowelScreen participants with f-Hb below 45µg/g in the first screening round who subsequently received a positive FIT result ($\geq 45\mu\text{g/g}$) in the second round, increased f-Hb in the first round was significantly associated with increased advanced pathology (CRC and high-risk adenomas) in the second round.⁽⁵⁹⁴⁾ The rates of advanced pathology in the second round rose from 7% in participants with f-Hb $< 5\mu\text{g/g}$ in the first screening round, to 50% in participants with f-Hb of 40.1–45µg/g.⁽⁵⁹⁴⁾ Breekveldt et al., using data from the Dutch CRC screening programme, found that 1.08% of those with a f-Hb concentration just below the screening threshold ($> 40\text{--}46.9\mu\text{g/g}$) had an interval CRC detected within 24 months of the first screening round, compared with 0.06% of those with f-Hb below the detection limit.⁽²⁵⁶⁾ Similarly, the number needed to screen (NNS) and number needed to scope (NSSc) to detect at least one advanced neoplasm (AN) was higher in individuals with no detectable f-Hb in the previous screening round, compared to those with detectable f-Hb.⁽⁵⁹³⁾

A 2025 meta-analysis reported that all 13 included studies reported a positive association between f-Hb in prior screenings and colorectal neoplasia detection.⁽⁵⁹⁵⁾ A

pooled analysis indicated a 5-, 8-, and 13-fold increased risk of colorectal neoplasia at the subsequent screening round among participants with f-Hb concentrations of 10, 20, and 40µg/g, respectively, compared to individuals with very low or undetectable f-Hb, although heterogeneity was high.⁽⁵⁹⁵⁾ As a result, some authors have suggested the potential for risk-stratified screening according to prior f-Hb concentration, for example, by extending screening intervals for those with undetectable f-Hb.^(593, 595, 596) Potential benefits of this approach could include a reduction of unnecessary screenings, while maintaining higher detection rates for those at greater risk.⁽⁵⁹⁵⁾ In the Netherlands, a study is underway to evaluate the yield, feasibility, acceptability and (cost-) effectiveness of personalised CRC screening using tailored invitation intervals based on prior f-Hb concentration.⁽⁵⁹⁷⁾

Novel screening modalities

As discussed in Chapter 4, while CRC screening has the potential to reduce incidence through the detection and removal of pre-cancerous lesions, advanced adenomas may bleed sporadically, and are therefore less likely to be detected by FIT. As a result, the sensitivity of FIT for the detection of AA is low, ranging from 13.7% to 24.1% at a threshold of 40µg/g in two studies included in the review of FIT test accuracy (Chapter 4).^(271, 277) While improved detection of pre-cancerous lesions could lead to a decrease in CRC incidence, efforts to improve the detection of pre-cancerous lesions are likely to decrease specificity and increase colonoscopy workloads.⁽⁵⁸⁵⁾ Higher diagnostic sensitivity also increases the potential for overdiagnosis and excision of lesions that are not clinically relevant, resulting in overtreatment.⁽⁵⁸⁵⁾ This has prompted ongoing research to improve sensitivity while maintaining high levels of specificity.

According to the NSAC criteria, there should ideally be evidence from high-quality RCTs that the screening programme is effective in reducing mortality or morbidity.⁽³⁾ As reported in Chapter 5 and discussed in section 10.4.1, several randomised trials have demonstrated the effectiveness of CRC screening in reducing CRC mortality, at follow ups ranging from 11 to 30 years.

CRC screening programmes are now well-established in many jurisdictions, reducing the feasibility of traditional RCTs due to the potential for contamination bias among the control group.⁽⁵⁹⁸⁾ To guide the development and validation of non-invasive screening tests without the need for RCTs with CRC mortality as the end point, 12 principles, based on expert consensus, have been outlined.⁽⁵⁸⁵⁾ The consensus group suggested that the evaluation of a new test should follow a sequential four-phase process, with FIT highlighted as a suitable comparator in the context of two-step screening programmes. When compared to an established test with a demonstrated positive impact on CRC mortality, a new non-invasive test should ideally improve sensitivity for CRC and advanced precursor lesions while maintaining an acceptable

level of specificity; improve the detection of precursor lesions; improve uptake rates; and demonstrate flexibility to allow a screening programme to achieve its desired goals within the context of its healthcare environment.⁽⁵⁸⁵⁾ While a comprehensive review of novel screening modalities was beyond the scope of this assessment, some of the ongoing developments in non-invasive screening tests are outlined in Chapter 2 and discussed further below.

Multi-target FIT and stool DNA tests

Multi-target FIT (mtFIT) targets three protein biomarkers: haemoglobin, calprotectin, and serpinF2.⁽⁴¹⁾ Compared with FIT at a threshold of 47µg/g, mtFIT has been found to detect a greater number of advanced neoplasia and AA, albeit with a higher test positivity rate.⁽⁴²⁾

In the US, a multi-target stool DNA test (mtsDNA) for colorectal cancer screening was approved by the Food and Drug Administration (FDA) in 2014, with a multi-target stool RNA test (mtsRNA) receiving approval in May 2024. While the USPSTF includes mtsDNA in its list of recommended screening options,⁽⁸²⁾ the 2021 American College of Gastroenterology clinical guideline includes a 'conditional' recommendation, based on 'very low' quality evidence, suggesting that mtsDNA could be considered for individuals who are unable or unwilling to undergo colonoscopy or FIT-based screening.⁽⁷⁶⁾ Stool DNA testing was not recommended by the American College of Physicians (ACP) in its 2023 guidance statement, with the ACP citing a lack of comparative evidence, as well as higher costs when compared with other stool-based tests, as justification for its decision.⁽⁸¹⁾ More recently, in 2024, a next-generation mtsDNA test, featuring a new panel of biomarkers selected to increase specificity, has demonstrated high sensitivity for detecting colorectal cancer and high specificity for advanced neoplasia.⁽⁴⁷⁾ While the next-generation mtsDNA appears to be more sensitive than FIT for detecting CRC and advanced pre-cancerous lesions, it is also less specific, with specificity further decreasing with increasing age.⁽⁴⁷⁾ In the context of a screening programme, lower specificity leads to an increased number of false positive test results and unnecessary colonoscopies,⁽⁴⁷⁾ which in turn increases healthcare costs and the risk of complications.⁽⁴⁶⁾ Further, mtsDNA and mtsRNA require significantly greater stool volumes than FIT, which could adversely impact uptake rates.⁽⁵⁹⁹⁾

Liquid biopsy

Testing for blood-based biomarkers, referred to as liquid biopsy, involves a non-invasive blood test to detect circulating tumour cells or other tumour-related components in the blood. In July 2024, the FDA approved SHIELD™, the first liquid biopsy to be approved for CRC cancer screening.^(600, 601) In a clinical study of test performance compared to colonoscopy, the test had a sensitivity for the detection of CRC of 83%, although the sensitivity for advanced pre-cancerous lesions was low at

13%. The sensitivity for other pre-cancerous lesions was not reported.⁽¹⁴¹⁾ Specificity for advanced neoplasia was 90%. Adequately-powered clinical trials have not been conducted to examine the long-term clinical effectiveness of SHIELD or other liquid biopsy tests in average-risk screening populations.⁽⁶⁰²⁾

A modelling study of a hypothetical liquid biopsy test concluded that while CRC incidence and mortality is reduced compared with no screening, it was less effective than FIT or colonoscopy.⁽⁵²⁾ Scenario analysis showed that these conclusions held with the test characteristics observed in the SHIELD clinical trial.⁽⁵²⁾ The poorer performance of liquid biopsy primarily occurs because liquid biopsy performs less well than FIT and colonoscopy in the early identification and removal of polyps before their potential transformation into cancer.^(52, 602) Further, the test's poorer specificity (at FIT thresholds used in Ireland), would place a greater burden on endoscopy capacity, given colonoscopy is required for those with a positive result. Nevertheless, liquid biopsy may be preferred by some patients as a testing modality.⁽⁶⁰²⁾ It has been suggested that if liquid biopsy adds unscreened people to the screening pool, it may be a useful adjunct to other screening methods.^(52, 602) In contrast, if it were used as a substitute for FIT, it is likely to adversely affect clinical outcomes and cost.^(52, 602)

Gut microbiome

Increasing evidence suggests a role of the gut microbiome in the development of colorectal cancer, which may serve as a biomarker for early diagnosis.⁽⁴⁹⁾ CRC risk factors such as age, Western diet, an unhealthy lifestyle and smoking can influence gut microbiota and may contribute to the carcinogenic process, with patients with CRC presenting with a different microbial composition compared to healthy controls.⁽⁶⁰³⁾ Studies have also explored differences in gut microflora and metabolic alterations in people with colorectal adenoma.⁽⁶⁰⁴⁾ Increasing research has explored faecal microbiota profiles as potential targets for the development of novel screening tools, either independently or in combination with FIT.^(605, 606) However, while differences in several microbial markers have been demonstrated between patients with colorectal cancer, adenomas and healthy controls, challenges remain regarding the identification of a unified biomarker, in addition to a lack of large, prospective, multi-centre studies demonstrating diagnostic performance.⁽⁶⁰⁶⁾ 'Micro-AI-biome', an international research project to explore the use of artificial intelligence in the analysis of gut or stool microbiome data, commenced in 2023, and will involve the recruitment of 1,500 BowelScreen participants.^(607, 608) Further developments in novel, non-invasive CRC screening tests may present alternative screening options in the future, and may lead to changes in the BowelScreen screening pathway prior to or in tandem with the planned expansion of the programme to include those aged 55–74.

10.4 The screening programme

The BowelScreen programme commenced in 2012, following the publication of two HIQA reports in 2009 and 2010 that examined colorectal cancer screening and resource use in cancer screening programmes.^(12, 13) The 2009 HTA concluded that FIT-based screening for people aged 55–74 years was the optimal screening option.⁽¹²⁾ As of April 2025, BowelScreen invites adults aged 59–70 for screening every two years, with an expansion to ages 55–74 committed to in the 2020 Programme for Government and the National Cancer Strategy 2017–2026.^(1, 2)

As outlined in the NSAC criteria, evidence that a screening programme is effective in reducing mortality and morbidity should ideally be underpinned by high-quality RCTs.⁽³⁾ Further, the criteria state that the opportunity cost of the programme should be economically balanced in relation to expenditure on medical care as a whole, with regard to evidence from cost benefit and or cost-effectiveness analyses. The following section summarises the evidence on the clinical effectiveness (section 10.4.1) and the cost-effectiveness (section 10.4.3) of extending BowelScreen to those aged 50–54.

10.4.1 Clinical effectiveness, benefits and harms of lowering the screening age

Evidence of the clinical effectiveness of CRC screening is based primarily on RCTs of guaiac-based faecal occult blood tests (gFOBT), colonoscopy or flexible sigmoidoscopy.^(73, 80) Compared to gFOBT, FIT is superior in detecting advanced adenomas and colorectal cancer, with higher sensitivity and specificity for lower gastrointestinal bleeding and improved uptake.⁽³¹⁾ As the analysis of samples is automated for quantitative FITs, interpretation of results is less subjective, which has led to the increased adoption of FIT in many screening programmes internationally.^(31, 34, 35)

While no RCTs of FIT-based screening were identified as part of this assessment, the evidence from randomised trials of gFOBT or flexible sigmoidoscopy, as well as from observational FIT studies, suggests that screening reduces CRC mortality compared to no screening, in participants ranging in age from 45–80 (Chapter 5). The observational FIT studies generally reported larger reductions in CRC mortality, although estimates varied widely, ranging from 10% with six years of follow-up to 65% with 11 years of follow-up in participants ranging in age from 50 to 74.^(314, 316) Some evidence, based on observational studies with a higher risk of bias, also suggested that FIT-based screening may reduce CRC incidence. While screening from age 50 is likely to be clinically effective compared to no screening, none of the clinical effectiveness studies identified as part of this assessment considered the effectiveness of commencing screening at age 50 compared to screening from age 55. Evidence from modelling studies suggests that lowering the starting age for

screening from 55 to 50 avoids between one and two additional CRC deaths per 1,000 people screened (Chapter 6). However, these estimates are uncertain. As both CRC and pre-cancerous lesions tend to bleed intermittently, the long-term effectiveness of FIT screening is increased through repeated screening rounds.⁽³¹⁵⁾

All studies of the clinical effectiveness of FIT screening identified as part of the review presented in Chapter 5 used a threshold of 20µg/g to identify individuals for referral to colonoscopy. Higher FIT thresholds result in the detection of fewer cancers. Thus, the clinical effectiveness estimates of FIT-based screening may overestimate the effect compared to what would be observed with a threshold of 45µg/g. However, given the improved test accuracy of FIT for the detection of CRC relative to gFOBT, and the consistent evidence of clinical effectiveness of gFOBT screening, it is unlikely that screening with FIT at a threshold of 45µg/g would be less effective than screening with gFOBT. While estimates of FIT sensitivity and specificity have varied widely, all studies included in the review of FIT test accuracy presented in Chapter 4 demonstrated higher levels of sensitivity for CRC at thresholds of 40 to 50µg/g, compared to the pooled estimates of gFOBT sensitivity reported by previous systematic reviews.^(31, 73)

According to the NSAC criteria, the benefit gained by populations and individuals from the screening programme should outweigh the harms.⁽³⁾ Three studies were identified that reported age-stratified data regarding harms of colonoscopy following a positive FIT result,^(325, 330, 331) which suggested that the risk of adverse events of colonoscopy following a positive stool-based test increases with age.

10.4.2 International guidelines and screening age ranges

CRC screening for those aged 50–74 has been recommended by the Council of the European Union since 2003.⁽¹⁶⁾ The 2022 updated European Council Recommendation outlined FIT as the preferred screening test for referring individuals aged 50–74 for follow-up colonoscopy.⁽⁶⁸⁾ The Council also acknowledged, however, that decisions made at national and regional level are likely to depend on the disease burden and healthcare resources available, as well as the benefit-harm balance and cost effectiveness of screening.⁽⁶⁸⁾ In 2023, the European Commission Initiative on Colorectal Cancer examined whether screening or no screening should be recommended for those aged 50 to 69 at average risk of colorectal cancer.⁽⁷⁰⁾ A strong recommendation, based on moderate quality evidence, was issued in favour of screening in this age group. Seven of the eight international colorectal cancer screening guidelines reviewed as part of this assessment recommended colorectal cancer screening from the age of 50 (see Chapter 2). Two guidelines included additional 'grade B' or 'conditional' recommendations for screening in those aged 45–49, based on very low-quality evidence or moderate certainty that screening in this age group has a moderate net benefit, respectively.^(76, 83)

In England, screening has recently expanded to those aged 50–74 as part of a gradual four-year initiative that commenced in April 2021.⁽⁹⁹⁾ The decision to lower the screening age was informed by a cost-effectiveness analysis, consideration of clinical effectiveness evidence, and a public consultation. The cost-effectiveness analysis concluded that FIT screening in those aged 50–74 at as low a threshold as possible (20µg/g) was the most cost-effective approach.⁽⁶⁰⁹⁾ Further, the UK National Screening Committee noted that, while fewer cancers and pre-cancerous lesions are detected among those aged 50–60 as a result of lower incidence and lower uptake, evidence from RCTs includes this age range, and the quality-adjusted life years (QALYs) and life years gained (LYG) in younger people are greater.⁽⁶¹⁰⁾

In Australia, the screening age was lowered from 50 to 45 in July 2024,⁽⁹⁸⁾ in line with the 2023 *Clinical practice guidelines for the prevention, early detection and management of colorectal cancer: Population Screening*.⁽⁶¹¹⁾ The 2023 guideline was informed by two systematic reviews and two modelling reports, including a microsimulation model. The microsimulation model suggested that lowering the screening age for two-yearly FIT screening to 45 or 40 could reduce CRC incidence and mortality compared to screening those aged 50–74, while being 'cost-effective and a relatively efficient use of colonoscopy services'.⁽⁶¹²⁾ Based on implementation considerations and the findings of this study, the Cancer Council Australia Colorectal Cancer Screening Working Party concluded that FIT screening in those aged 45–74 every two years was the most favourable.⁽⁶¹²⁾

A 2022 evaluation of the Dutch CRC screening programme assessed whether improvements to the programme could be achieved by expanding the age range from 55–75 to 50–80, calibrating the FIT threshold, amending the screening interval, or applying risk stratification.⁽⁵²²⁾ Based on this evaluation, the Health Council of the Netherlands recommended that no modifications be made to the programme at that time.

The role of decision modelling and epidemiological evidence: US recommendations

USPSTF recommendations on the net benefit of screening in particular groups are based on a range of evidence; the evidence base referred to in its recommendation statements considers various study designs examining each of effectiveness, test accuracy, and harms of screening, and is supplemented by epidemiological studies and microsimulation models.⁽⁸²⁾ However, not all recommendation bodies consider modelled data within their assessment of net benefit; for example, ECICC European guidelines on CRC primary prevention, screening, and diagnosis considered modelling studies but only in the context of assessment of cost effectiveness.⁽⁸⁰⁾ As such, it is important to consider the nature of the evidence base underlying recommendations, and the assumptions informing the evidence.

The 2021 USPSTF recommendation took consideration of recent evidence reporting increasing CRC incidence rates among recent US birth cohorts, and such evidence was also incorporated in decision models that helped to inform the recommendation. Prior to the 2021 USPSTF update, the American Cancer Society (ACS) in 2018 issued a modification of the USPSTF 2016 recommendations; this guideline update in part addressed the question of initiation age and made a qualified recommendation to begin screening at age 45 years (a qualified recommendation indicates that there is clear evidence of benefit or harm, but less certainty either about the balance of benefits and harms or about patients' values and preferences, which could lead to different individual decisions).⁽⁶¹³⁾ In order to inform this guideline update, the ACS used the 2016 USPSTF evidence review and report of simulation modelling findings, and commissioned an extension of the modelling studies to incorporate new epidemiological evidence on CRC incidence published between 2016 and 2018, which suggested increased rates of CRC in younger cohorts.⁽³⁵³⁾ No additional empirical evidence had been published in the interim, however. The ACS noted that the recommendation to begin screening at age 45 years was based on disease burden, results from microsimulation modelling, and 'the reasonable expectation that screening will perform similarly in adults aged 45 to 49 years as in persons for whom screening is currently recommended.'⁽⁶¹³⁾

Subsequent to the issuing of the ACS recommendation, and further following the 2021 USPSTF recommendation, the American College of Gastroenterology (ACG) suggested that CRC screening should begin at 50 years of age, but practitioners should 'consider offering it at 45 years of age for average-risk patients', noting that these guidelines mainly support the 2021 USPSTF update. However, notably, the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) both continue to recommend, as of January 2025, that screening begin at 50 years of age, as does the Canadian Task Force on Preventive Health Care and the European Council.^(74, 81, 133, 543) The AAFP noted the lack of clinical evidence and that the USPSTF recommendation centred on indirect evidence from modelling studies; they furthermore suggested that, while the incidence of CRC in younger individuals is increasing, the increased risk in this age group is small and may be overestimated, and that there is no evidence that early detection in the 45 to 49-year age group would be as beneficial as in the older age group.⁽⁶¹⁴⁾ The 2023 American College of Physicians guidance statement states that clinicians should consider not screening asymptomatic, average-risk patients between 45 and 49 years old. Reasons for this recommendation from the ACP included a lack of sensitivity and specificity data of CRC screening tests in this age group, the potential for the exacerbation of health disparities; concerns over assumptions used in modelling studies, and a reduced net benefit of screening in those aged 45 to 49 when compared to older age groups.⁽⁸¹⁾

Reflecting on how different recommendation bodies have arrived at different conclusions illustrates the challenges in interpretation of the available data. Generally, given the uncertainties in the evidence base, it has been argued that 'evidence-based medicine recommendations are not definitive answers but rather educated and thoughtful data-based advice' and such recommendations involve subjectivity.⁽⁶¹⁵⁾ However, it is also important to consider that, in comparison with Ireland, and amongst various important differences in healthcare funding approaches and organisation, screening within the US is not offered within a structured national screening programme such as occurs with BowelScreen. Concerns regarding access, and US-specific considerations regarding disparities, may be influential in guideline development.

10.4.3 Cost-effectiveness

None of the cost-effectiveness studies included in the review presented in Chapter 6 specifically sought to establish whether lowering the starting age at which individuals at average risk of CRC are invited for screening is cost-effective. Overall, however, the evidence consistently suggests that lowering the age range for screening from 55–74 to 50–74 would likely be cost-effective, based on a willingness-to-pay threshold of €20,000 per QALY gained. The lower starting age for screening appears to produce more favourable QALY gains and reductions in CRC incidence and mortality, albeit at marginally higher cost due to increased overall duration of screening.

10.5 Implementation

10.5.1 Organisational, resource and budget implications

Decision-making regarding an extension of BowelScreen to include those aged 50–54 requires careful consideration of the ability to effectively deliver the increased resources necessary to support increased screening. As outlined in the NSAC criteria, there should be evidence that the complete screening programme is acceptable and can be implemented, including the availability of adequate staffing and facilities for testing, diagnosis, treatment and programme management prior to the commencement of the screening programme.⁽³⁾ As an established screening programme, the screening, treatment and surveillance pathways are in place. However, while a commitment to screen people aged 55–74 was included in the 2020 Programme for Government,⁽²⁾ as of May 2025, this has not been achieved.

Colorectal cancer screening requires timely access to endoscopy for participants who receive a positive FIT result, histopathology to process samples taken during colonoscopy, and diagnostic radiology for suspected cancer cases. These services have experienced ongoing capacity challenges, including long waiting lists and deteriorating report turnaround times. Since its inception, the programme has

experienced challenges regarding endoscopy capacity in particular. Lowering the starting age from 55 to 50 would increase the eligible population by 27% when fully implemented, necessitating careful planning and allocation of health service resources to accommodate the larger eligible population. Chapter 7 outlined the estimated resources required for an extension of BowelScreen to include those aged 50–54. Compared to offering screening to those aged 55 to 74 only, this age extension would require approximately 2,000, 2,400 and 2,300 additional colonoscopies (index, additional planned procedures and surveillance) as part of the BowelScreen programme in year one, year five and year ten, respectively, with an estimated 800 additional participants requiring histopathology. For resources relating to staging and grading of cancers, such as diagnostic radiology, the increased demand from cases identified through screening is expected to be partially offset by reduced demand from patients presenting symptomatically.

Faster implementations are predicted to incur higher cumulative incremental costs over 10 years, with immediate, one-yearly, and two-yearly expansions costing an additional approximately €66 million, €57 million, and €45 million, respectively, compared to screening those aged 55–74 (Chapter 7). However, these estimates should be considered in light of uncertainties surrounding the ongoing BowelScreen expansion to 55–74, which is likely to require substantial investment. The 2025 HSE National Service Plan outlined the expansion of the programme to include those aged 58–70 on an incremental basis by 2026 as a key area of focus,⁽¹⁵⁾ with €1.9 million announced as part of Budget 2025 to support this expansion.⁽⁴¹⁹⁾

Both a potential extension of the programme to include those aged 50–54, as well as the planned expansion to 55–74, are likely to be impacted by ongoing capacity constraints and workforce shortages. The resource and organisational implications of expanded screening are discussed in detail in Chapter 8 and briefly summarised below.

Workforce shortages

The NSAC Criteria highlight that 'adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme.'⁽³⁾ Screening colonoscopies are generally performed by consultant gastroenterologists or general surgeons, while samples removed at colonoscopy are reported on by histopathologists. As outlined in Chapter 8, screening colonoscopies are more complex and require a greater level of experience and expertise, with the programme highlighting that colonoscopy capacity in Ireland is constrained by a short supply of endoscopists with an appropriate skill level.⁽¹⁸⁾ Workforce shortages have been highlighted across general surgery, gastroenterology and histopathology. Training for these roles typically spans a period of five to eight years, with constraints on a potential expansion of training

programmes including the supply of trainees, sufficient training capacity, and availability of funding for training posts.^(425, 438, 462)

Infrastructure

Cancer screening is a complex public health strategy, which requires significant resources, infrastructure and coordination.⁽⁴¹⁴⁾ As outlined in Chapter 8, the National Cancer Screening Service (NCSS) in 2008 recommended the establishment of four dedicated screening centres with two endoscopy suites each, geographically dispersed throughout the country and within close proximity of cancer centres, but operating discretely from the symptomatic service.⁽¹⁶²⁾ Acknowledging the significant organisational structures and systems required by colorectal cancer screening, the NCSS stressed that these should not interfere with the delivery of symptomatic services for people with gastrointestinal complaints.⁽¹⁶²⁾ However, since its inception in 2012, the BowelScreen programme has operated within the general symptomatic services. As the programme continues to expand, the participation of additional endoscopy units will be required, with each requiring approximately two years to become fully embedded within the programme. Requirements for BowelScreen endoscopy units are outlined in the programme quality assurance standards.⁽³⁰⁵⁾ Sourcing capacity from additional units is challenging given the requirements for units to meet quality assurance standards, pressures from symptomatic waiting lists, and the finite pool of endoscopists who would meet the BowelScreen performance thresholds.

The 2025 Programme for Government committed to the building of four new elective treatment centres (previously referred to as elective hospitals) in Cork, Dublin (two sites), and Galway, in addition to the establishment of six surgical hubs in Cork, Dublin (two sites), Galway, Limerick and Waterford.^(14, 474) The new elective treatment centres are expected to provide 42 additional endoscopy suites nationally, which are estimated to provide capacity for an additional 128,100 endoscopies annually.⁽⁴⁷²⁾ However, delivering both the infrastructure and resourcing of the new facilities is expected to be challenging.⁽⁴⁷²⁾

Long waiting times for endoscopy procedures illustrate a significant existing unmet demand, which is likely to be compounded by the significant increase in endoscopy capacity that will be required to support the planned expansion of BowelScreen to those aged 55–74 years. Given a finite number of endoscopists with the required level of experience and expertise to perform screening colonoscopies, as well as capacity constraints in histopathology and radiology services (see Chapter 8), the potential impact of the new elective treatment centres, including the additional capacity that will be provided in practice, is unclear.

Quality assurance

According to the NSAC criteria, a plan should be in place to manage and monitor the screening programme against an agreed set of quality assurance standards.⁽³⁾ The quality standards, quality requirements and key performance indicators (KPIs) for the BowelScreen programme are outlined in the BowelScreen Standards for Quality Assurance in Colorectal Screening.⁽³⁰⁵⁾ The standards are kept under review and revised as necessary, as further evidence or data become available.⁽³⁰⁵⁾ As highlighted in Chapter 8, at existing levels of capacity, the requirement for additional procedures and cases as a result of an age extension could impact both BowelScreen quality assurance standards and KPI targets for symptomatic services, including longer waiting lists and worsening turnaround times.

Initiatives to relieve demand and maximise capacity

Capacity is likely to be impacted by a myriad of factors, including developments and advances in screening and diagnostic techniques, as well as demographic changes. Some of these are summarised in Chapter 8.

Chapter 8 also outlines potential strategies to maximise capacity or reduce demand, including efforts to reduce colonoscopy waiting lists, such as the use of FIT for symptomatic colonoscopy triage and post-polypectomy surveillance, increasing weekend and out-of-hours activity and sourcing additional capacity from private hospitals. However, efforts to maximise endoscopy capacity may have deleterious consequences for downstream histopathology and radiology services, while relieving demand from symptomatic procedures may not result in a proportionate decrease in demand for histopathology or radiology. Strategies to increase endoscopy activity should therefore be matched by initiatives to increase downstream histopathology and radiology capacity to prevent delays in accessing diagnostic services for people with abnormal screening results, as well as for those presenting symptomatically.⁽⁴⁹⁷⁾ Significant planning and investment is likely to be required to ensure the necessary resources are in place to support both the planned expansion, as well as any potential future extension of the programme.

Information and awareness

Individuals considering screening should be fully informed about the potential benefits, risks, and limitations of screening, especially in the context of the lower screening age.⁽⁴¹⁵⁾ It is important for screening programmes to ensure informed consent, including providing information about the potential for over-diagnosis and unnecessary procedures. The BowelScreen programme has developed multiple leaflets to help educate and inform people about the programme, including information about the programme itself, the screening test, and colonoscopy.⁽⁴⁹⁶⁾ While screening for colorectal cancer may be less effective in those aged 50–54 than

in older age groups due to an overall lower CRC incidence, the harms of screening may also be lower. If the screening age is lowered to 50, it may be necessary to revise BowelScreen materials to ensure the information remains relevant to all age groups of the target population. There may also be benefits to targeting elements of a campaign to appeal to a younger audience.

10.5.2 Future developments

Any decision to implement screening should also consider future developments that will impact services and which could affect their ability to absorb an increased workload arising from an expansion of screening. Future developments in alternative screening methods have already been described within this chapter, while developments and advances in diagnostic techniques and treatment, such as advanced endoscopic techniques, molecular testing and total neoadjuvant therapy, have been described in Chapter 8. Separate to these developments, the integration of artificial intelligence (AI) into CRC screening programmes has the potential to improve diagnostic accuracy and efficiency while reducing workload. Image classification has become a hallmark of AI applications in healthcare. In brief, AI algorithms – sometimes referred to as machine learning – may be fine-tuned to recognise specific features in images (such as colorectal polyps during endoscopy) after being trained on large sets of annotated images. In radiology, where the most significant advancements have occurred, numerous commercialised products are available, for example, to detect and highlight suspicious areas and to quantify and extract features from images.⁽⁶¹⁶⁾

AI-assisted endoscopy and histopathology have seen rapid development in recent years, with studies indicating promising accuracy figures. In endoscopy, computer-assisted detection (CAdE) has the potential to enhance the detection of colorectal polyps and cancer, which may otherwise be missed by the human eye. A 2024 meta-analysis reported the CAdE sensitivity for detection of colon polyps and neoplasia at 93% and 94%, and the specificity at 87% and 98%, respectively.⁽⁶¹⁷⁾ However, evidence on the effectiveness of CAdE colonoscopy over standard colonoscopy in real-world settings is mixed.^(618, 619) In histopathology, the digitalisation of medical imaging and analysis, known as digital pathology, is seeing rapid adoption. Within this development, the integration of AI-assisted image processing tools is a pivotal step.⁽⁶²⁰⁾ Several AI algorithms have shown the ability to replicate the performance of histopathologists with high accuracy in identifying CRC in microscopy slides.⁽⁶²¹⁻⁶²³⁾ In some cases, prototype interfaces have been developed to assist pathologists with complex and challenging cases to reduce the need for a second pathologist within the existing workflow.⁽⁶²³⁾

The adoption of AI in healthcare settings is progressing at a rapid pace. However, there remain broad challenges and concerns regarding the application of AI-assisted

tools to medical settings. These include bias in AI algorithms, often due to insufficient or non-representative training datasets, acceptability of AI-assisted technologies, data security and privacy, and regulatory frameworks and approval processes.^(624, 625) As such, there is uncertainty around how developments in this field might impact the BowelScreen programme in the future.

10.6 Strengths and limitations

This assessment has a number of strengths related to its methodological rigour. The assessment followed a robust approach, including publication of a protocol and adherence to national and international best practice guidelines for the conduct and reporting of HTA and systematic review.^(266, 306, 416, 626) All aspects of the screening pathway and all HTA domains were considered. Systematic searches were developed and or updated for the reviews of clinical effectiveness, cost effectiveness and test accuracy. The HTA was supported by an expert advisory group and engagement with key stakeholders.

A number of limitations should be acknowledged. There were limited data available to address specific elements of the HTA, including the clinical and cost effectiveness and test accuracy. As a result, the benefits and harms of extending BowelScreen to those aged 50–54 are subject to a degree of uncertainty, as data relating to this age group specifically were limited. Limited data were also available to inform several of the parameters included in the cohort model presented in Chapter 7. The resource estimates presented in this assessment are therefore subject to uncertainty, and the true numbers required to support an extension of screening could be higher or lower in practice.

The scope of this HTA was limited to consideration of extending BowelScreen to people aged 50–54. Alternative testing modalities, such as primary screening tools other than FIT, or specifications (for example, alternative FIT thresholds or alternative screening intervals) were not considered. Ongoing developments in novel, non-invasive screening tests may lead to changes in the screening pathway prior to or in tandem with the planned expansion of the programme to those aged 55–74, increasing the uncertainty in the estimates presented in this report. Similarly, developments and advances in diagnostic techniques and treatment, such as advanced endoscopic techniques, molecular testing and total neoadjuvant therapy, will continue to increase demands for endoscopy, histopathology and radiology resources. The estimates presented in this report are therefore likely to underestimate the future demand on these services that would result from an extension of CRC screening.

Further, while the available evidence suggests that lowering the age range for screening would likely be cost-effective, there may be more efficient screening

combinations than screening all adults from age 50–74 using a FIT threshold of 45µg/g and two-yearly intervals. For example, the cost-effectiveness study by McFerran et al. referred to in Chapter 6 suggested that extending the screening interval to four years, reducing the FIT cut-off to 10µg/g, and limiting the age range for screening to 60–72 years could provide a screening strategy that returns maximum net health benefit within finite capacity constraints.⁽³⁶⁵⁾ In contrast, Whyte et al. found that the 20 most cost-effective strategies examined within their analysis (that is, optimal strategies with the highest net monetary benefit (NMB) at £20,000 per QALY gained threshold) involved starting screening at age 50 to 53 years, using two-yearly intervals with seven or eight rounds of screening, and a FIT threshold of 127 to 166µg/g.⁽³⁶⁸⁾ However, the difference between strategies may be marginal, as in the study by Whyte et al., where the percentage difference in NMB between the highest and lowest strategy (among the top 20 most cost-effective strategies) was 10%.⁽³⁶⁸⁾ The available evidence suggests that starting screening earlier is likely cost-effective at commonly used WTP thresholds in Ireland.

Finally, this assessment did not include a de novo economic model to assess the costs and consequences of extending CRC screening in Ireland. While the cohort model presented in Chapter 7 was devised to examine the resource and budget impact of lowering the starting age of BowelScreen from 55 to 50 over a ten-year time horizon, the results of this model should not be used in isolation to assess the clinical effectiveness or cost effectiveness of screening. Although some uncertainty remains regarding the generalisation of international evidence to the Irish setting, there is likely sufficient evidence to suggest that lowering the age range from 55–74 to 50–74 would be cost-effective in the context of Ireland. While it is possible that developing a bespoke economic model would reduce uncertainty, it is also important to consider the benefit of developing a new model against the resources required. Across the studies included in the review of cost-effectiveness reported in Chapter 6, the key finding – that is, that lowering the starting age of CRC screening to 50 (from 54, 55, or 60) is cost-effective – was consistent regardless of geographical context and FIT-threshold. Therefore, it is unlikely that an Ireland-specific model would lead to a different conclusion.

10.7 Conclusion

Colorectal cancer screening from the age of 50 has been demonstrated to be both clinically and cost-effective compared to no screening. While there was a lack of evidence that directly assessed the effectiveness of lowering the screening age from 55 to 50, the available evidence suggests that screening from 50–74 is likely to be cost-effective compared to screening from 55–74. Similarly, there was consistent evidence, based on a range of screening modalities and study designs, that screening from age 50 reduces CRC mortality compared to no screening, with a reduced risk of adverse events among younger screening participants.

Lowering the screening age would increase the size of the population eligible for screening by 27%, and is estimated to incur additional costs of between approximately €45 million and €66 million over 10 years compared to screening those aged 55–74, depending on the pace of implementation. Once established, the overall incremental cost would be expected to decline over time as a result of earlier cancer detection, which reduces the need for more costly advanced-stage treatments.

While a commitment to screen those aged 55–74 is in place, as of May 2025 this has not been achieved. Ongoing developments in novel, non-invasive screening tests may lead to changes in the screening pathway prior to or in tandem with the planned expansion of the programme to those aged 55–74, increasing the uncertainty in the estimates presented in this report.

The services required for screening, including endoscopy, histopathology and diagnostic radiology are experiencing significant ongoing capacity constraints, including workforce shortages. Extending the programme without coordinated efforts to address the existing constraints is likely to negatively impact the ability of both BowelScreen and symptomatic services to provide care in accordance with quality assurance standards and KPI targets, which could lead to longer waiting lists and worsening turnaround times. Significant investment and planning would be required to ensure the necessary resources are in place to support a potential extension of the programme to those aged 50 to 54.

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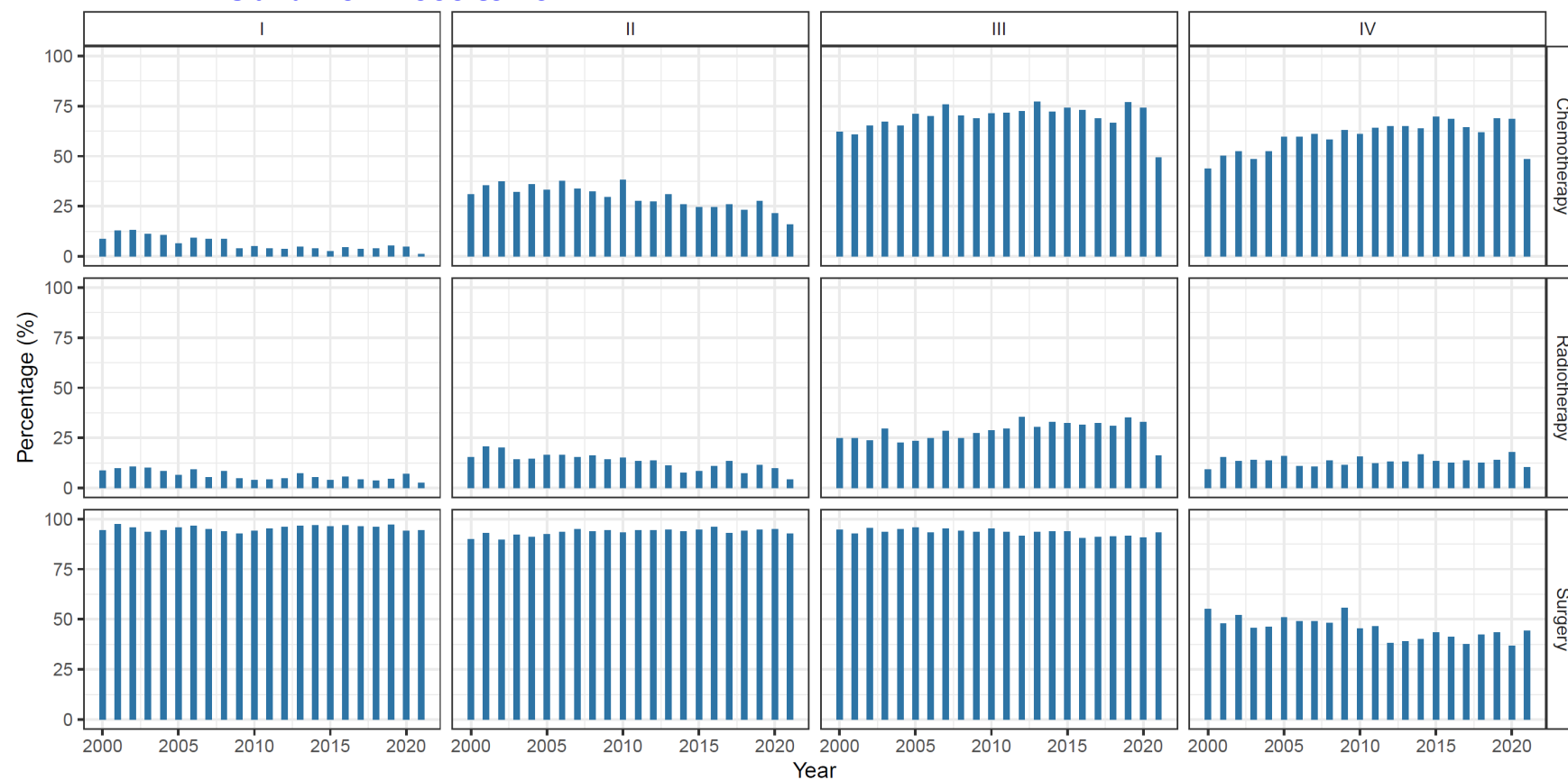
Appendices

Appendix A Epidemiology

A.1 Temporal trends in treatment

The following presents an analysis of treatment receipt over the years 2000–2020; thus it is possible that some trends started earlier than 2000. It is important to note that the availability and nature of treatment approaches have evolved over this time period,⁽⁶²⁷⁾ which may have influenced treatment patterns over time. All analyses of temporal trends in this chapter were carried out in R using the segmented package (detailed methods and estimated patterns are provided in section A.2). For Stage I and II CRC, the use of chemotherapy and radiotherapy generally decreased at least since the year 2000 (-9.3 to -3.2 average annual percentage change, AAPC), while surgery for Stage II increased until 2007 (+0.6 AAPC). For Stage III and IV, the use of surgery decreased since 2000 (-0.2 and -1.5 AAPC, respectively), while chemotherapy increased until 2006 and 2008 (+2.4 and +3.7 AAPC, respectively) and remained stable since. The use of radiotherapy for Stage III has also increased at least since 2000 (+1.9 AAPC; Figure A.1). More detailed analyses of age-specific treatment trends were published by NCRI in 2017 and noted an increase in chemotherapy use between the 1996–2000 and 2010–2013 periods for older CRC patients (+58% and +140% for 65–74 and 75+, respectively) and for advanced stages (+30% and +68% for Stages III and IV respectively); a decrease in chemotherapy for those aged <45 (-18%) and Stage I (-36%); and an increase in pre-operative radiotherapy from 2000.⁽⁶²⁸⁾

Figure A.1 Colorectal cancer treatment by stage, carried out within one year of colorectal cancer diagnosis in Ireland from 2000 to 2021



Source: NCRI. Data displayed are of patients between 40 and 84 years old. Note that the treatment receipt data from 2018 to 2020 were incomplete at the time of analysis.

Key: NCRI – National Cancer Registry Ireland.

A.2 Breakpoint regression analysis

Breakpoint regression, also known as segmented or joinpoint regression, identifies points where the relationship between the response and predictor variables changes and estimates slopes associated with individual segments. In Chapter 3, the segmented package^(629, 630) in R was used to fit piecewise linear models with breakpoints to the data outlined in Table A.1.

Table A.1 List of breakpoint regression analyses carried out in Chapter 3

Response	Predictor	Grouped by	Index
Case number	Year		A
Crude incidence rate per 100,000	Year		B
Crude incidence rate per 100,000	Year	Age group	C
Crude incidence rate per 100,000	Year	Country; Age group	D
Proportional share of population	Year	Age group	E
Crude mortality rate per 100,000	Year	Age group	F
Proportion of cases	Year	Stage; Treatment	G
Proportion of cases detected via screening	Year	Age group	H
Proportion of cases	Age group	Stage	I

Key: Index refers to the index label indicated in Table A.2 showing the estimated breakpoints and piecewise regression slopes.

All responses were log-transformed such that a given estimated slope for a segment represents the proportional difference in the log scale per unit of the predictor. Thus, when the predictor is time in coded years, the slope multiplied by 100 gives the annual percentage change in the log-scale. Data from 2020 were excluded as there was an 18% drop in reported CRC due to COVID-19, compared to the preceding year.⁽²⁰⁴⁾ The registered CRC numbers were subsequently restored to the pre-pandemic level by 2021, according to an NCRI analysis of projected and registered cases.⁽²⁰⁵⁾

Table A.2 Estimated breakpoints and piecewise regression slopes

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
A	Case number	Year	All	I, II, III, IV	Ireland	NA	Breakpoint	1	2009.1	2007	2011.2	
A	Case number	Year	All	I, II, III, IV	Ireland	NA	Slope	1	0.0288	0.0242	0.0334	Up
A	Case number	Year	All	I, II, III, IV	Ireland	NA	Slope	2	0.0118	0.008	0.0156	Up
B	Crude incidence rate per 100,000	Year	All	I, II, III, IV	Ireland	NA	Breakpoint	1	2015.3	2012.1	2018.4	
B	Crude incidence rate per 100,000	Year	All	I, II, III, IV	Ireland	NA	Slope	1	0.0079	0.0057	0.0101	Up
B	Crude incidence rate per 100,000	Year	All	I, II, III, IV	Ireland	NA	Slope	2	-0.0051	-0.0157	0.0054	
C	Crude incidence rate per 100,000	Year	<50	I, II, III, IV	Ireland	NA	Slope	1	0.0184	0.0123	0.0245	Up
C	Crude incidence rate per 100,000	Year	50-54	I, II, III, IV	Ireland	NA	Slope	1	-0.0032	-0.0085	0.0021	
C	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	Ireland	NA	Slope	1	-0.0058	-0.011	-6.00E-04	Down
C	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Ireland	NA	Slope	1	-0.0037	-0.0115	0.0042	
C	Crude incidence rate per 100,000	Year	65-69	I, II, III, IV	Ireland	NA	Breakpoint	1	2014	2011.6	2016.4	
C	Crude incidence rate per 100,000	Year	65-69	I, II, III, IV	Ireland	NA	Slope	1	0.0011	-0.0088	0.011	
C	Crude incidence rate per 100,000	Year	65-69	I, II, III, IV	Ireland	NA	Slope	2	-0.0529	-0.0781	-0.0276	Down
C	Crude incidence rate per 100,000	Year	70-74	I, II, III, IV	Ireland	NA	Breakpoint	1	2008.3	2005.5	2011.1	
C	Crude incidence rate per 100,000	Year	70-74	I, II, III, IV	Ireland	NA	Slope	1	0.0078	-0.0094	0.025	
C	Crude incidence rate per 100,000	Year	70-74	I, II, III, IV	Ireland	NA	Slope	2	-0.034	-0.0447	-0.0233	Down
C	Crude incidence rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	1	2009	2007.1	2010.9	
C	Crude incidence rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	2	2019	2017.5	2020.5	
C	Crude incidence rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Slope	1	0.0124	0.0051	0.0198	Up
C	Crude incidence rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Slope	2	-0.0154	-0.0217	-0.0092	Down
C	Crude incidence rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Slope	3	-0.0625	-0.1027	-0.0222	Down
D	Crude incidence rate per 100,000	Year	50-54	I, II, III, IV	Denmark	NA	Slope	1	0.004	-0.0043	0.0123	

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	Denmark	NA	Breakpoint	1	2017	2015.5	2018.5	
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	Denmark	NA	Slope	1	0.012	0.0039	0.0201	Up
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	Denmark	NA	Slope	2	-0.0885	-0.14	-0.0369	Down
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Denmark	NA	Breakpoint	1	2016.3	2014.1	2018.5	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Denmark	NA	Slope	1	0.0137	0.0054	0.0221	Up
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Denmark	NA	Slope	2	-0.0687	-0.1222	-0.0151	Down
D	Crude incidence rate per 100,000	Year	50-54	I, II, III, IV	England	NA	Slope	1	0.0054	0.0026	0.0082	Up
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	England	NA	Breakpoint	1	2019	2018.7	2019.3	
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	England	NA	Slope	1	0.0043	0.0012	0.0074	Up
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	England	NA	Slope	2	-0.212	-0.3072	-0.1168	Down
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Breakpoint	1	2006.5	2005.5	2007.5	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Breakpoint	2	2008.2	2007.5	2009	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Breakpoint	3	2015.7	2013	2018.4	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Slope	1	8.00E-04	-0.0123	0.014	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Slope	2	0.0994	0.0215	0.1772	Up
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Slope	3	-0.0156	-0.026	-0.0052	Down
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	England	NA	Slope	4	0.0084	-0.009	0.0258	
D	Crude incidence rate per 100,000	Year	50-54	I, II, III, IV	Netherlands	NA	Slope	1	0.0027	-4.00E-04	0.0058	
D	Crude incidence rate per 100,000	Year	55-59	I, II, III, IV	Netherlands	NA	Slope	1	0.0119	0.0033	0.0206	Up
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Netherlands	NA	Breakpoint	1	2013	2012	2014	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Netherlands	NA	Breakpoint	2	2015	2014.3	2015.7	
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Netherlands	NA	Slope	1	0.005	-0.0064	0.0165	

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Netherlands	NA	Slope	2	0.1735	0.0643	0.2828	Up
D	Crude incidence rate per 100,000	Year	60-64	I, II, III, IV	Netherlands	NA	Slope	3	-0.1367	-0.1736	-0.0997	Down
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Breakpoint	1	2004.6	2004	2005.1	
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Breakpoint	2	2008.1	2007.9	2008.3	
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Breakpoint	3	2015	2013.8	2016.1	
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Breakpoint	4	2018.9	2017.2	2020.5	
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Slope	1	-0.0024	-0.0028	-0.0019	Down
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Slope	2	0.0015	8.00E-04	0.0022	Up
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Slope	3	-0.0075	-0.0079	-0.0072	Down
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Slope	4	-0.0059	-0.0065	-0.0052	Down
E	Proportional share of population	Year	<50	I, II, III, IV	Ireland	NA	Slope	5	-0.0072	-0.0077	-0.0067	Down
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Breakpoint	1	2005	2003.9	2006	
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Breakpoint	2	2008.3	2008	2008.6	
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Breakpoint	3	2014.8	2014.4	2015.2	
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Breakpoint	4	2019.4	2018.8	2020	
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Slope	1	-0.0021	-0.0034	-7.00E-04	Down
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Slope	2	-0.0072	-0.0091	-0.0054	Down
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Slope	3	0.0145	0.0135	0.0155	Up
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Slope	4	0.0011	-2.00E-04	0.0024	
E	Proportional share of population	Year	50-54	I, II, III, IV	Ireland	NA	Slope	5	0.0164	0.0135	0.0194	Up
E	Proportional share of population	Year	55-59	I, II, III, IV	Ireland	NA	Breakpoint	1	2003.6	2003.3	2004	
E	Proportional share of population	Year	55-59	I, II, III, IV	Ireland	NA	Breakpoint	2	2008.3	2007.6	2009	

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
E	Proportional share of population	Year	55-59	I, II, III, IV	Ireland	NA	Slope	1	0.0404	0.0348	0.0459	Up
E	Proportional share of population	Year	55-59	I, II, III, IV	Ireland	NA	Slope	2	-0.0067	-0.0106	-0.0028	Down
E	Proportional share of population	Year	55-59	I, II, III, IV	Ireland	NA	Slope	3	0.0105	0.0098	0.0113	Up
E	Proportional share of population	Year	60-64	I, II, III, IV	Ireland	NA	Breakpoint	1	2004.3	2003.4	2005.2	
E	Proportional share of population	Year	60-64	I, II, III, IV	Ireland	NA	Breakpoint	2	2010	2009.2	2010.8	
E	Proportional share of population	Year	60-64	I, II, III, IV	Ireland	NA	Slope	1	0.0098	0.0065	0.0132	Up
E	Proportional share of population	Year	60-64	I, II, III, IV	Ireland	NA	Slope	2	0.0241	0.0215	0.0266	Up
E	Proportional share of population	Year	60-64	I, II, III, IV	Ireland	NA	Slope	3	0.0108	0.01	0.0116	Up
E	Proportional share of population	Year	65-69	I, II, III, IV	Ireland	NA	Breakpoint	1	2008	2007.7	2008.3	
E	Proportional share of population	Year	65-69	I, II, III, IV	Ireland	NA	Breakpoint	2	2014.2	2013.8	2014.7	
E	Proportional share of population	Year	65-69	I, II, III, IV	Ireland	NA	Slope	1	-0.004	-0.0062	-0.0018	Down
E	Proportional share of population	Year	65-69	I, II, III, IV	Ireland	NA	Slope	2	0.0417	0.039	0.0444	Up
E	Proportional share of population	Year	65-69	I, II, III, IV	Ireland	NA	Slope	3	0.0089	0.007	0.0108	Up
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Breakpoint	1	2008.2	2007.6	2008.9	
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Breakpoint	2	2012.4	2011.7	2013.1	
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Breakpoint	3	2018.6	2017.9	2019.3	
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Slope	1	-0.0096	-0.0113	-0.0079	Down
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Slope	2	0.017	0.0111	0.0229	Up
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Slope	3	0.0404	0.0373	0.0436	Up
E	Proportional share of population	Year	70-74	I, II, III, IV	Ireland	NA	Slope	4	0.0141	0.0097	0.0186	Up
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	1	2005.5	2004.7	2006.2	
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	2	2007.6	2007.3	2007.9	

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	3	2018.3	2017.5	2019.1	
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Slope	1	-3.00E-04	-0.0019	0.0013	
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Slope	2	-0.0162	-0.0257	-0.0067	Down
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Slope	3	0.0195	0.0188	0.0201	Up
E	Proportional share of population	Year	>=75	I, II, III, IV	Ireland	NA	Slope	4	0.0301	0.0278	0.0324	Up
F	Crude mortality rate per 100,000	Year	<50	I, II, III, IV	Ireland	NA	Slope	1	-0.0055	-0.0427	0.0317	
F	Crude mortality rate per 100,000	Year	50-54	I, II, III, IV	Ireland	NA	Slope	1	-0.0061	-0.0361	0.024	
F	Crude mortality rate per 100,000	Year	55-59	I, II, III, IV	Ireland	NA	Slope	1	-0.0143	-0.0305	0.0019	
F	Crude mortality rate per 100,000	Year	60-64	I, II, III, IV	Ireland	NA	Slope	1	-0.0243	-0.0417	-0.007	Down
F	Crude mortality rate per 100,000	Year	65-69	I, II, III, IV	Ireland	NA	Slope	1	-0.032	-0.0504	-0.0136	Down
F	Crude mortality rate per 100,000	Year	70-74	I, II, III, IV	Ireland	NA	Slope	1	-0.0326	-0.0436	-0.0217	Down
F	Crude mortality rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Breakpoint	1	2012.4	2010.1	2014.7	
F	Crude mortality rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Slope	1	0.0048	-0.0133	0.0228	
F	Crude mortality rate per 100,000	Year	>=75	I, II, III, IV	Ireland	NA	Slope	2	-0.0324	-0.0467	-0.0181	Down
G	Proportion of cases	Year	40-84	I	Ireland	Surgery	Slope	1	6.00E-04	-4.00E-04	0.0017	
G	Proportion of cases	Year	40-84	I	Ireland	Chemotherapy	Breakpoint	1	2015	2012.6	2017.4	
G	Proportion of cases	Year	40-84	I	Ireland	Chemotherapy	Slope	1	-0.0927	-0.1219	-0.0634	Down
G	Proportion of cases	Year	40-84	I	Ireland	Chemotherapy	Slope	2	0.0922	-0.0247	0.2092	
G	Proportion of cases	Year	40-84	I	Ireland	Radiotherapy	Slope	1	-0.0405	-0.0596	-0.0214	Down
G	Proportion of cases	Year	40-84	II	Ireland	Surgery	Breakpoint	1	2007	2003	2011	
G	Proportion of cases	Year	40-84	II	Ireland	Surgery	Slope	1	0.0057	0.0021	0.0094	Up
G	Proportion of cases	Year	40-84	II	Ireland	Surgery	Slope	2	6.00E-04	-0.0011	0.0024	
G	Proportion of cases	Year	40-84	II	Ireland	Chemotherapy	Breakpoint	1	2006	2001.9	2010.1	
G	Proportion of cases	Year	40-84	II	Ireland	Chemotherapy	Slope	1	0.0099	-0.0269	0.0468	

Index	Response	Predictor	Age group	Stage	Country	Treatment	Parameter	ID	Mean	Lower CI	Upper CI	Trend
G	Proportion of cases	Year	40-84	II	Ireland	Chemotherapy	Slope	2	-0.0319	-0.0448	-0.019	Down
G	Proportion of cases	Year	40-84	II	Ireland	Radiotherapy	Slope	1	-0.0361	-0.0497	-0.0224	Down
G	Proportion of cases	Year	40-84	III	Ireland	Surgery	Slope	1	-0.002	-0.003	-0.001	Down
G	Proportion of cases	Year	40-84	III	Ireland	Chemotherapy	Breakpoint	1	2006.8	2003.3	2010.2	
G	Proportion of cases	Year	40-84	III	Ireland	Chemotherapy	Slope	1	0.024	0.0078	0.0401	Up
G	Proportion of cases	Year	40-84	III	Ireland	Chemotherapy	Slope	2	5.00E-04	-0.0052	0.0062	
G	Proportion of cases	Year	40-84	III	Ireland	Radiotherapy	Slope	1	0.0186	0.0125	0.0247	Up
G	Proportion of cases	Year	40-84	IV	Ireland	Surgery	Slope	1	-0.015	-0.021	-0.0089	Down
G	Proportion of cases	Year	40-84	IV	Ireland	Chemotherapy	Breakpoint	1	2008.1	2005.2	2011	
G	Proportion of cases	Year	40-84	IV	Ireland	Chemotherapy	Slope	1	0.0366	0.024	0.0492	Up
G	Proportion of cases	Year	40-84	IV	Ireland	Chemotherapy	Slope	2	0.0069	-0.0012	0.0151	
G	Proportion of cases	Year	40-84	IV	Ireland	Radiotherapy	Slope	1	0.008	-0.0034	0.0194	
H	Proportion of cases detected via screening	Year	60-64	I, II, III, IV	Ireland	NA	Breakpoint	1	2015.3	2015	2015.6	
H	Proportion of cases detected via screening	Year	60-64	I, II, III, IV	Ireland	NA	Slope	1	1.9086	1.6175	2.1998	Up
H	Proportion of cases detected via screening	Year	60-64	I, II, III, IV	Ireland	NA	Slope	2	-0.1254	-0.2556	0.0048	
H	Proportion of cases detected via screening	Year	65-69	I, II, III, IV	Ireland	NA	Slope	1	-0.0245	-0.1179	0.069	
I	Proportion of cases	Age group	40-84	I	Ireland	NA	Slope	1	0.03	-0.1005	0.1606	
I	Proportion of cases	Age group	40-84	II	Ireland	NA	Breakpoint	1	2.3	1.4	3.3	
I	Proportion of cases	Age group	40-84	II	Ireland	NA	Slope	1	-0.1765	-0.4004	0.0473	
I	Proportion of cases	Age group	40-84	II	Ireland	NA	Slope	2	0.0866	0.0571	0.116	Up
I	Proportion of cases	Age group	40-84	III	Ireland	NA	Slope	1	-0.0297	-0.0507	-0.0087	Down
I	Proportion of cases	Age group	40-84	IV	Ireland	NA	Slope	1	-0.0499	-0.2066	0.1068	

Key: CI – 95% Confidence interval; Age group as a predictor in I is coded as integer from 1 to 9 corresponding to 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79 and 80-84.

Note: Trends, when statistically significant, are listed as 'Up' or 'Down'.

A.3 Five-year net survival rates

Table A.3 Estimated five-year net survival rate and corresponding 95% confidence interval across age groups for colorectal cancer patients in Ireland before and after the introduction of BowelScreen

Age group	2000-2011 five-year net survival (95% CI; Number of cases)	2013-2018
40-44	0.67 (0.63-0.72; 467)	0.73 (0.68-0.78; 302)
45-49	0.62 (0.59-0.65; 897)	0.74 (0.70-0.78; 511)
50-54	0.64 (0.62-0.67; 1,499)	0.69 (0.66-0.73; 824)
55-59	0.63 (0.61-0.65; 2,180)	0.68 (0.66-0.71; 1,237)
60-64	0.61 (0.59-0.63; 2,985)	0.72 (0.70-0.74; 1,901)
65-69	0.59 (0.57-0.61; 3,510)	0.71 (0.69-0.73; 2,368)
70-74	0.56 (0.55-0.58; 4,095)	0.65 (0.62-0.67; 2,135)
75-79	0.52 (0.50-0.54; 3,965)	0.62 (0.60-0.65; 2,203)
80-84	0.45 (0.43-0.48; 3,105)	0.55 (0.52-0.59; 1,758)

Source: NCRI and CSO (life tables). BowelScreen was introduced to people aged 60 to 69 years old in 2012. The net survival analysis was implemented using the relSurv package⁽²¹⁴⁾ in R 4.3. with the Pohar-Perme estimator.⁽²¹⁰⁾ The life tables used in the analyses were estimated by LSHTM⁽²¹⁵⁾ using the population and mortality data from CSO.⁽²⁰⁶⁾

Key: CI – Confidence interval, CSO – Central Statistics Office, LSHTM – London School of Hygiene and Tropical Medicine, NCRI – National Cancer Registry Ireland.

Appendix B Test accuracy of FIT

Table B.1 Studies excluded after two-step full text review

Author, year	Country	Age range	Age-stratified results	FIT thresholds	Reasons for exclusion
Brenner 2017	Germany	50–79	No	5 to 50µg/g	Overlap with included studies
Bretagne 2021	France	50–74	Partial	30µg Hb/g	Threshold <40µg/g
Burón 2019	Spain	50–69	Partial	20µg/g	Threshold <40µg/g
Canévet 2023	France	50–77	No	30µg Hb/g	Threshold <40µg/g
Chen 2017	Germany	50–79	No	Various, 41.8µg Hb/g	Overlap with included studies; higher thresholds determined according to positivity rates
Chen 2018	Taiwan	50–69	Yes	20µg/g	Threshold <40µg/g
Gies 2021	Germany	50–79	Yes	2 to 17µg/g	Threshold <40µg/g
Gies 2018	Germany	50–79	No	2 to 17µg/g, various	Higher thresholds determined by fixing specificity
Gill 2021	US	50–70+	Yes	100ng/ml	Threshold <40µg/g
Grancher 2022	France	50–80	Partial	Various, 30µg Hb/g	Included both qualitative and quantitative FITs
Imperiale 2024	US	40–76+	Yes	20µg Hb/g	Threshold <40µg/g
Itoh 1996	Japan	40+	No	50, 200ng Hb/mL	Higher FIT threshold determined from ROC analysis
Kang 2020	China	40–75	No	50 to 200µg/L	Sample included hospital inpatients and outpatients
Kim 2017	Korea	30–50+	Yes	20µg Hb/g	Threshold <40µg/g
Kortlever 2021	Netherlands	50–75	Partial	20, 50µg Hb/g	Individualised FIT cut-offs calculated based on age and sex
Liles 2018	US	49–75	Partial	150ng/ml	Threshold <40µg/g
Lu 2021	China	50–74	Yes	20µg Hb/g	Threshold <40µg/g
Niedermaier 2018	Germany	50–79	No	Various, 27µg/g	Overlap with included studies; cutoffs determined by fixing specificity
Njor 2022	Denmark	50–75	Yes	100ng Hb/mL	Threshold <40µg/g
Selby 2018	US	50–75	Yes	10 to 30µg/g	Threshold <40µg/g
Yeh 2021	Taiwan	20–50+	Yes	100ng Hb/mL	Threshold <40µg/g
Yuan 2019	China	45–75	No	150 to 400ng/mL	Health examination population

Note: Some studies were excluded for multiple reasons. Key: FIT – faecal immunochemical test; Hb – haemoglobin.

B.1 Studies excluded after two-step full text review

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Table B.2 Sample characteristics of included studies

Author Year	Sample description and exclusions	Demographic characteristics	Timing of reference standard
Aniwan 2017 ⁽²⁵⁷⁾	All asymptomatic participants aged 50-75 who participated in a health promotion programme in six university hospitals across Thailand were invited. Exclusion criteria were prior colon examination, previous colonic resection, previous history of CRC, IBD, family history of hereditary CRC such as FAP, positive FOBT in the last year.	Male: n=566 (38.3%) Female: n=913 (61.7%) 50-59 yrs: n=732 (49.5%) 60-69 yrs: n=559 (37.8%) 70-75 yrs: n=188 (12.7%)	Colonoscopy within 3 days of FIT.
Breekveldt 2023 ⁽²⁵⁶⁾	Included patients were those who participated in the Dutch national CRC screening programme between 2014 and 2017. All individuals aged 55 to 74 were invited biennially for FIT-based screening. The programme was gradually rolled out by birth cohort.	Round1 Male: n= 1,113,736 (48.4%) Female: n= 1,188, 975 (51.6%) 55-59yrs: n= 353,178 (15.3%) 60-64yrs: m=813,106 (35.3%) 65-69yrs: n=673,110 (29.2%) 70-74yrs: n=187,583 (8.1%) >=75yrs: n=275,734 (12.0%)	Screen-detected CRC was defined as CRC diagnosed within 180 days after colonoscopy following positive FIT (time interval between FIT and colonoscopy not reported). Interval cancer was defined as CRC diagnosed before invitation to the next screening round (<=24 months).
Brenner 2018 ⁽²⁷¹⁾	Participants of screening colonoscopy recruited by a network of up to 20 gastroenterology practices. Excluded: age <50 years or ≥80 years (N=170); history of CRC or inflammatory bowel disease (N=41); colonoscopy in the previous 5 years (N=270); inadequate bowel preparation before colonoscopy (N=472); incomplete colonoscopy (cecum not reached, N=29).	Male: n=1559 (48.6%) Female: n=1652 (51.4%) 50-64 yrs: n=2124 (66.1%) 65-79 yrs: n=1087 (33.9%)	Not reported in this paper.
Digby 2023 ⁽²⁸⁰⁾	All participants in the Scottish Bowel Screening Programme from November 2017 to March 2018.	Male: n=111,141 (47.9%) Female: n=129,935 (52.1%) 50-54 yrs: n=57,767 (24.9%) 55-59 yrs: n=44,777 (20.2%) 60-64 yrs: n=53,150 (22.9%) 65-69 yrs: n=36,886 (15.9%) 70-74 yrs: n=39,496 (17.0%)	Not reported for colonoscopy. Interval cancers were CRCs that arose within 2 years of a screening FIT result <80µg/g.
Grobbee 2017 ⁽²⁷⁸⁾	Individuals with a history of inflammatory bowel disease or CRC, as well as those who had undergone a full colonic examination in the past five years, those with an estimated life expectancy of <5 years, and people who were unable to give informed consent were excluded from the study.	Male: n=638 (50.8%) Female: n=618 (49.2%) Median age Male: 61 yrs (IQR 56, 66) Female: 60 yrs (IQR 55, 65)	Participants were instructed to perform FIT at home, within 48 hours before the colonoscopy, but before starting the bowel preparation.

Author Year	Sample description and exclusions	Demographic characteristics	Timing of reference standard
Hernandez 2014 ⁽²⁷⁹⁾	Exclusion criteria included personal history of CRC, adenoma or inflammatory bowel disease, family history of hereditary or familial CRC (i.e., > 2 first-degree relatives with CRC or one diagnosed before the age of 60 years), severe comorbidity, previous colectomy, FIT screening in the past 2 years, sigmoidoscopy or colonoscopy within the past 5 years, or symptoms requiring additional workup. Individuals were also excluded if they did not accept the study or refused to undergo the colonoscopy.	Male: n=386 (49.6%) Female: n=393 (50.4%) Age: Mean=57.55 ± 4.55 yrs	All participants collected 2 stool samples from 2 consecutive days the week before the colonoscopy was scheduled.
Niedermaier 2023 ⁽²⁷²⁾	Excluded participants aged <50 or >80, with a history of CRC or IBD, colonoscopy in the past 5 years, inadequate bowel prep, incomplete colonoscopy, undefined polyp from colonoscopy findings, and stool sampling after colonoscopy.	Male: n=3,583 (48.4%) Female: n=3,815 (51.6%) 50-59 yrs: n=3,605 (48.7%) 60-79 yrs: n=3,793 (51.3%)	90% of screening colonoscopies were done within 9 days after the stool test, 94% within 2 weeks.
Njor 2021 ⁽²⁷⁵⁾	All citizens aged 50 to 74 who provided an analysable stool sample between March 2014 and December 2015, as part of the Danish CRC screening programme. n=488 sent in an unanalysable stool sample and were excluded.	Not reported	Participants were followed for CRC diagnoses using the Danish National Pathology Data Bank and National Patient Register, linked to the CRC Screening Database, for 2 years after the stool sample was analysed. 90.1% of participants with a positive FIT had a colonoscopy within 6 months.
RibbingWilén 2019 ⁽²⁷³⁾	1155 persons who had accepted participation in the colonoscopy arm of SCREESCO were invited to send in two FIT. Inclusion period was one year starting from March 2016. n=123 did not have colonoscopy, n=192 did not complete FIT, n=8 did not complete study questionnaire, n=26 with polyps not sent for pathology.	Male: n=416 (51.6%) Female: n=390 (48.4%) 60 yrs: n=806	Not reported.
RibbingWilén 2022, 2024 ^(89, 274)	The program invited all 60- to 69-year-olds residing in the region without exclusions, except participants from previous rounds referred to an adenoma surveillance program or surgery.	Round 1 Male: n=68,838 (46.8%) Female: n=78,140 (53.2%) 60-64 yrs: n=88,619 (60.3%) 65-69 yrs: n=58,359 (39.7%)	Two year follow up. Time interval between FIT and colonoscopy (for 'FIT positive') not described.
Sekiguchi 2021 ⁽²⁷⁷⁾	All residents on the island aged 40–79 years without uncontrollable complications, including unstable angina, acute myocardial infarction, heart failure, chronic respiratory disease, and bleeding tendency, that made the safe performance of colonoscopy difficult were recruited to the Oshima study. Individuals who did not have colonoscopy (n=42), underwent incomplete colonoscopy (poor bowel preparation and/or not reaching the cecum) (n=7), did not hand in 2-day FIT samples (n=21), had a history of colorectal surgery or colonoscopic treatment (n=128), or lacked the information required for score calculation (n=1) were excluded from this study.	Male: n=518 (43.5%) Female: n=673 (56.5%) 40-49 yrs: n=210 (17.6%) 50-59 yrs: n=256 (21.5%) 60-69 yrs: n=415 (34.8%) 70+ yrs: n=310 (26.0%)	FIT samples returned within 30 days of colonoscopy.

Author Year	Sample description and exclusions	Demographic characteristics	Timing of reference standard
Vanaclocha-Espi 2021 ⁽²⁷⁶⁾	All participations of the cohort of men and women aged 50–69 invited to take part in the CRCSPs from 2006 until December 2012. n=13,124 with a qualitative test were excluded.	Not reported	Not reported for colonoscopy. Interval cancers were those diagnosed within 0-24 months of a negative FIT, or longer in the event that the following invitation was delayed.

Key: CRC – colorectal cancer; CRCSP – colorectal cancer screening programme; FAP – familial adenomatous polyposis; FIT – faecal immunochemical test; FOBT – faecal occult blood test; IQR – interquartile range; n – number; yrs – years.

Table B.3 Extracted or derived 2x2 tables for studies with a colonoscopy reference standard

Author, year	FIT device, threshold ^{\$}	FIT participants <i>n</i>	Colorectal cancer				Advanced neoplasia				Advanced adenomas	
			TP	FN	TN	FP	TP	FN	TN	FP	TP	FN
Aniwan, 2017 ⁽²⁵⁷⁾	OC-Sensor™ 40µg/g	1479	9	5	1,401	64	23	114	1,292	50	NR	NR
Brenner, 2018 ^{*(271)}	FOB Gold® 40µg/g	3,211	20	5	3,040	146	89	222	2,823	77	69	217
	FOB Gold® 50µg/g	3,211	18	7	3,059	127	77	234	2,832	68	59	227
Grobbee, 2017 ⁽²⁷⁸⁾	OC-Sensor™ 40µg/g	1,256	NR	NR	NR	NR	28	91	1,121	16	NR	NR
Hernandez, 2014 ⁽²⁷⁹⁾	OC-Sensor™ 40µg/g	779	4	1	733	41	27	70	664	18	NR	NR
Niedermaier, 2023 ^{*(272)}	FOB Gold® 45µg/g	7,398	43	11	6,999	345	197	531	6,479	191	NR	NR
RibbingWilén, 2019 ⁽²⁷³⁾	OC-Sensor™ 40µg/g	806	NR	NR	NR	NR	8	73	714	11	NR	NR
Sekiguchi, 2021 ⁽²⁷⁷⁾	OC-Sensor™ 40µg/g	1,191	6	4	1,141	40	20	92	1,053	26	14	88

* Overlapping study samples.

\$ converted from ng/ml for OC-Sensor™ if appropriate.

Key: FIT – faecal immunochemical test; FN – false negatives; FP – false positives. n – number; NR – not reported; TN – true negatives; TP – true positives.

Table B.4 Extracted or derived 2x2 tables for studies with a registry reference standard

Author, year	FIT device, threshold ^{\$}	FIT participants	Colorectal cancer			
		<i>n</i>	TP	FN	TN	FP
Breekveldt 2023 ⁽²⁵⁶⁾	FOB Gold®, 47µg/g	2,302,711	12,183	2,256	2,151,326	136,946
Digby 2023 ⁽²⁸⁰⁾	Not reported, 40µg/g	232,076	309	118	219,610	12,039
Vanaclocha-Espi 2021 ⁽²⁷⁶⁾	Various, 40µg/g	545,505	1,737	448	521,726	21,594
Njor 2021 ⁽²⁷⁵⁾	OC-Sensor™, 45µg/g	531,828	1,923	624	509,168	20,113

^{\$} converted from ng/ml for OC-Sensor™ if appropriate.

Key: FIT – faecal immunochemical test; FN – false negatives; FP – false positives; TN – true negatives; TP – true positives.

Table B.5 Sensitivity and specificity of FIT for the detection of advanced neoplasia by sex

Author, year	FIT brand, threshold ^{\$}	Sex	FIT participants <i>n</i>	Positivity rate	Cases (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity (95% CI)
Niedermaier 2023 ⁽²⁷²⁾	FOB Gold® 45µg/g	Male	3,583	6.7%	133/446	29.8 ^Ω	96.6 ^Ω
		Female	3,815	3.9%	64/282	22.7 ^Ω	97.6 ^Ω
Grobbee 2017 ⁽²⁷⁸⁾	OC-Sensor™ 40µg/g	Male	638	3.8%	17/68	25.0 (16.1, 36.6)	98.8 (97.4, 99.4)
		Female	618	3.2%	11/51	21.6 (12.4, 34.9)	98.4 (97.0, 99.2)

Note: Colonoscopy reference standard. 95% CI as reported. ^Ω Estimates derived from available data.

Key: CI – confidence intervals; FIT – faecal immunochemical test; *n* – number; SD – screen detected.

Table B.6 Sensitivity and specificity of FIT for the detection of colorectal cancer by sex

Author, year	FIT brand, threshold	Sex	FIT participants <i>n</i>	Positivity rate	Cases (SD/all) <i>n</i>	Sensitivity (95% CI)	Specificity (95% CI)
Breekveldt 2023 ⁽²⁵⁶⁾	FOB Gold® 47µg/g	Male	1,113,736	8.0%	7,584/8,762	86.6 (85.8, 87.3)	92.6 ^Ω
		Female	1,188,975	5.0%	4,599/5,677	81.0 (80.0, 82.0)	95.3 ^Ω

Note: Registry reference standard. 95% CI as reported. ^Ω Estimates derived from available data.

Key: CI – confidence intervals; FIT – faecal immunochemical test; SD – screen detected.

Table B.7 Sensitivity of FIT for the detection of proximal and distal AN

Author, year	FIT brand, threshold ^{\$}	FIT participants <i>n</i>	Target condition	Cases (SD/all) <i>n</i>	Sensitivity 95% CI
Aniwan 2017 ⁽²⁵⁷⁾	OC-Sensor™ 40µg/g	1,479	Proximal AN	9/44	20.5 (9.8, 35.3)
			Distal AN	13/85	15.3 (8.4, 24.7)
Sekiguchi 2021 ^{*(277)}	OC-Sensor™ 40µg/g	1,191	Right-sided AN	NR	4.9 (0.6, 16.5)
			Left-sided AN	NR	24.1 (13.9, 37.2)

Note: colonoscopy reference standard. 95% CI as reported.

* Sensitivity for right-sided/left-sided AN calculated based on participants who had either right- or left-sided AN only (excluding those who had both).

\$ converted from ng/ml for OC-Sensor™ if appropriate.

Key: AN – advanced neoplasia; CI – confidence intervals; FIT – faecal immunochemical test; *n* – number; NR – not reported; SD – screen detected.

Table B.8 Sensitivity of FIT for the detection of proximal and distal CRC

Author, year	FIT brand, threshold	FIT participants <i>n</i>	Target condition	Cases (SD/all) <i>n</i>	Sensitivity 95% CI
Ribbing Wilén 2022 ⁽²⁷⁴⁾	OC-Sensor™ 40µg/g (women) 80µg/g (men)	146,978	Proximal CRC	65/125	52.0
			Distal CRC	192/255	75.3

Note: registry reference standard. 95% confidence intervals not reported.

Key: CI – confidence intervals; CRC – colorectal cancer; FIT – faecal immunochemical test; SD – screen detected.

Figure B.1 Risk of bias and applicability concerns summary

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Aniwan 2017	—	+	+	?	—	+	+
Breekveldt 2023	+	+	—	?	+	+	+
Brenner 2018	—	+	+	—	—	+	+
Digby 2023	+	?	—	?	+	?	+
Hernandez 2014	—	+	+	—	—	+	+
Grobbee 2017	—	+	+	?	+	+	+
Niedermaier 2023	—	+	+	—	—	+	+
Njor 2021	+	+	—	?	+	+	+
RibbingWilén 2019	?	+	+	—	?	+	+
RibbingWilén 2024	+	—	—	?	+	—	+
Sekiguchi 2021	—	+	+	—	—	+	+
Vanaclocha-Espi 2021	+	?	—	?	+	?	+

Low risk
 High risk
 Unclear risk

Note: Risk of bias and applicability assessed using QUADAS-2.

Appendix C Review of colorectal cancer screening in those aged 50 to 54 years

Table C.1 Screening uptake rates of included FIT-based cohort studies

Study (Primary Modality / Follow-up Modality)	Invitation Years	Sex	Eligible	Invited	Returned FIT	FIT Uptake Rate		Colonoscopy follow-up rate for those with positive FIT %
						No. of FIT users as a % of those invited	No. of FIT users as a % of those eligible	
Baldacchini 2021 ⁽³¹⁴⁾ FIT/Colonoscopy	2005-2008	Male	253,424	220,599	107,577	48.8%	42.4%	77%
		Female	269,698	237,285	124,769	52.6%	46.3%	74.8%
	2009-2012	Male	262,296	252,235	126,139	50.0%	48.1%	79.8%
		Female	280,101	271,546	145,823	53.7%	52.1%	78.3%
	2013-2016	Male	278,507	268,963	133,101	49.5%	47.8%	79.3%
		Female	298,248	289,041	153,888	53.2%	51.6%	77.4%
	2005-2016	All	1,642,274	1,539,669	791,297	51.4%	48.2%	77.8%
Chiu 2015 ⁽³¹²⁾ FIT/Colonoscopy	2004-2009	All	5,417,699	<i>NR</i>	1,160,895	<i>NR</i>	21.4%	80%
Chiu 2021 ⁽³¹¹⁾ FIT/Colonoscopy	2004-2009	All	5,417,699	<i>NR</i>	3,067,853	<i>NR</i>	56.6%	70% Not specified if complete
Hsiao 2024 ⁽³¹⁶⁾ FIT/Colonoscopy	2010-2013	All	1,596,995	<i>NR</i>	719,073	<i>NR</i>	45.0%	62.9%
Njor 2022 ⁽³¹⁵⁾ FIT/Colonoscopy	2014-2017	All	<i>NR</i>	262,893	175,480	66.7%	<i>NR</i>	<i>NR</i>

Key: FIT – faecal immunochemical test; FSIG – flexible sigmoidoscopy; gFOBT – guaiac-based faecal occult blood test; HR – Hazard Ratio; NORCCAP – Norwegian colorectal cancer prevention; NR – not reported.

Table C.2 Screening uptake rates of gFOBT or FSIG included studies

Study (Primary Modality / Follow-up Modality)	Invitation Years	Sex	Invited	Attended Primary Test	Primary Modality Uptake rate (%)	Colonoscopy follow-up rate for those with positive primary tests (%)
Burgundy Trial, Faivre 2004 ⁽³¹⁹⁾ gFOBT/ Colonoscopy	1988-1989 (Round 1)	All	45,642	24,099	52.8%	<i>NR</i>
	1990 (Round 2)	All	43,852	23,680	54.0%	<i>NR</i>
	1992 (Round 3)	All	41,404	23,724	57.3%	<i>NR</i>
	1994 (Round 4)	All	38,887	22,671	58.3%	<i>NR</i>
	1996 (Round 5)	All	37,502	21,076	56.2%	<i>NR</i>
	1998 (Round 6)	All	34,623	18,627	53.8%	<i>NR</i>
	1988-1998 (All)	All	<i>NR</i>	<i>NR</i>	55.4%	87%
Funen Trial, Kronborg 2004 ⁽³²⁰⁾ gFOBT/ Colonoscopy	1985-1986 (Round 1)	All	30,762	20,672	67.2%	83.7%
	1987-1988 (Round 2)	All	20,113	18,781	93.4%	89.3%
	1989-1990 (Round 3)	All	18,236	17,279	94.8%	82.1%
	1991-1992 (Round 4)	All	16,746	15,845	94.6%	84%
	1993-1994 (Round 5)	All	15,279	14,203	93.0%	81.6%
	1995-1996 (Round 6)	All	13,602	12,533	92.1%	82.4%
	1997-1998 (Round 7)	All	11,902	11,058	92.9%	83.7%
	1999-2000 (Round 8)	All	10,615	9,774	92.1%	74.1%
	2000-2002 (Round 9)	All	9,367	8,558	91.4%	74.6%
	1988-2002 (All rounds)	All	146,622	128,703	87.8%	82.3%

Study (Primary Modality / Follow-up Modality)	Invitation Years	Sex	Invited	Attended Primary Test	Primary Modality Uptake rate (%)	Colonoscopy follow-up rate for those with positive primary tests (%)
Minnesota Colon Cancer Control Study, Shaukat 2013 ⁽⁸⁴⁾ gFOBT/Colonoscopy	1976-1992	All	NR	NR	90% completed 1 or more rounds	83% Not specified if complete
Nottingham Trial, Scholefield 2012 ⁽⁸⁵⁾ gFOBT/Colonoscopy	1981-1995	All	NR	76,056	Uptake at first invitation of approximately 57%	NR
NORCCAP Trial Holme 2018 ⁽³¹⁷⁾ Sigmoidoscopy or Sigmoidoscopy with FIT/ Colonoscopy	1991-2001	All	20,552	NR	63.05%	96%
		Male	10,255	NR	61.4%	NR
		Female	10,297	NR	64.7%	NR

Key: FIT – faecal immunochemical test; FSIG – flexible sigmoidoscopy; gFOBT – guaiac-based faecal occult blood test; NORCCAP – Norwegian colorectal cancer prevention; NR – not reported.

Appendix D Review of cost-effectiveness

D.1 Outline of extracted cost-effectiveness data

Table D.1 Data extracted from each cost-effectiveness study

Extracted data	
General study characteristics	- Author name, year - Country setting - Type of analysis - Measure of health outcome(s) - Assumed willingness-to-pay threshold - Model structure (and type) - Health states - Perspective - Time horizon - Cycle length - Discount rate - Price year - Currency
Population characteristics	- Target population - Source of disease data
Intervention / comparator characteristics	- Number of screening strategies - FIT threshold(s) - Screening start age(s) - Screening stop age(s) - Uptake/adherence - FIT test administration method - Surveillance schedule after polyp removal - Treatment of individuals who have a negative scope after positive FIT
Costs and consequences	- Type of costs included - Cost sources - Source of utility data - Utility value
Sensitivity and scenario analysis	- Type of uncertainty analysis (e.g., probabilistic sensitivity analysis) - Scenario analyses investigated (e.g., incomplete adherence) - Impact of scenario analyses on cost-effectiveness findings
Author-reported conclusions and limitations	- Reported conclusions - Reported limitations - Funding source
Costs	- Type - Parameter - Frequency - Value
Diagnostic performance	- Type - Threshold

Extracted data	
	▪ CRC stage ▪ Sensitivity ▪ Specificity
Cost-effectiveness findings	▪ Analysis (e.g., base case vs scenario) ▪ Strategy ▪ Comparator ▪ Outcome ▪ Unit ▪ Value

Key: CRC – colorectal cancer; FIT – faecal immunochemical test.

D.2 Assessment of relevance and credibility of cost-effectiveness studies

Table D.2 Summary of responses to ISPOR questionnaire: relevance

Study	Question				Decision
	1. Is the population relevant?	2. Are any critical interventions missing?	3. Are any relevant outcomes missing?	4. Is the context applicable?	
Heinävaara 2022 ⁽³⁶²⁾	Yes	Yes	Yes	Yes	Sufficient
Ladabaum 2014 ⁽³⁶³⁾	Yes	Yes	No	No	Insufficient
Lansdorp-Vogelaar 2018 ⁽³⁶⁴⁾	Yes	Yes	Yes	No	Insufficient
McFerran 2022 ⁽³⁶⁵⁾	Yes	Yes	No	Yes	Sufficient
Thomas 2021 ⁽³⁶⁶⁾	Yes	Yes	No	Yes	Sufficient
van der Meulen 2017 ⁽³⁶⁷⁾	Yes	Yes	No	Yes	Sufficient
Whyte 2021 ⁽³⁶⁸⁾	Yes	No	Yes	Yes	Sufficient
van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾	Yes	No	No	Yes	Sufficient

Table D.3 Summary of responses to ISPOR questionnaire: credibility

Domain	Question	Heinävaara 2022 ⁽³⁶²⁾	McFerran 2022 ⁽³⁶⁵⁾	Thomas 2021 ⁽³⁶⁶⁾	van der Meulen 2017 ⁽³⁶⁷⁾	Whyte 2021 ⁽³⁶⁸⁾	van de Schootbrugge- Vandermeer 2024 ⁽³⁶⁹⁾
Validation	5. Is external validation of the model sufficient?	Yes	Yes	No	Unclear	Yes	Yes
	6. Is internal verification of the model sufficient?	Unclear	Unclear	No	Unclear	Yes	Unclear
	7. Does the model have sufficient face validity?	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Conclusion (validation)</i>	<i>Strength</i>	<i>Strength</i>	<i>Neutral</i>	<i>Neutral</i>	<i>Strength</i>	<i>Strength</i>
Design	8. Is the design of the model adequate?	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Conclusion (Design)</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>
Data	9. Are the data used in populating the model suitable?	Yes	Yes	Unclear	Yes	Yes	Yes
	<i>Conclusion (Data)</i>	<i>Strength</i>	<i>Neutral</i>	<i>Weakness</i>	<i>Neutral</i>	<i>Strength</i>	<i>Strength</i>
Analysis	10. Were the analyses adequate?	Yes	Yes	Yes	Yes	Yes	Yes
	11. Was there adequate assessment of uncertainty?	No	Yes	Yes	No	Yes	Yes
	<i>Conclusion (Analysis)</i>	<i>Neutral</i>	<i>Neutral</i>	<i>Strength</i>	<i>Neutral</i>	<i>Strength</i>	<i>Strength</i>
Reporting	12. Was the reporting adequate?	Yes	No	No	Yes	Yes	No
	<i>Conclusion (Reporting)</i>	<i>Neutral</i>	<i>Weakness</i>	<i>Weakness</i>	<i>Weakness</i>	<i>Neutral</i>	<i>Weakness</i>
Interpretation	13. Was interpretation fair and balanced?	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Conclusion (Interpretation)</i>	<i>Neutral</i>	<i>Strength</i>	<i>Neutral</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>
Conflict of interest	14. Were there any potential conflicts of interest?	No	No	No	Unclear	No	No
	15. Were steps taken to address conflicts?	Not applicable	Not applicable	Not applicable	Unclear	Not applicable	Not applicable

Domain	Question	Heinävaara 2022 ⁽³⁶²⁾	McFerran 2022 ⁽³⁶⁵⁾	Thomas 2021 ⁽³⁶⁶⁾	van der Meulen 2017 ⁽³⁶⁷⁾	Whyte 2021 ⁽³⁶⁸⁾	van de Schootbrugge- Vandermeer 2024 ⁽³⁶⁹⁾
	<i>Conclusion (COI)</i>	<i>Strength</i>	<i>Strength</i>	<i>Strength</i>	<i>Weakness</i>	<i>Strength</i>	<i>Strength</i>
Decision		Sufficient	Sufficient	Sufficient	Insufficient	Sufficient	Sufficient

Key: COI – conflict of interest.

D.3 Assessment of methodological quality of cost-effectiveness studies

Table D.4 Summary of methodological assessment based on Philips checklist: Heinävaara 2022

Heinävaara 2022 ⁽³⁶²⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	Starting screening earlier may be cost-effective, but other extensions of the screening program may be even more efficient
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	Investigated the cost effectiveness of different CRC screening strategies to identify the optimal extension of the program
	Is the primary decision-maker specified?	No	
S2	Is the perspective of the model stated clearly?	No	
	Are the model inputs consistent with the stated perspective?	Yes	The model was calibrated to observed CRC incidence and stage distribution in the Dutch population in the years before the introduction of screening (2009-2013), to ensure that the model imitates the Dutch population accurately and model predictions of the course of CRC correspond closely to reality
	Has the scope of the model been stated and justified?	Yes	Used the MISCAN-Colon model to simulate a cohort of ten million 50-year-olds in 2018, to which we applied 588 different screening strategies by varying four parameters: 1) screening interval of 1, 2 or 3 years, 2) FIT cut-off of 15, 20, 47 or 60 µg/g, 3) start age of 50, 52, 54, 55, 56, 58 or 60 years, and 4) stop age of 70, 72, 74, 75, 76, 78 or 80 years
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	For each strategy, life-time quality-adjusted life-years (QALYs) gained, costs and colonoscopy demand were calculated. QALYs and costs were discounted at 3%
S3	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	MISCAN model well known and published, validated

Heinävaara 2022 ⁽³⁶²⁾			
Quality criterion	Questions	Response	Comments
S4	Are the sources of data used to develop the structure of the model specified?	Yes	Used Dutch population-based life-tables from 2019 to determine background mortality rates, FIT characteristics per FIT positivity cut-off were calibrated on observed outcomes of the Dutch CRC screening program, Costs for the different elements of the screening process, such as the costs for FIT (including costs for the invitation, test kit, FIT analysis and organization of the screening program) and the costs for diagnostic follow-up (colonoscopy), were obtained from the Dutch National Institute for Public Health and the Environment in 2018. Treatment costs were obtained through matching of treatments and complications in medical records with the associated costs from the National Health Care Institute in 2018. Quality-of-life losses were assumed to be the same as in a previous publication
	Are the causal relationships described by the model structure justified appropriately?	Yes	Not outlined in the paper but based on MISCAN model, published elsewhere
	Are the structural assumptions transparent and justified?	Yes	Published re MISCAN in other reports
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	As above
S5	Is there a clear definition of the options under evaluation?	Yes	Age extension of current program looked at older and younger age extensions
	Have all feasible and practical options been evaluated?	Yes	Included relevant ages and FIT thresholds, looked at scope capacity also
	Is there justification for the exclusion of feasible options?	NA	
S6	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Widely validated for CRC screening

Heinävaara 2022 ⁽³⁶²⁾				
Quality criterion	Questions	Response		Comments
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime	
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Not outlined here but based on MISCAN model, published elsewhere	
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Yes	Not outlined here but based on MISCAN model, published elsewhere	
	Is the cycle length defined and justified in terms of the natural history of disease?	No	Cycle length not reported	
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Uses Dutch epidemiological and cost data; source of utilities is unclear	
	Where choices have been made between data sources, are these justified appropriately?	NA		
	Has particular attention been paid to identifying data for the important parameters in the model?	Yes	Used incidence data prior to screening programme	
	Has the quality of the data been assessed appropriately?	No	Not described	
	Where expert opinion has been used, are the methods described and justified?	NA		
D2	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Well validated model	

Heinävaara 2022 ⁽³⁶²⁾			
Quality criterion	Questions	Response	Comments
D2a	Is the choice of baseline data described and justified?	Yes	Simulated one birth cohort born in 1968 (thus eligible for screening in 2023 when screening starts at age 55) and used Dutch population-based life-tables from 2019 to determine background mortality rates
	Are transition probabilities calculated appropriately?	Yes	Transition probabilities between different states in the disease process are based on observed outcomes in the Netherlands and in clinical trials.
	Has a half-cycle correction been applied to both cost and outcome?	No	Not mentioned
	If not, has this omission been justified?	NA	
D2b	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Are the costs incorporated into the model justified?	Yes	Costs for the different elements of the screening process, such as the costs for FIT (including costs for the invitation, test kit, FIT analysis and organization of the screening program) and the costs for diagnostic follow-up (colonoscopy), were obtained from the Dutch National Institute for Public Health and the Environment in 2018. Treatment costs were obtained through matching of

Heinävaara 2022 ⁽³⁶²⁾			
Quality criterion	Questions	Response	Comments
			treatments and complications in medical records with the associated costs from the National Health Care Institute in 2018. Quality-of-life losses were assumed to be the same as in a previous publication
	Has the source for all costs been described?	Yes	as above
	Have discount rates been described and justified given the target decision-maker?	No	described but not justified
D2d	Are the utilities incorporated into the model appropriate?	Yes	Utility values look appropriate, along with age-dependent QoL scores based on EQ-5D-3L index values
	Is the source for the utility weights referenced?	No	Only specifies that EQ-5D was used. Source apparently reported in another publication that was not referenced
	Are the methods of derivation for the utility weights justified?	NA	
	Have all data incorporated into the model been described and referenced in sufficient detail?	No	Source of QoL not reported
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found
D3	Is the process of data incorporation transparent?	Yes	Additional info provided in supplement, and largely referenced to other publications
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	No	Didn't discuss this for all parameters but do report that costs and quality-of-life losses were drawn from a Gamma distribution for PSA
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	Yes	PSA undertaken
D4	Have the four principal types of uncertainty been addressed?	No	Parameter only

Heinävaara 2022 ⁽³⁶²⁾			
Quality criterion	Questions	Response	Comments
	If not, has the omission of particular forms of uncertainty been justified?	No	
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	No	
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	Costs and quality-of-life losses were drawn from a Gamma distribution, with shape and scale parameter such that the mean was equal to the base-case assumption in Table Sb and 50% and 200% of the mean were four standard deviations apart
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	No	Mention for one parameter Sensitivity CRC (range in PSA)
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Well established MISCAN model
C2	Are any counterintuitive results from the model explained and justified?	NA	Not discussed
	If the model has been calibrated against independent data, have any differences been explained and justified?	NA	Although relies on calibration, no apparent differences were observed
	Have the results of the model been compared with those of previous models and any differences in results explained?	No	

Key: C – consistency; CRC – colorectal cancer; D – data; FIT – faecal immunochemical test; PSA – probabilistic sensitivity analysis; QALY – quality adjusted life year; S – structure.

Table D.5 Summary of methodological assessment based on Philips checklist: McFerran 2022

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	Most cost-effectiveness analyses (CEAs) of CRC screening do not consider the binding colonoscopy capacity constraints when assessing CE
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	The objective of this study is to further explore the potential for improved effectiveness and cost-effectiveness within a capacity-constrained system, and assess whether longer screening intervals enhance screening effectiveness within colonoscopy constraints
	Is the primary decision-maker specified?	No	Uses Irish screening program as a case study but relies on Dutch CRC incidence data. Ultimately no clear decision maker; paper is illustrative using a mix of data
S2	Is the perspective of the model stated clearly?	No	But costs are consistent with healthcare payer perspective
	Are the model inputs consistent with the stated perspective?	No	Uses Irish CRC screening program as a case study but applies Dutch CRC incidence data, along with non-Irish costs and discount rates inconsistent with Ireland
	Has the scope of the model been stated and justified?	Yes	To broaden the scope for optimizing screening within colonoscopy capacity constraints by simulating 525 screening strategies in addition to no screening.
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	CRC benefits, QALYs, costs (consistent with a healthcare payer perspective), ICER
S3	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	Natural disease history model with screening module
	Are the sources of data used to develop the structure of the model specified?	Yes	Model based on established MISCAN model, which is detailed elsewhere
	Are the causal relationships described by the model structure justified appropriately?	Yes	The relationships are well established in MISCAN

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
S4	Are the structural assumptions transparent and justified?	Yes	Detailed elsewhere but again no issues observed in the established MISCAN model
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	No issues found in established MISCAN
S5	Is there a clear definition of the options under evaluation?	Yes	Modelled 5 FIT cutoffs of 10, 15, 20, 30, and 40 µg Hb/g (equivalent to 50, 75, 100, 150, and 200ng Hb/mL); considered intervals of 1, 2, 3, 4, and 5yr; in addition to the current program start and stop age of 60 and 70 yr, respectively, simulated screening start ages of 45, 50, 55, 60, 65, and 70 yr, with stop ages of 70, 75, and 80 yr or close approximations thereof depending on the screening interval
	Have all feasible and practical options been evaluated?	Yes	Broad range of strategies considered
	Is there justification for the exclusion of feasible options?	NA	
S6	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Microsimulation model based on MISCAN-Colon model
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Treatment effect is essentially modelled as the effect of screening on CRC incidence and mortality reduction; hence no treatment or treatment duration modelled outside of standard treatment of CRC
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological	Yes	Based on natural disease history of CRC

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
D1	process of the disease in question and the impact of interventions?		
	Is the cycle length defined and justified in terms of the natural history of disease?	No	Cycle length not reported
	Are the data identification methods transparent and appropriate given the objectives of the model?	No	Source of natural disease history not reported, along with utility source; costs derive from historical Dutch analysis (not updated)
	Where choices have been made between data sources, are these justified appropriately?	No	Unclear why Dutch data used
	Has particular attention been paid to identifying data for the important parameters in the model?	No	Since using Ireland as case study, Irish data on CRC more relevant; no discussion on why not used; similarly Irish cost data would be more relevant with Irish discount rates applied
	Has the quality of the data been assessed appropriately?	No	No discussion on quality of parameters included
D2	Where expert opinion has been used, are the methods described and justified?	NA	None used
	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Natural disease history model, reportedly based on Dutch population
D2a	Is the choice of baseline data described and justified?	Yes	Single birth cohort of average-risk individuals (i.e., adults aged 45+ without CRC)
	Are transition probabilities calculated appropriately?	Yes	Calibrated to known CRC incidence in a Dutch population, details of which are cited elsewhere
	Has a half-cycle correction been applied to both cost and outcome?	No	Cycle length not reported and no mention of half-cycle correction
	If not, has this omission been justified?	No	No information provided

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
D2b	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Are the costs incorporated into the model justified?	No	Although choice of costs is appropriate, these are historical (possibly priced in 2010) and reflect costs specific to the Netherlands
	Has the source for all costs been described?	Yes	Published source
	Have discount rates been described and justified given the target decision-maker?	Unclear	Discount rate of 3% justified as being in accordance with previous Dutch analysis; inconsistent with recommended Irish rate. Target decision-maker is unclear.
D2d	Are the utilities incorporated into the model appropriate?	No	Source not reported
	Is the source for the utility weights referenced?	No	Source not reported
	Are the methods of derivation for the utility weights justified?	No	Source not reported

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	No	Source of CRC data not reported, along with utility source, while cost data are historical
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found
	Is the process of data incorporation transparent?	No	Unclear why Dutch data chosen over Irish given focus of the paper; sources not well reported
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	No	PSA not performed; MISCAN is stochastic but distributions not presented
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	NA	As above
D4	Have the four principal types of uncertainty been addressed?	No	Parameter only
	If not, has the omission of particular forms of uncertainty been justified?	No	
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	

McFerran 2022 ⁽³⁶⁵⁾			
Quality criterion	Questions	Response	Comments
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	No	
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	Only varies a single parameter in different scenario analyses (e.g., incidence, participation, discount rate); likely due to complexity in microsimulation model for more advanced/efficient sensitivity analyses
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	Yes	Ranges used in scenario analysis described
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Based on established and widely validated MISCAN-Colon model
C2	Are any counterintuitive results from the model explained and justified?	NA	None observed
	If the model has been calibrated against independent data, have any differences been explained and justified?	NA	Although relies on calibration, no apparent differences were observed
	Have the results of the model been compared with those of previous models and any differences in results explained?	Yes	Compared with Whyte 2021 with different results obtained; MISCAN found net costly vs net saving in Whyte; authors conclude that difference is largely due to difference in CRC incidence and adenoma

Key: C – consistency; CE – cost effective; CEA – cost-effectiveness analysis; CRC – colorectal cancer; D – data; FIT – faecal immunochemical test; Hb – haemoglobin; ICER – incremental cost-effectiveness ratio; PSA – probabilistic sensitivity analysis; QALY – quality adjusted life year; S – structure.

Table D.6 Summary of methodological assessment based on Philips checklist: Thomas 2021

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	To consider the cost effectiveness of sex-specific and uniform screening strategies in the context of constrained resources
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	In order to inform the planned reduction in starting age of screening in England and other countries, we aimed to investigate whether, in a situation of constrained resources, planned reductions in FIT screening start age should be uniform across the population, or stratified by sex
	Is the primary decision-maker specified?	No	Only specifies healthcare payer (English NHS)
S2	Is the perspective of the model stated clearly?	Yes	NHS in England
	Are the model inputs consistent with the stated perspective?	Yes	Cancer Research UK incidence data; costs specific to England; QALYs applied to inform health outcomes
	Has the scope of the model been stated and justified?	Yes	Given plans to reduce the start age for screening in the UK, authors asked whether it would be more cost-effective and beneficial to health to reduce screening start age by 2 years to age 58 in all individuals (nine screening episodes in total for all individuals), or whether instead screening start age should be reduced by 4 years to age 56 in males, and kept at age 60 in females (10 screening episodes for males and 8 in females, approximate average of 9 screening episodes in total)
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	CRC benefits, QALYs, costs, ICER
	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	Natural disease history model with screening module
S3	Are the sources of data used to develop the structure of the model specified?	Yes	Informed by natural disease history of CRC, although sources not reported

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
S4	Are the causal relationships described by the model structure justified appropriately?	Yes	The relationships are aligned with other models such as established MISCAN-Colon model
	Are the structural assumptions transparent and justified?	Yes	Described greater detail in discussion paper; health states consistent with MISCAN, although model not validated against international trial data
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	Broadly aligned with MISCAN-Colon; also microsimulation model used
S5	Is there a clear definition of the options under evaluation?	Yes	Biennial screening with different FIT thresholds and age start and stop ranges applied; however, total number of strategies simulated not reported
	Have all feasible and practical options been evaluated?	Yes	Broad range of strategies considered
	Is there justification for the exclusion of feasible options?	NA	
S6	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Microsimulation model (MiMiC) aligned with MISCAN-Colon model
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Treatment effect is essentially modelled as the effect of screening on CRC incidence and mortality reduction; hence no treatment or treatment duration modelled outside of standard treatment of CRC
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Yes	Based on natural disease history of CRC

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
	Is the cycle length defined and justified in terms of the natural history of disease?	Yes	1 year; rationale not reported but likely aligned with incidence data
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Based on available evidence from current screening, natural history, published studies including meta analyses
	Where choices have been made between data sources, are these justified appropriately?	NA	No clear choices were presented regarding different sources to the best that I can see
	Has particular attention been paid to identifying data for the important parameters in the model?	Yes	e.g., sex-specific FIT parameters
	Has the quality of the data been assessed appropriately?	No	No discussion on quality of parameters included
	Where expert opinion has been used, are the methods described and justified?	NA	None used
D2	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Natural disease history model based on UK population
D2a	Is the choice of baseline data described and justified?	Yes	Normal colorectal epithelium at model start (adults are assumed to be age 30 at model start)
	Are transition probabilities calculated appropriately?	Yes	Calibrated to known CRC incidence, adenoma prevalence and screening outcomes using Metropolis Hastings algorithm
	Has a half-cycle correction been applied to both cost and outcome?	Yes	Half cycle correction and discounting is applied to costs, QALYs and life years, and incremental results are estimated
	If not, has this omission been justified?	No	
D2b	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Are the costs incorporated into the model justified?	Yes	Consistent with other studies in screening for CRC also
	Has the source for all costs been described?	Yes	All source data described
	Have discount rates been described and justified given the target decision-maker?	Yes	Consistent with NHS perspective
D2d	Are the utilities incorporated into the model appropriate?	Yes	Vary by age with decrements applied to AEs
	Is the source for the utility weights referenced?	Yes	Systematic review and meta-analysis for CRC studies (CRC stage) and Ara and Brazier 2011
	Are the methods of derivation for the utility weights justified?	Yes	Based on relevant published papers with utility decrements and age-adjusted values applied
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	Yes	No issues found

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found
	Is the process of data incorporation transparent?	Yes	But largely detailed in discussion paper rather than principal publication
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	Yes	Ranges for PSA well reported and valid
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	Yes	Parameter uncertainty reflected
D4	Have the four principal types of uncertainty been addressed?	No	Parameter and heterogeneity
	If not, has the omission of particular forms of uncertainty been justified?	No	
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	Yes	A range of scenario analyses were performed assessing sex stratified strategies
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	PSA with ranges reported in discussion paper

Thomas 2021 ⁽³⁶⁶⁾			
Quality criterion	Questions	Response	Comments
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	Yes	No issues found
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	No	Internal validation not performed
	Are any counterintuitive results from the model explained and justified?	NA	None observed
C2	If the model has been calibrated against independent data, have any differences been explained and justified?	NA	Although relies on calibration, no apparent differences were observed
	Have the results of the model been compared with those of previous models and any differences in results explained?	No	Paper does not compare against other studies nor identify limitations associated with the analysis; major disadvantage versus other models is that MiMiC does not appear to have been validated against international trial data, for example

Key: C – consistency; CRC – colorectal cancer; D – data; FIT – faecal immunochemical test; ICER – incremental cost-effectiveness ratio; NHS – national health service; QALY – quality adjusted life year; PSA – probabilistic sensitivity analysis; S – structure; UK – United Kingdom.

Table D.7 Summary of methodological assessment based on Philips checklist: van de Schootbrugge-Vandermeer 2024

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	Starting screening earlier may be cost-effective, but other extensions of the screening program may be even more efficient
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	Investigated the cost effectiveness of different CRC screening strategies to identify the optimal extension of the program
	Is the primary decision-maker specified?	No	
S2	Is the perspective of the model stated clearly?	No	
	Are the model inputs consistent with the stated perspective?	Yes	The model was calibrated to observed CRC incidence and stage distribution in the Dutch population in the years before the introduction of screening (2009-2013), to ensure that the model imitates the Dutch population accurately and model predictions of the course of CRC correspond closely to reality
	Has the scope of the model been stated and justified?	Yes	Used the MISCAN-Colon model to simulate a cohort of ten million 50-year-olds in 2018, to which we applied 588 different screening strategies by varying four parameters: 1) screening interval of 1, 2 or 3 years, 2) FIT cut-off of 15, 20, 47 or 60 µg/g, 3) start age of 50, 52, 54, 55, 56, 58 or 60 years, and 4) stop age of 70, 72, 74, 75, 76, 78 or 80 years
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	For each strategy, life-time quality-adjusted life-years (QALYs) gained, costs and colonoscopy demand were calculated. QALYs and costs were discounted at 3%
S3	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	MISCAN model well known and published, validated

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
S4	Are the sources of data used to develop the structure of the model specified?	Yes	Used Dutch population-based life-tables from 2019 to determine background mortality rates, FIT characteristics per FIT positivity cut-off were calibrated on observed outcomes of the Dutch CRC screening program, Costs for the different elements of the screening process, such as the costs for FIT (including costs for the invitation, test kit, FIT analysis and organization of the screening program) and the costs for diagnostic follow-up (colonoscopy), were obtained from the Dutch National Institute for Public Health and the Environment in 2018. Treatment costs were obtained through matching of treatments and complications in medical records with the associated costs from the National Health Care Institute in 2018. Quality-of-life losses were assumed to be the same as in a previous publication
	Are the causal relationships described by the model structure justified appropriately?	Yes	Not outlined in the paper but based on MISCAN model, published elsewhere
	Are the structural assumptions transparent and justified?	Yes	Published re MISCAN in other reports
S5	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	As above
	Is there a clear definition of the options under evaluation?	Yes	Age extension of current program looked at older and younger age extensions
	Have all feasible and practical options been evaluated?	Yes	Included relevant ages and FIT thresholds, looked at scope capacity also
S6	Is there justification for the exclusion of feasible options?	NA	
	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Widely validated for CRC screening

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Not outlined here but based on MISCAN model, published elsewhere
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Yes	Not outlined here but based on MISCAN model, published elsewhere
	Is the cycle length defined and justified in terms of the natural history of disease?	No	Cycle length not reported
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Uses Dutch epidemiological and cost data; source of utilities is unclear
	Where choices have been made between data sources, are these justified appropriately?	NA	
	Has particular attention been paid to identifying data for the important parameters in the model?	Yes	Used incidence data prior to screening programme
	Has the quality of the data been assessed appropriately?	No	Not described
	Where expert opinion has been used, are the methods described and justified?	NA	

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
D2	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Well validated model
	Is the choice of baseline data described and justified?	Yes	Simulated one birth cohort born in 1968 (thus eligible for screening in 2023 when screening starts at age 55) and used Dutch population-based life-tables from 2019 to determine background mortality rates
D2a	Are transition probabilities calculated appropriately?	Yes	Transition probabilities between different states in the disease process are based on observed outcomes in the Netherlands and in clinical trials.
	Has a half-cycle correction been applied to both cost and outcome?	No	Not mentioned
	If not, has this omission been justified?	NA	
	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening
D2b	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Are the costs incorporated into the model justified?	Yes	Costs for the different elements of the screening process, such as the costs for FIT (including costs for the invitation, test kit, FIT analysis and organization of the screening program) and the costs for diagnostic follow-up (colonoscopy), were obtained from the Dutch National Institute for Public Health and the Environment in 2018. Treatment costs were obtained through matching of treatments and complications in medical records with the associated costs from the National Health Care Institute in 2018. Quality-of-life losses were assumed to be the same as in a previous publication
	Has the source for all costs been described?	Yes	as above
	Have discount rates been described and justified given the target decision-maker?	No	described but not justified
D2d	Are the utilities incorporated into the model appropriate?	Yes	Utility values look appropriate, along with age-dependent QoL scores based on EQ-5D-3L index values
	Is the source for the utility weights referenced?	No	Only specifies that EQ-5D was used. Source apparently reported in another publication that was not referenced
	Are the methods of derivation for the utility weights justified?	NA	
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	No	Source of QoL not reported
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
	Is the process of data incorporation transparent?	Yes	Additional info provided in supplement, and largely referenced to other publications
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	No	Didn't discuss this for all parameters but do report that costs and quality-of-life losses were drawn from a Gamma distribution for PSA
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	Yes	PSA undertaken
D4	Have the four principal types of uncertainty been addressed?	No	Parameter only
	If not, has the omission of particular forms of uncertainty been justified?	No	
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	No	
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	Costs and quality-of-life losses were drawn from a Gamma distribution, with shape and scale parameter such that the mean was equal to the base-case assumption in Table Sb and 50% and 200% of the mean were four standard deviations apart

van de Schootbrugge-Vandermeer 2024 ⁽³⁶⁹⁾			
Quality criterion	Questions	Response	Comments
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	No	Mention for one parameter Sensitivity CRC (range in PSA)
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Well established MISCAN model
C2	Are any counterintuitive results from the model explained and justified?	NA	Not discussed
	If the model has been calibrated against independent data, have any differences been explained and justified?	NA	Although relies on calibration, no apparent differences were observed
	Have the results of the model been compared with those of previous models and any differences in results explained?	No	

Key: C – consistency; CRC – colorectal cancer; D – data; FIT – faecal immunochemical test; PSA – probabilistic sensitivity analysis; QALY – quality adjusted life year; QoL; quality of life; S – structure.

Table D.8 Summary of methodological assessment based on Philips checklist: van der Meulen 2017

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	Differences in test characteristics might affect the optimal cutoff for a positive FIT, but might also affect the optimal screening age range and interval. Microsimulation modelling can take these gender differences in test characteristics, but also in life expectancy and colorectal cancer incidence into account and estimate costs and quality-adjusted life years (QALY) gained of various screening strategies
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	To determine optimal screening strategies for men and women and to study whether screening stratified by gender is beneficial in terms of cost-effectiveness.
	Is the primary decision-maker specified?	No	Only specifies that third party payer perspective is assumed
S2	Is the perspective of the model stated clearly?	Yes	Third-party payer (healthcare payer)
	Are the model inputs consistent with the stated perspective?	Yes	Uses sex-specific FIT parameters and sex-specific CRC incidence and mortality data specific to the Netherlands
	Has the scope of the model been stated and justified?	Yes	To consider the costs and benefits of all 480 different screening strategies by gender, including no screening
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	QALYs, costs, ICER; didn't consider CRC benefits (e.g., CRC incidence and mortality reductions)
S3	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	Natural disease history model with screening module
	Are the sources of data used to develop the structure of the model specified?	Yes	Model based on established MISCAN model, which is detailed elsewhere

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
S4	Are the causal relationships described by the model structure justified appropriately?	Yes	The relationships are well established in MISCAN
	Are the structural assumptions transparent and justified?	Yes	MISCAN contains three modules: demography, natural disease history, and screening
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	No issues found in established MISCAN
S5	Is there a clear definition of the options under evaluation?	Yes	Individuals were offered screening according to different FIT screening schedules varying by: Age to start screening: 40, 45, 50, 55, 60, and 65 years; Age to stop screening: 70, 75, 80, and 85 years; and Screening interval: 1, 1.5, 2, and 3 years
	Have all feasible and practical options been evaluated?	Yes	Broad range of strategies considered
	Is there justification for the exclusion of feasible options?	NA	
S6	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Microsimulation model based on MISCAN-Colon model
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Treatment effect is essentially modelled as the effect of screening on CRC incidence and mortality reduction; hence no treatment or treatment duration modelled outside of standard treatment of CRC
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological	Yes	Based on natural disease history of CRC

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
	process of the disease in question and the impact of interventions?		
	Is the cycle length defined and justified in terms of the natural history of disease?	No	Cycle length not reported
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Based on available evidence from CORERRO-1 trial, natural history, published studies
	Where choices have been made between data sources, are these justified appropriately?	NA	No clear choices were presented regarding different sources to the best that I can see
	Has particular attention been paid to identifying data for the important parameters in the model?	Yes	e.g., sex-specific FIT parameters; utilises trial data where feasible (e.g., FIT characteristics calibrated to CORERRO-1 trial)
	Has the quality of the data been assessed appropriately?	No	No discussion on quality of parameters included
	Where expert opinion has been used, are the methods described and justified?	NA	None used
D2	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Natural disease history model based on Dutch population
D2a	Is the choice of baseline data described and justified?	Yes	Dutch population aged 25-85 years in 2015
	Are transition probabilities calculated appropriately?	Yes	Calibrated to known CRC incidence in a Dutch population, details of which are provided in supplement
	Has a half-cycle correction been applied to both cost and outcome?	NA	Not reported
	If not, has this omission been justified?	NA	

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
D2b	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Are the costs incorporated into the model justified?	Yes	Consistent with other studies in screening for CRC also; however, costs are now somewhat outdated, based on 2012 prices
	Has the source for all costs been described?	Yes	All source data described
	Have discount rates been described and justified given the target decision-maker?	No	3% applied, presumably in line with Dutch guidelines
D2d	Are the utilities incorporated into the model appropriate?	Yes	Also considers utility loss associated with colonoscopy and CRC treatment
	Is the source for the utility weights referenced?	Yes	Ness 2006 - specific to CRC care

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
	Are the methods of derivation for the utility weights justified?	Yes	Based on study specific to CRC treatment; however, limited information is provided on methods for derivation
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	Yes	No issues found
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found
	Is the process of data incorporation transparent?	Yes	Extensive information on MISCAN model and CRC incidence and mortality data provided in supplement, along with cost, utility and FIT performance
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	No	PSA not performed; MISCAN is stochastic but distributions not presented
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	NA	As above
D4	Have the four principal types of uncertainty been addressed?	No	Parameter and heterogeneity
	If not, has the omission of particular forms of uncertainty been justified?	No	
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	

van der Meulen 2017 ⁽³⁶⁷⁾			
Quality criterion	Questions	Response	Comments
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	Yes	A range of scenario analyses were performed assessing sex stratified FIT performance, differential adherence, CRC incidence
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	But essentially limited to one-way sensitivity analysis
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	Yes	Ranges used in scenario analysis described
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Based on established and widely validated MISCAN-Colon model
C2	Are any counterintuitive results from the model explained and justified?	Yes	Despite differences in costs and QALYs gained between men and women vs no screening, ICERs remain similar in both sexes, likely due to earlier detection in men and lower sensitivity in women (returning higher yield)
	If the model has been calibrated against independent data, have any differences been explained and justified?	No	Some differences appear to exist in calibrated data (as detailed in supplement), upon which corrections were made, but no further info was provided
	Have the results of the model been compared with those of previous models and any differences in results explained?	No	No meaningful comparisons with published studies included; authors regarded this study as first to CE by gender

Key: C – consistency; CRC – colorectal cancer; D – data; FIT – faecal immunochemical test; ICER – incremental cost-effectiveness ratio; QALY - quality adjusted life year; S – structure.

Table D.9 Summary of methodological assessment based on Philips checklist: Whyte 2021

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
S1	Is there a clear statement of the decision problem?	Yes	The aim was to determine the optimal strategy in terms of screening age range, screening frequency, and FIT threshold to inform policy making, while considering constraints on endoscopy capacity
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Yes	For a fixed screening referral colonoscopy capacity, the aim was to determine the following: 1. What is the optimal screening age range? 2. What is the optimal screening interval? 3. For a fixed screening age range, is a higher FIT threshold at a shorter screening interval or a lower FIT threshold at a longer screening interval preferable? 4. Is it preferable to screen a narrower age range more intensively (short interval, low FIT threshold) or a wider age range less intensively?
	Is the primary decision-maker specified?	Yes	UK National Screening Committee (NSC)
S2	Is the perspective of the model stated clearly?	Yes	NHS and PSS
	Are the model inputs consistent with the stated perspective?	Yes	Cancer Research UK (mortality); England cancer registry data (as detailed in Whyte 2011); costs specific to England; QALYs applied to inform health outcomes
	Has the scope of the model been stated and justified?	Yes	Screening strategies considered included those with starting ages between 50 and 60 years; maximum screening age of up to 74 years; screening intervals of 1, 2, 3, 4, 5, or 6 years; 3 or more screening episodes; and any FIT integer threshold between 20 and 180µg haemoglobin (Hb)/g feces.
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Yes	CRC benefits, QALYs, costs, NMB
S3	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Yes	Based on cohort Markov model which was necessary to efficiently simulate wide range of strategies; health states consistent with established MISCAN; however, microsimulation probably preferred approach

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
S4	Are the sources of data used to develop the structure of the model specified?	Yes	Informed by natural disease history of CRC, although sources not reported
	Are the causal relationships described by the model structure justified appropriately?	Yes	Simulates the life experience of a cohort of 50-yearold individuals in the general population of England with normal epithelium through to the development of adenomas (low risk and intermediate/high risk), CRC (by Duke's stage), and subsequent death. Also extensively validated
	Are the structural assumptions transparent and justified?	Yes	Likely detailed in earlier publication by Whyte 2012; however, health states consistent with MISCAN and booth models have been extensively validated
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Yes	As above, microsimulation probably preferred, but would likely be too inefficient to simulate >60,000 strategies
S5	Is there a clear definition of the options under evaluation?	Yes	Screening strategies considered included those with starting ages between 50 and 60 years; maximum screening age of up to 74 years; screening intervals of 1, 2, 3, 4, 5, or 6 years; 3 or more screening episodes; and any FIT integer threshold between 20 and 180µg haemoglobin (Hb)/g faeces.
	Have all feasible and practical options been evaluated?	Yes	As above
	Is there justification for the exclusion of feasible options?	NA	None excluded
S6	Is the chosen model type appropriate given the decision problem and specified causal relationships within the model?	Yes	Although microsimulation probably preferred; cohort Markov is appropriate but perhaps limited
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Yes	Lifetime
	Are the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Yes	Treatment effect is essentially modelled as the effect of screening on CRC incidence and mortality reduction; hence no treatment or treatment duration modelled outside of standard treatment of CRC

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Yes	Based on natural disease history of CRC
	Is the cycle length defined and justified in terms of the natural history of disease?	No	Likely annual, but not reported
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Yes	Based on available evidence from current screening, natural history, published studies including meta analyses
	Where choices have been made between data sources, are these justified appropriately?	No	Sensitivity analyses were carried out where multiple sources were identified: e.g., "A sensitivity analysis was performed in which the Reed values were used in place of the SchARR values. No reason was given to base case choice
	Has particular attention been paid to identifying data for the important parameters in the model?	Yes	Uptake, for example; more realistic values were applied, rather than simple assumption of 100% uptake. Endoscopy constraints also well considered along with diagnostic performance
	Has the quality of the data been assessed appropriately?	No	No discussion on quality of parameters included
	Where expert opinion has been used, are the methods described and justified?	NA	None used
D2	Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Yes	Natural disease history model based on UK population
D2a	Is the choice of baseline data described and justified?	Yes	50-yearold individuals in the general population of England with normal epithelium
	Are transition probabilities calculated appropriately?	Yes	Calibrated to known CRC incidence, adenoma prevalence and screening outcomes using Metropolis Hastings algorithm

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
D2b	Has a half-cycle correction been applied to both cost and outcome?	No	Cycle length not reported and no mention of half-cycle correction
	If not, has this omission been justified?	No	As above; since Markov cohort, both cycle length and half cycle approach should have been mentioned
	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	Treatment effect is screening
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
D2c	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	NA	As above; no treatment effect other than screening which identifies/detects (i.e., no extrapolation included of treatment effects)
	Are the costs incorporated into the model justified?	Yes	Consistent with other studies in screening for CRC also
	Has the source for all costs been described?	Yes	All source data described
	Have discount rates been described and justified given the target decision-maker?	Yes	Consistent with NHS and PSS perspective

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
D2d	Are the utilities incorporated into the model appropriate?	Yes	Vary by age with decrements applied to bleeding and perforation
	Is the source for the utility weights referenced?	Yes	Health Survey for England for the years 2003 to 2014 and systematic review and meta-analysis for CRC studies (CRC stage)
	Are the methods of derivation for the utility weights justified?	Yes	Also considered utility decrement for screening, but concluded the duration of disutility would be too short to be meaningful. Justified choice of utility source and decrements. However, choice of source differs between paper and supplement (paper incorrectly refers to source used for AEs)
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	Yes	No issues found
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	NA	No issues found
	Is the process of data incorporation transparent?	Yes	Detailed in the publication's Appendix 1
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	No	Choice of distribution used in PSA not reported
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	Yes	Monte Carlo simulation used to reflect second order uncertainty
D4	Have the four principal types of uncertainty been addressed?	No	Parameter and heterogeneity (i.e., varying cancer risk by sex); others not explicitly mentioned
	If not, has the omission of particular forms of uncertainty been justified?	No	Not discussed

Whyte 2021 ⁽³⁶⁸⁾			
Quality criterion	Questions	Response	Comments
D4a	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	No	
D4b	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	No	
D4c	Has heterogeneity been dealt with by running the model separately for different subgroups?	Yes	Varied cancer risk by sex
D4d	Are the methods of assessment of parameter uncertainty appropriate?	Yes	PSA (although choice of distributions not presented) and scenario analysis
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	No	With the exception of scenario analysis (cost of bowel scope: £150 and £450)
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Yes	Applied in earlier model by Whyte and then validated separately by Thomas 2019
C2	Are any counterintuitive results from the model explained and justified?	NA	None observed
	If the model has been calibrated against independent data, have any differences been explained and justified?	NA	Although relies on calibration, no apparent differences were observed. Perhaps some exist in validation paper by Thomas 2019
	Have the results of the model been compared with those of previous models and any differences in results explained?	Yes	Only findings from Wilschut differed, which authors could not explain

Key: C – consistency, D – data, S – structure.

D.4 Source and values used to adjust costs

Table D.10 CPI data used to inflate historical costs in origin country

Year	England – UK PSSRU Unit Costs and Social Care 2023 ⁽⁶³¹⁾	Finland – Statistics Finland '06 Health' ⁽⁶³²⁾	Netherlands – Statistics Netherlands '060000 Health' ⁽⁶³³⁾
2010	1.000	99.994	99.210
2011	1.030	100.743	98.750
2012	1.052	101.077	99.640
2013	1.070	102.851	100.910
2014	1.081	105.967	101.220
2015	1.091	109.328	100.000
2016	1.095	116.813	98.040
2017	1.118	118.809	98.650
2018	1.132	120.247	100.010
2019	1.150	121.331	102.550
2020	1.175	122.315	104.510
2021	1.204	122.142	105.400
2022	1.235	122.814	107.630
2023	1.322	120.948	113.410

Key: CPI – consumer price index, PSSRU – Personal Social Services Research Unit.

Table D.11 Summary GDP PPP data used to convert international costs to Irish Euro using 2023 price year

Country	Finland	Ireland	Netherlands	England*
Reference	National currency per US dollar, Euro	National currency per US dollar, Euro	National currency per US dollar, Euro	National currency per US dollar, Pound sterling
2023 GDP PPP	0.771	0.756	0.744	0.673
Ratio to Ireland	0.980	NA	1.016	1.122

* Reflects UK GDP PPP

Key: GDP PPP – Gross Domestic Product Purchasing Power Parity, NA – not applicable.

Appendix E Resource and budget impact

E.1 Detailed methods

This section provides a more detailed description of the cohort model and the analysis and the parameters used to simulate the model. Modelling, analysis and visualisation were performed in R.4.3.3.

Model overview

The model consists of cohorts of average-risk people of a particular initial age, i.e. the cohorts are then tracked over time. Those with known elevated CRC risks (for example, those with hereditary conditions such as Lynch syndrome and familial adenomatous polyposis) are outside the scope of the model.

Each cohort is stratified according to the CRC natural history:

1. No CRC/adenoma, W
2. Non-high-risk adenoma(s), X
3. High-risk adenoma(s), Y
4. CRC, Z

where letters W , X , Y and Z represent the size of each stratum. Two adenoma categories (that is, non-high-risk and high-risk) are modelled separately to reflect the difference in how these are managed as part of the surveillance pathway.⁽⁶⁶⁾ The BowelScreen programme defines high-risk findings as a) at least two premalignant polyps, with at least one advanced polyp or b) at least five or more premalignant polyps, which include both serrated polyps (excluding 1-5 mm rectal hyperplastic polyps) and conventional adenomas.⁽⁶⁶⁾ Thus, the conventional and serrated pathways of CRC development are implicitly combined in the present model. The model does not distinguish cancer sites (that is, colon or rectum), nor does it track distinct TNM cancer stages (that is, I, II, III, and IV): where appropriate, these heterogeneities are incorporated indirectly using cancer registry data.

Every year, each cohort is assumed to experience a series of events, namely, CRC pathogenesis, symptomatic presentation, screening if eligible, death and net migration (Figure E.1). At the end of each year, the cohort age is incremented and the events are repeated until the time horizon is reached.

The model evaluation procedures are outlined in Appendix E.4.

Cohorts

The model is simulated from 2012, that is the first year of programme implementation. The model focuses on outcomes in the target screening age range (from 50 to 74) from the intervention base year of 2031 for the duration of a 10-

year time horizon, that is until 2040. In total, 53 cohorts were modelled from the initial age of 23 to 74, the youngest of which turns 50 in 2040. The size of the initial age cohorts at the start of the simulation was parameterised using the CSO-estimated population size.⁽³⁸⁰⁾

Events

Five events were modelled sequentially to describe the natural history of CRC and modes of detection (Figure E.1). These include:

- a) CRC disease progression
- b) Symptomatic presentation
- c) Screening
- d) Death
- e) Net migration

These events modify the number of people along the CRC natural history (that is, W , X , Y and Z). The subscript on the stratum identity refers to the event label: for example, Z_a refers to the number of people with CRC after pathogenesis. The parameters governing these events are described in Table E.1. The follow-up of people with detected high-risk adenomas and CRC survivors are tracked outside the general cohort model and described below (Section 7.4.1 Resources and associated costs).

- a) CRC disease progression: The transitions among the stages along the natural history of CRC are indicated by transition probabilities, α . Specifically, α_{WX} , α_{XY} and α_{YZ} each refer to the probability of moving from W to X , X to Y and Y to Z , respectively ($\cdot$). For a given cohort and year, the numbers of people after pathogenesis are given by:

$$\begin{aligned} W_a &= (1 - \alpha_{WX}) W_0 \\ X_a &= (1 - \alpha_{XY}) X_0 + \alpha_{WX} W_0 \\ Y_a &= (1 - \alpha_{YZ}) Y_0 + \alpha_{XY} X_0 \\ Z_a &= Z_0 + \alpha_{YZ} Y_0 \end{aligned}$$

where the subscript 0 indicates the number carried over from the previous year (or the initial condition when $t = 0$).

- b) Symptomatic presentation: A fraction of people with CRC, β_z , is assumed to receive a colonoscopy for presentation of symptoms consistent with CRC. If colonoscopy detects cancer, the patient enters the treatment and subsequent surveillance pathway and is assumed not to re-join the pool of average-risk people. The number of CRC cases detected through colonoscopy (indicated by the asterisk) and who receive treatments is:

$$Z_b^* = \beta_z \gamma_z Z_a$$

where γ_Z is the sensitivity of colonoscopy to CRC. The remaining people with CRC – that is, those who do not present symptoms ($1 - \beta_Z$) or those who present symptoms but whose CRC was not detected via colonoscopy ($1 - \gamma_Z$) – is given by:

$$Z_b = (1 - \beta_Z \gamma_Z) Z_a.$$

In the absence of data informative across age groups of interest (50–74), the probability of false symptomatic presentation was approximated to 0 for those without CRC (that is, $\beta_W = \beta_X = \beta_Y = 0$) such that:

$$W_b = W_a; X_b = X_a; Y_b = Y_a.$$

- c) Screening: When a given cohort is eligible for CRC screening, a fraction, δ , is assumed to enrol in the programme and take FIT. The probability of returning a positive FIT test, ε , is parameterised to depend on the CRC natural history stage.

For those without CRC/adenoma and FIT-tested, a fraction ε_W returns a (false) positive result and a fraction, θ of which accepts the invitation for colonoscopy. For those with non-high-risk adenoma(s) and FIT-tested, a fraction ε_X returns a positive result, a fraction, θ of which accepts the invitation for colonoscopy and a fraction, γ_X of those are confirmed positive for non-high-risk adenoma via colonoscopy. These individuals are assumed to have their non-high-risk adenoma(s) removed during colonoscopy and regain the no CRC/adenoma status. Therefore, the number of people without CRC/adenoma after screening (and associated procedures) is given by,

$$W_c = W_b + \delta \varepsilon_X \theta \gamma_X X_b.$$

Conversely, a fraction $1 - \delta \varepsilon_X \theta \gamma_X$ of people with non-high-risk adenoma(s) remain undetected and carry over to the next event:

$$X_c = (1 - \delta \varepsilon_X \theta \gamma_X) X_b.$$

For those with high-risk adenoma(s) and FIT-tested, a fraction ε_Y returns a positive result, a fraction, θ of which accepts the invitation for colonoscopy and a fraction, γ_Y of those are confirmed positive for high-risk adenomas via colonoscopy. These individuals have their high-risk adenoma(s) removed and join the high-risk adenoma surveillance pathway (described in detail below). The number of these individuals is given by:

$$Y_c' = \delta \varepsilon_Y \theta \gamma_Y Y_b,$$

where the prime sign indicates the confirmed high-risk adenoma status. Similarly to those with non-high-risk adenoma(s), a fraction $1 - \delta \varepsilon_Y \theta \gamma_Y$ of people with high-risk adenomas remains undetected and carries over to the next event:

$$Y_c = (1 - \delta \varepsilon_Y \theta \gamma_Y) Y_b.$$

Finally, for those with CRC and FIT-tested, a fraction ε_Z returns a positive result, a fraction, θ of which accepts the invitation for colonoscopy and a fraction, γ_Z of those are confirmed positive for CRC via colonoscopy. Those confirmed CRC-positive (indicated by the asterisk) will then receive treatment.

$$Z_c^* = \delta \varepsilon_Z \theta \gamma_Z Z_b.$$

Similarly to those with adenoma(s), a fraction $1 - \delta \varepsilon_Z \theta \gamma_Z$ of those with CRC remains undetected following screening and carries over to the next event:

$$Z_c = (1 - \delta \varepsilon_Z \theta \gamma_Z) Z_b.$$

- d) Death: The probability of surviving a given year consists of two components: 1) general population survival, μ (which is assumed independent of the specific cause of interest due to its low prevalence in the overall population)⁽²¹⁰⁾ and 2) CRC-specific survival, π , for those with CRC (that is, Z). Therefore, the numbers of surviving individuals carried over to the next year are given by:

$$W_d = \mu W_c$$

$$X_d = \mu X_c$$

$$Y_d = \mu Y_c$$

$$Z_d = \mu \pi Z_c.$$

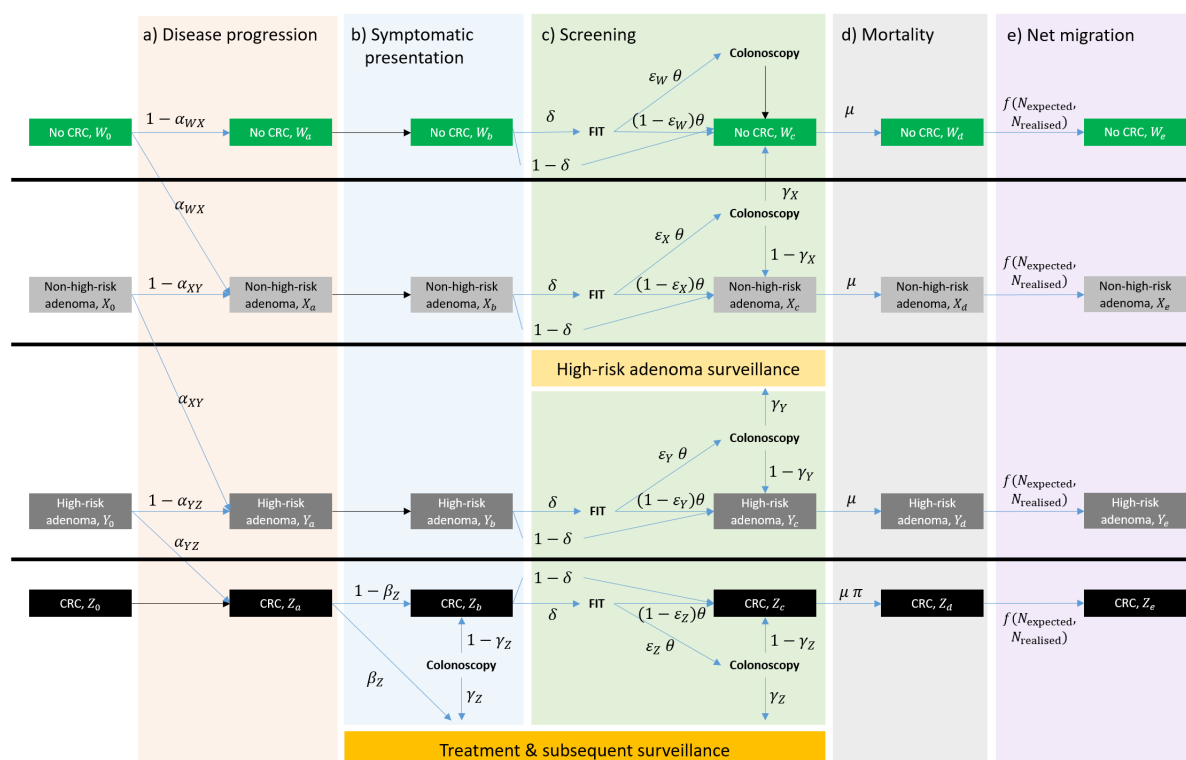
- e) Net migration: The population size in Ireland is projected to increase, due largely to the positive net migration rate; that is, more people are expected to immigrate to, than emigrate from, Ireland.⁽³⁸²⁾ In order to keep up with the projected population increase, the cohort size in the model was adjusted for net migration at the end of each year as follows:

$$\begin{aligned} W_e &= W_d + (N_{\text{expected}} - N_{\text{realised}}) \times \frac{W_d}{W_d + X_d + Y_d + Z_d} \\ X_e &= X_d + (N_{\text{expected}} - N_{\text{realised}}) \times \frac{X_d}{W_d + X_d + Y_d + Z_d} \\ Y_e &= Y_d + (N_{\text{expected}} - N_{\text{realised}}) \times \frac{Y_d}{W_d + X_d + Y_d + Z_d} \\ Z_e &= Z_d + (N_{\text{expected}} - N_{\text{realised}}) \times \frac{Z_d}{W_d + X_d + Y_d + Z_d} \end{aligned}$$

where N_{expected} is the observed (until 2023) and projected (from 2024) age-specific population size for a given year (published by CSO⁽³⁸¹⁾) and N_{realised} is the corresponding surviving cohort size (inclusive of the cumulative number of

surviving people under surveillance; described in detail below) estimated by the model (that is, after Event d). This formulation assumes that the migrating population is not presently under surveillance for CRC or high-risk adenomas and the immigrating population exhibits the same prevalence of CRC and adenomas as the resident population.

Figure E.1 Events describing the demography, natural history of colorectal cancer and associated health services in Ireland



Note: The black arrows indicate transitions with the probability of 1. The overview of model parameters are given in Table E.1.

Screening scenarios

Timeline of CRC screening in Ireland

The BowelScreen programme, launched in October 2012, targeted individuals aged 60–69. Initially, invitations were prioritised for older people nearing the upper limit of the eligible age range. An expansion to those aged 55–74 was committed to in the 2020 Programme for Government and the National Cancer Strategy 2017–2026.^(1, 2) The programme expanded to include those aged 59 in October 2023. The planned expansion to 55–74 is anticipated to be completed by 2030.⁽⁶³⁴⁾ As of April 2025, those aged 59–70 were eligible for screening, while a further expansion to 58–70 is planned for 2026.⁽¹⁵⁾ Upon consultation with the BowelScreen programme,

2031 was chosen as the intervention base year (that is, the start of the rollout) for the proposed expansion to 50–54.

The model was simulated from 2012 (that is, the first year of implementation), taking into account the historical change in eligibility and patterns of invitation in eligible cohorts (that is, the proportion of people who were invited to the programme). The historical context of CRC screening is required to reflect the feedback between health services and epidemiology (for example, previously screened cohorts have a reduced risk of CRC) and resources incurred through follow-up of previously detected cases. As the time is simulated in yearly intervals, changes to the eligibility criteria were modelled to take place at the turn of the year. For example, the expansion to age 59, which occurred in October 2023, was modelled to have been implemented at the beginning of 2024. Similarly, the subsequent expansion to age 70, which took place in April 2025, was modelled to have commenced at the beginning of 2025. A 10-year time horizon was chosen such that the present analysis focuses on the outcome during the time period between 2031 and 2040.

Comparator and interventions

The current evaluation considers screening of 55–74 as the baseline or comparator scenario of CRC screening. The further extension to those aged 50–54 serves as the intervention. The pace of extension will depend on the existing capacity (see Chapter 8) and available budget. As such, three rollout scenarios were considered (Figure E.2):

- Immediate: instantaneous implementation from the base year
- One-yearly: lowering the starting age by one every year from the base year
- Two-yearly: lowering the starting age by one every two years from the base year.

Eligible ages

As the expansion to those aged 50–54 would maintain the existing two-year screening interval, the model assumes that cohorts within the eligible age range are invited every second year. It was also assumed that half of the newly eligible population would be invited to participate in the first year of eligibility, with the remaining half invited in the following year.

The proposed expansion to those aged 50–74 from 55–74 would increase the maximum number of screening events per cohort from 10 to 13 counting from the first year of eligibility:

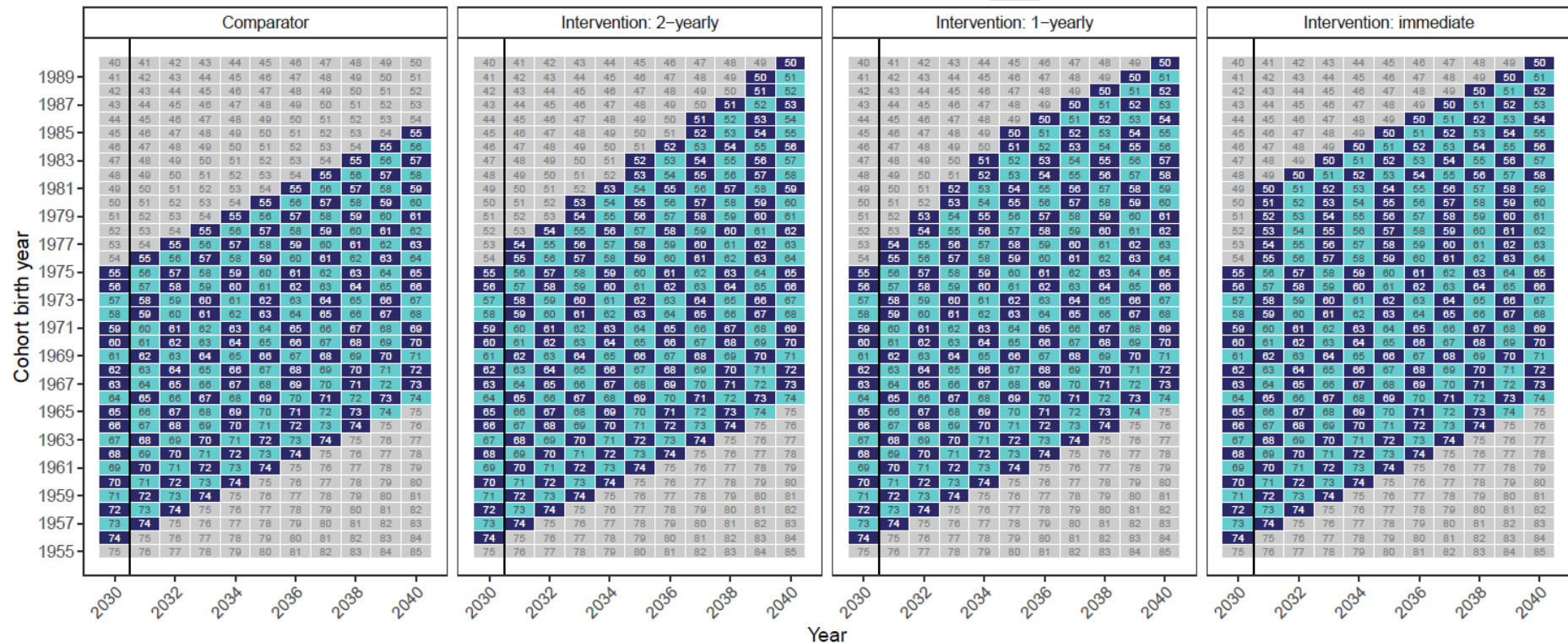
- 50–74: 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 (13 times)
- 55–74: 55, 57, 59, 61, 63, 65, 67, 69, 71, 73 (10 times).

For reference, the original age range from 60 to 69 offered up to four screening events per participant:

- 60–69: 60, 62, 64, 68.

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Figure E.2 Colorectal cancer screening eligibility under comparator and intervention screening scenarios. Three intervention scenarios differing in the pace of expansion were considered



Note: The model assumes that half of the newly eligible population is invited to participate in their first year of eligibility (as shown in this figure), with the remaining half invited the following year. The years in which the first half of a given cohort is eligible for screening and invited are indicated in dark blue, while those within the eligible age range but not invited are indicated in light blue. The number in each tile indicates the cohort age. The solid vertical lines mark the beginning of the programme expansion to those aged 50–54 (2031).

Cohort model parameters

Parameters of the cohort model were sourced from the Irish context and international systematic reviews. Table E.1 summarises parameter values. Further details of parameterisation are provided in this section.

Table E.1 Overview of cohort model parameters

Parameter	Description	Value(s)	Source
$N_{0,i}$	Initial population size	Sourced directly from CSO	CSO (PEA11 ⁽³⁸⁰⁾ and PEC19 ⁽³⁸¹⁾)
$X_{0,i}/N_{0,i}$	Initial prevalence of non-high-risk adenoma(s)	Table E.2	Thomas et al. 2020 & 2021 ^(366, 406)
$Y_{0,i}/N_{0,i}$	Initial prevalence of high-risk adenoma(s)		
$Z_{0,i}/N_{0,i}$	Initial prevalence of CRC		
α_{WX}	Probability of developing non-high-risk adenoma(s) de-novo	Table E.3	Thomas et al. 2020 & 2021 ^(366, 406)
α_{XY}	Probability of developing high-risk adenoma(s) from non-high-risk adenoma(s)		
α_{YZ}	Probability of developing CRC from high-risk adenoma(s)		
β_Z	Probability that a person with CRC receives a colonoscopy for suspected CRC	0.197	Thomas et al. ⁽³⁶⁶⁾
γ_X	Colonoscopy sensitivity to non-high-risk adenomas	0.765	Thomas et al. 2020 & 2021 ^(366, 406)
γ_Y	Colonoscopy sensitivity to high-risk adenomas	0.925	
γ_Z	Colonoscopy sensitivity to CRC	0.957	HSE ⁽⁶³⁵⁾
δ	BowelScreen FIT uptake	Empirically-informed: Table E.5	BowelScreen Canadian Partnership Against Cancer ⁽⁹⁵⁾
		Quality assurance target: 0.6	National Screening Service 2023 ⁽³⁰⁵⁾
ϵ_W	FIT positivity rate for those without CRC	0.023	Chapter 6 on Test Accuracy: Niedermaier et al. 2023 ⁽²⁷²⁾ ; Brenner et al. 2018 ⁽²⁷¹⁾ ; Hernandez et al. 2014 ⁽²⁷⁹⁾ ; Grobbee et al. 2017 ⁽²⁷⁸⁾
ϵ_X	FIT positivity rate for those with non-high-risk adenoma(s)		
ϵ_Y	FIT positivity rate for those with high-risk adenoma(s)		
ϵ_Z	FIT positivity rate for those with CRC	0.772	Chapter 6 on Test Accuracy: Niedermaier et al. 2023 ⁽²⁷²⁾ ; Brenner et al. 2018 ⁽²⁷¹⁾ ; Hernandez et al. 2014 ⁽²⁷⁹⁾ ;
θ	Colonoscopy uptake rate given a positive FIT test	0.806	BowelScreen ⁽¹⁴⁹⁾
μ	Probability of survival of the general population	Table E.6	NCRI ⁽²¹²⁾
π	Probability of surviving CRC		

Initial population size

The initial population size, $N_{0,i}$, was parameterised from the CSO population estimates (PEA11) until 2023 and population projection (PEC19) from 2024 onwards.^(380, 381) The CSO population projections were generated assuming three migration scenarios: low, moderate and high. The moderate scenario was chosen as the default while the impact of the migration assumption was explored in scenario analysis.

Initial prevalence of adenomas and CRC

The initial condition of the model includes the disease prevalence inclusive of both diagnosed and undiagnosed cases in the population, which is not directly observable by definition. Estimates of the initial prevalence of non-high-risk adenoma(s), high-risk adenoma(s), and CRC (that is, $X_{0,i}/N_{0,i}$, $Y_{0,i}/N_{0,i}$ and $Z_{0,i}/N_{0,i}$, respectively) were extrapolated from a 2021 modelling study set in England (Table E.2).

Table E.2 Initial prevalence estimates of adenomas (non-high-risk and high-risk) and colorectal cancer by age group.

Age group	Non-high-risk, $X_{0,i}/N_{0,i}$	High-risk, $Y_{0,i}/N_{0,i}$	CRC, $Z_{0,i}/N_{0,i}$
40-44	0.0552	0.0049	0.0007
45-49	0.1159	0.0155	0.0013
50-54	0.1686	0.0310	0.0025
55-59	0.1998	0.0454	0.0042
60-64	0.2205	0.0561	0.0062
65-69	0.2321	0.0631	0.0089
70-74	0.2363	0.0680	0.0128

Source: Thomas et al.: MiMiC model (Fig.9-11),^(366, 406) digitised using WebPlotDigitizer.

Female and male values from the source were averaged to compute the combined prevalence.

Transition probabilities

The cohort model explicitly tracks four states in each initial age cohort: those without CRC or adenoma, W ; non-high-risk adenomas, X ; high-risk adenomas, Y and CRC, Z . In the natural history pathway, transitions between these states were assumed unidirectional and they were governed by three parameters, α_{WX} , α_{XY} , and α_{YZ} designating the probabilities of developing non-high-risk adenoma(s) de-novo, developing high-risk adenoma(s) from non-high-risk adenoma(s) and developing CRC from high-risk adenoma(s), respectively. Estimates of the transition probabilities were obtained from a 2021 modelling study set in England (Table E.3).⁽³⁶⁶⁾

Table E.3 Transition probability estimates by age group

Age group	No CRC or adenoma to non-high-risk adenoma(s), α_{WX}	Non-high-risk adenoma(s) to high-risk adenoma(s), α_{XY}	High-risk adenoma(s) to CRC, α_{YZ}
40-44	0.0151	0.0288	0.0137
45-49	0.0215	0.0299	0.0185
50-54	0.0189	0.0244	0.0207
55-59	0.0132	0.0175	0.0226
60-64	0.0105	0.0143	0.0261
65-69	0.0082	0.0132	0.0321
70-74	0.0060	0.0157	0.0463
75-79	0.0042	0.0177	0.0576
80-84	0.0033	0.0155	0.0557

Source: Thomas et al.: MiMiC model (Table 5).^(366, 406)

The probabilities were reported in ten-year intervals by the source. The values corresponding to five-year age groups were predicted from LOESS regression, which accommodates possible non-linear relationships. Female and male estimates were averaged to compute the combined probabilities.

Probability of symptomatic presentation

The probability that a CRC patient undergoes a diagnostic colonoscopy for symptomatic presentation, β_Z , was parameterised based on Thomas et al., who calibrated the parameter based on English data.^(366, 406) As the present model does not model cancer stages explicitly, the weighted average of 0.197 was estimated based on the calibrated stage-specific probabilities reported by Thomas et al.⁽³⁶⁶⁾ and stage distribution data from NCRI. In the absence of data, it was assumed the probability of (false-positive) symptomatic presentation was negligible for those without CRC (that is, $\beta_W = \beta_X = \beta_Y = 0$).

Colonoscopy & CT colonography sensitivity

Colonoscopy is used to diagnose CRCs through symptomatic presentation and for FIT-positive individuals in the screening programme. CT colonography is offered to a small fraction of cases in the event of an incomplete colonoscopy, if an individual refuses colonoscopy or is deemed unsuitable (for example, as a result of poor health or a higher risk of perforation). In the BowelScreen programme, CT colonography was used for 1.6% of participants between 2020-2021.⁽¹⁸⁾ In the present study, sensitivity parameters for the two methods were parameterised based on colonoscopy studies, as colonoscopy is significantly more common than CT colonography. Systematic reviews of screening studies have indicated that both methods are comparatively sensitive in detecting CRC and adenomas.⁽⁶³⁶⁾

CRC

The quality of a colonoscopy is influenced by various factors, such as the population being screened, the quality of bowel preparation, and the endoscopist's expertise. Post-colonoscopy colorectal cancer, also known as interval cancer, is defined as CRC diagnosed within three years of a colonoscopy that did not detect any cancer. The rate of interval cancer serves as an indicator of colonoscopy quality, as most cases occur due to a pre-existing lesion that was either not completely removed or missed by the endoscopist.⁽¹¹⁷⁾ According to estimates published by the National Screen Service, the average three-year interval cancer rate following a BowelScreen colonoscopy between 2012 and 2017 was 4.3%.⁽⁶³⁵⁾ Based on this estimate, the current study sets $\gamma_Y = 1 - 0.043 = 0.957$.

Adenomas

No specific information on the sensitivity of colonoscopy to adenomas was available from the Irish context. Thus, following an English study by Thomas et al.,^(366, 406) the colonoscopy sensitivity for non-high-risk and high-risk adenomas was set to $\gamma_X = 0.765$ and $\gamma_Y = 0.925$, respectively.

Screening programme invitation coverage

The proportion of the population invited to enroll in BowelScreen was indirectly estimated by considering the number of invitations sent and the cohort size for each year. The annual invitation numbers were calculated by averaging the numbers per screening round (that is, typically two years except for the first round which took place 2012–2015). As the invitation coverage increased during the first round, the NCRI data on the number of screening detected cancer was leveraged to estimate per-year numbers during the first round. Specifically, cases detected through screening in 2013, 2014 and 2015 were from 1, 10, and 70 for those aged 60–64 while they were 66, 111 and 106 for those aged 65–69. The numbers of invitations during 2013 to 2015 were then assumed proportional to the number of screening detected cases in each the age group during this period. The estimated invitation coverage was markedly lower than 100% at the beginning of the programme (that is, prior to 2015) and during the years affected by the COVID-19 pandemic (2020–2021). From 2024, the invitation was assumed to be sent to 100% of those eligible, reflecting the achievable performance threshold set by the quality assurance standard for BowelScreen.⁽³⁰⁵⁾

Table E.4 Estimated proportion of population invited to enrol in BowelScreen

Year	Age group	
	60–64	65–69
2013	0.017	0.731
2014	0.08	0.914
2015	1.14	1.10
2016	1.29	1.16
2017	1.25	1.13
2018	1.32	0.944
2019	1.28	0.928
2020	0.552	0.641
2021	0.537	0.626
2022	1.22	1.04
2023	1.18	1.02

Source: BowelScreen and CSO⁽³⁸⁰⁾.

Note: Values larger than 100% likely indicate catch-up invitations from previous years.

Screening programme uptake

Among the screening eligible cohort, FIT uptake rates have ranged from 0.381-0.434 for those aged 60-64 and 0.413-0.499 for those aged 65-69 (Chapter 2: Table 2.2).

To extrapolate the expected uptake rate for the proposed expansion age groups (that is, 50–54, 55-59 and 70-74), uptake rate data were sought from an international programme where those aged 50–74 are already screening-eligible and the uptake rates for those aged 60–69 are within the range of values observed in Ireland.⁽⁹⁵⁾ Based on these criteria, the uptake rates of the Canadian CRC screening programme were used to inform the relative difference in the uptake rate between a reference age group already screening-eligible in Ireland (that is, 65-69) and those that are yet to be eligible (that is, 50–54, 55-59 and 70-74). The relative values for 50–54, 55–59 and 70–74 compared to 65–69 were 0.630, 0.783 and 1.065, respectively.

Using the Irish uptake from the latest period (2022–2023) and extrapolating from the relative rates from Canada,⁽⁹⁵⁾ the age-specific uptake rate, δ , per age group was parameterised as shown in Table E.5:

Table E.5 Observed and extrapolated uptake rates of the BowelScreen.

Age group	Uptake rate
50–54	0.312*
55–59	0.388*
60–64	0.426
65–69	0.495
70–74	0.527*

Source: BowelScreen (for the currently screening-eligible age groups: 60–64 and 65–69; Chapter 2: Table 2.2). Canadian Partnership Against Cancer (for the relative difference in the uptake rate across age groups).

Note: the asterisks indicate the extrapolated estimates.

The quality assurance standard for CRC screening uptake in Ireland is set at 60%.⁽³⁰⁵⁾ Thus, two FIT uptake scenarios (empirically-informed (base case) and quality assurance target (scenario analysis)) are presented throughout.

FIT positivity rate

The FIT test sensitivity depends on the faecal haemoglobin concentration threshold, which is set at 45 µg Hb/g faeces in the BowelScreen programme. As part of the present HTA, a review of the test accuracy of FIT for the detection of CRC at thresholds relevant to the Irish context (40 to 50µg Hb/g: Chapter 4 on Test Accuracy). The cohort model was parameterised using test accuracy data reported in Chapter 4 and the references therein.

For those without CRC

The probability of testing positive in the absence of the condition of interest is also known as the false positivity rate. Taking the average of European studies with a colonoscopy reference standard,^(271, 272, 278, 279) the false positivity rate (that is, 1 – specificity for either CRC or advanced neoplasia), ε_W , was set to 0.023.

For those with non-high-risk adenoma(s) and high-risk adenoma(s)

FITs exhibit relatively low sensitivity for the detection of adenomas, although the evidence is limited. The review of test accuracy identified one European study that reported FIT sensitivity for the detection of advanced adenomas at thresholds similar to that used by BowelScreen, with a sensitivity of 0.206.⁽²⁷¹⁾ Due to a lack of specific evidence for non-high-risk and high-risk findings, the FIT sensitivity for high-risk findings, ε_Y , was set at 0.206. In the absence of evidence, the sensitivity for non-high-risk adenomas, ε_X , was set identical to that of those without CRC or advanced adenomas, ε_W .

For those with CRC

Taking the average of the available evidence,^(271, 272, 279) the FIT sensitivity to CRC, ε_z , was set to 0.772.

Colonoscopy uptake rate following a positive FIT result

The uptake rate of colonoscopy following a positive FIT result, θ , was reported by BowelScreen at 0.806 (2022–2023).⁽¹⁴⁹⁾ It was noted that the rates are relatively constant across rounds or age groups; thus, the average value over rounds and age groups was used. For reference, the currently observed value remains slightly lower than the BowelScreen QA target (minimum standard $\geq 85\%$; achievable standard $>90\%$).⁽³⁰⁵⁾

Probability of survival

The annual probabilities of surviving background (or, all-cause) mortality, μ , was parameterised per age using the life table from Ireland. The net survival specific to CRC (that is, the probability of surviving CRC-specific hazard), π , was calculated per five-year age group using the Pohar-Perme estimator from anonymised individualised data from NCRI (2014–2018). Annual survival probabilities were computed based on the five-year survival estimates assuming a constant rate process (that is, exponentially distributed events; Table E.6).

Table E.6 Annual probability of surviving background and colorectal cancer-specific mortality

Age	Age group	Background, μ	CRC-specific, π
40	40–44	0.9992	0.9357
41	40–44	0.9991	0.9357
42	40–44	0.999	0.9357
43	40–44	0.9989	0.9357
44	40–44	0.9988	0.9357
45	45–49	0.9986	0.9378
46	45–49	0.9983	0.9378
47	45–49	0.998	0.9378
48	45–49	0.9978	0.9378
49	45–49	0.9977	0.9378
50	50–54	0.9976	0.9273
51	50–54	0.9975	0.9273
52	50–54	0.9973	0.9273
53	50–54	0.9971	0.9273
54	50–54	0.9969	0.9273

55	55–59	0.9967	0.9275
56	55–59	0.9965	0.9275
57	55–59	0.9962	0.9275
58	55–59	0.9958	0.9275
59	55–59	0.9954	0.9275
60	60–64	0.995	0.9369
61	60–64	0.9944	0.9369
62	60–64	0.9939	0.9369
63	60–64	0.9932	0.9369
64	60–64	0.9924	0.9369
65	65–69	0.9915	0.9343
66	65–69	0.9905	0.9343
67	65–69	0.9894	0.9343
68	65–69	0.9881	0.9343
69	65–69	0.9866	0.9343
70	70–74	0.9849	0.919
71	70–74	0.983	0.919
72	70–74	0.9809	0.919
73	70–74	0.9784	0.919
74	70–74	0.9756	0.919
75	75–79	0.9726	0.9192
76	75–79	0.9691	0.9192
77	75–79	0.9652	0.9192
78	75–79	0.961	0.9192
79	75–79	0.9563	0.9192
80	80–84	0.951	0.903
81	80–84	0.9453	0.903
82	80–84	0.939	0.903
83	80–84	0.9323	0.903
84	80–84	0.925	0.903

Source: NCRI (anonymised individualised patient data); Life table supplied by NCRI, originally estimated by LSTMH using CSO data.

E.2 Further detail on the estimation of selected model costs

Table E.7 Estimation of BowelScreen histopathology procedure resource requirement and costs

Histopathology procedures					
	Procedures	Case	Units per case	Unit cost	Case cost
H&E	6,339	543	11.7	€11	€128.40
Special immunochemistry	131	131	1	€31	€31
Immunohistochemistry	504	131	4	€40	€160
Staffing requirements					
	Whole-time salary	WTE	Adjusted Salary	Other costs (PRSI, Pension, Overheads)*	Total cost
Consultant	€260,378	0.4	€104,151	€68,896	€173,047
Senior scientist	€77,923	0.8	€62,338	€42,324	€104,662
Medical laboratory aides	€43,993	0.5	€21,997	€12,131	€34,128
Grade IV	€44,864	0.5	€22,432	€12,371	€34,803
Total					€346,640
Staffing cost per procedure					
Staffing cost per procedure					
346,640 / (6339+131+504) =					€50
Case cost (with staffing)					
Histopathology (H&E)					€710
Further histopathology (Special immunochemistry)					€81
Further histopathology (Immunohistochemistry)					€359
Further histopathology (Total)					€440

Source: Laboratory Services Reform Programme (HSE); HSE 2025 pay scales.⁽³⁸³⁾

*Calculated in line with the National Guidelines for the Budget Impact Analysis of Health Technologies in Ireland 2025.⁽⁶³⁷⁾

Note: Special histochemistry includes elastin stains for the assessment of invasion and it was assumed that it is ordered as one per case though it may be ordered multiple times in some cases.

Immunohistochemistry tests include four mismatch repair antibody tests per case. The staffing costs were estimated from the midpoint of the scale. The staffing cost per procedure was estimated assuming that each procedure incurs equal staffing needs.

Key: H&E – haematoxylin and eosin stain; PRSI – Pay Related Social Insurance; WTE – whole-time equivalent.

Table E.8 Estimation of additional administrative BowelScreen Programme costs

Staffing requirements					
	HSE Grade	WTE	Whole time salary	Other costs (PRSI, Pension, Overheads) [#]	Total
Clinical co-ordinator	Grade VII (clerical)	1	€67,501	€37,227	€104,728
Assistant staff officer*	Grade V (clerical)*	1	€55,897	€30,827	€86,724
Assistant staff officer*	Grade IV (clerical)*	1	€44,864	€24,742	€69,606
Total					€261,058

*The BowelScreen programme reported that two assistant staff officers would be required at Grade IV/V level. Model assumed one officer at each grade.

[#]Calculated in line with the National Guidelines for the Budget Impact Analysis of Health Technologies in Ireland 2025.⁽⁶³⁷⁾

Key: PRSI – Pay Related Social Insurance; WTE – whole-time equivalent.

E.3 Absolute model outputs of base-case and alternative scenarios

Table E.9 Absolute values of estimated key outputs at 2031, 2035 and 2040 under two FIT-uptake scenarios

	Intervention	2031		2035		2040	
		Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate
Epidemiology: CRC	Immediate	3,057	3,345	3,136	3,157	3,286	3,161
	1-yearly	2,995	3,226	3,166	3,223	3,302	3,187
	2-yearly	2,995	3,226	3,153	3,200	3,325	3,234
	Comparator	2,976	3,189	3,122	3,148	3,324	3,243
Epidemiology: Non-high-risk adenoma	Immediate	1,218	1,733	1,340	1,890	1,452	2,018
	1-yearly	1,063	1,434	1,341	1,893	1,453	2,020
	2-yearly	1,063	1,434	1,267	1,751	1,454	2,023
	Comparator	1,023	1,358	1,136	1,500	1,266	1,664
Epidemiology: High-risk adenoma	Immediate	3,074	4,382	3,348	4,527	3,601	4,656
	1-yearly	2,710	3,684	3,374	4,613	3,618	4,700
	2-yearly	2,710	3,684	3,213	4,311	3,644	4,777
	Comparator	2,607	3,486	2,903	3,733	3,242	4,060
Resource: FIT invitation (thousands)	Immediate	834	834	899	897	947	943
	1-yearly	663	663	900	898	948	943
	2-yearly	663	663	814	812	948	944
	Comparator	624	624	680	678	746	743
Resource: FIT kit (thousands)	Immediate	347	500	375	538	400	566
	1-yearly	293	398	375	539	400	566
	2-yearly	293	398	349	487	400	567
	Comparator	281	375	307	407	337	446
Resource: Colonoscopy (thousands)	Immediate	22	27	25	31	27	33
	1-yearly	20	24	25	31	27	33
	2-yearly	20	24	24	29	27	33

	Intervention	2031		2035		2040	
		Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate
Resource: Histopathology (H & E) (people requiring)	Comparator	20	23	22	27	25	29
	Immediate	7,339	9449	7,807	9,550	8,321	9,811
	1-yearly	6,759	8,333	7,867	9,708	8,354	9,883
	2-yearly	6,759	8,333	7,618	9,243	8,405	10,010
	Comparator	6,597	8,023	7,147	8,362	7,817	8,947
Resource: Further histopathology (people requiring)	Immediate	3,047	3,335	3,120	3,133	3,268	3,137
	1-yearly	2,985	3,216	3,151	3,202	3,284	3,163
	2-yearly	2,985	3,216	3,138	3,181	3,307	3,210
	Comparator	2,966	3,179	3,108	3,129	3,308	3,222
Resource: Treatments (stage I)	Immediate	641	759	669	723	710	731
	1-yearly	615	710	676	741	713	738
	2-yearly	615	710	667	726	719	751
	Comparator	608	695	649	694	703	727
Resource: Treatments (stage II)	Immediate	718	781	736	737	770	737
	1-yearly	704	755	743	752	774	743
	2-yearly	704	755	740	748	779	754
	Comparator	700	747	733	737	780	758
Resource: Treatments (stage III)	Immediate	1,053	1,140	1,078	1,074	1,128	1,074
	1-yearly	1,035	1,104	1,088	1,096	1,133	1,083
	2-yearly	1,035	1,104	1,085	1,090	1,141	1,098
	Comparator	1,029	1,093	1,077	1,077	1,144	1,107
Resource: Treatments (stage IV)	Immediate	645	665	653	623	679	619
	1-yearly	641	657	660	634	682	624
	2-yearly	641	657	661	637	686	631
	Comparator	640	654	662	640	697	651
Cost:	Immediate	185	211	194	209	204	212

	Intervention	2031		2035		2040	
		Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate	Base-case (empirical)	QA-target uptake rate
Total	1-yearly	178	197	195	212	205	213
	2-yearly	178	197	192	206	206	216
	Comparator	176	193	187	197	200	206

Key: CRC – colorectal cancer; FIT – faecal immunochemical test; H & E – haematoxylin and eosin stain.

Note: Adenoma numbers are those detected from screening only as the model assumes no incidental or symptomatic adenoma detection. For resource, shown are most influential items which collectively account for over 95% of the total absolute incremental costs. The unit numbers related to FIT and colonoscopy are provided in thousands. The unit numbers related to histopathology refer to the number of people requiring the tests. Costs are in millions of euros. The values are rounded to the nearest whole number.

Table E.10 Absolute values of estimated key outputs at 2031, 2035 and 2040 under and three immigration scenarios

	Intervention	2031			2035			2040		
		Base-case (moderate)	High migration	Low migration	Base-case (moderate)	High migration	Low migration	Base-case (moderate)	High migration	Low migration
Epidemiology: CRC	Immediate	3,057	3,075	3,043	3,136	3,167	3,107	3,286	3,338	3,234
	1-yearly	2,995	3,012	2,982	3,166	3,198	3,137	3,302	3,354	3,249
	2-yearly	2,995	3,012	2,982	3,153	3,184	3,124	3,325	3,378	3,272
	Comparator	2,976	2,993	2,963	3,122	3,152	3,093	3,324	3,376	3,272
Epidemiology: Non-high-risk adenoma	Immediate	1,218	1,226	1,212	1,340	1,355	1,326	1,452	1,481	1,424
	1-yearly	1,063	1,069	1,058	1,341	1,356	1,327	1,453	1,481	1,424
	2-yearly	1,063	1,069	1,058	1,267	1,280	1,255	1,454	1,482	1,425
	Comparator	1,023	1,029	1,019	1,136	1,147	1,126	1,266	1,287	1,246
Epidemiology: High-risk adenoma	Immediate	3,074	3,092	3,059	3,348	3,384	3,314	3,601	3,670	3,531
	1-yearly	2,710	2,726	2,698	3,374	3,411	3,340	3,618	3,687	3,547
	2-yearly	2,710	2,726	2,698	3,213	3,246	3,182	3,644	3,714	3,573
	Comparator	2,607	2,622	2,595	2,903	2,930	2,877	3,242	3,296	3,189

	Intervention	2031			2035			2040		
		Base-case (moderate)	High migration	Low migration	Base-case (moderate)	High migration	Low migration	Base-case (moderate)	High migration	Low migration
Resource: FIT invitation (thousands)	Immediate	834	839	830	899	910	889	947	968	926
	1-yearly	663	667	660	900	911	890	948	968	926
	2-yearly	663	667	660	814	823	806	948	969	927
	Comparator	624	628	621	680	686	674	746	759	734
Resource: FIT kit (thousands)	Immediate	347	349	345	375	379	371	400	408	391
	1-yearly	293	295	292	375	379	371	400	408	391
	2-yearly	293	295	292	349	352	345	400	408	391
	Comparator	281	283	280	307	310	304	337	342	331
Resource: Colonoscopy (thousands)	Immediate	22	22	22	25	25	25	27	27	26
	1-yearly	20	20	20	25	25	24	27	27	27
	2-yearly	20	20	20	24	24	24	27	27	26
	Comparator	20	20	20	22	23	22	25	25	24
Resource: Histopathology (H & E) (people requiring)	Immediate	7,339	7,382	7,304	7,807	7,889	7,730	8,321	8,470	8,170
	1-yearly	6,759	6,797	6,727	7,867	7,950	7,789	8,354	8,504	8,203
	2-yearly	6,759	6,797	6,727	7,618	7,695	7,546	8,405	8,556	8,252
	Comparator	6,597	6,635	6,567	7,147	7,215	7,082	7,817	7,943	7,692
Resource: Further histopathology (people requiring)	Immediate	3,047	3,065	3,033	3,120	3,150	3,091	3,268	3,319	3,216
	1-yearly	2,985	3,002	2,971	3,151	3,182	3,122	3,284	3,335	3,231
	2-yearly	2,985	3,002	2,971	3,138	3,169	3,109	3,307	3,360	3,254
	Comparator	2,966	2,983	2,952	3,108	3,138	3,079	3,308	3,360	3,256
Resource: Treatments (stage I)	Immediate	641	644	638	669	676	663	710	721	698
	1-yearly	615	619	613	676	683	670	713	725	702
	2-yearly	615	619	613	667	674	661	719	731	707
	Comparator	608	611	605	649	655	643	703	714	692
Resource: Treatments (stage II)	Immediate	718	722	715	736	743	729	770	782	758
	1-yearly	704	708	701	743	750	736	774	786	762

	Intervention	Base-case (moderate)	2031		Base-case (moderate)	2035		Base-case (moderate)	2040	
			High migration	Low migration		High migration	Low migration		High migration	Low migration
	2-yearly	704	708	701	740	747	733	779	792	767
	Comparator	700	704	697	733	741	727	780	792	768
Resource: Treatments (stage III)	Immediate	1,053	1,059	1,048	1,078	1,089	1,068	1,128	1,145	1,110
	1-yearly	1,035	1,041	1,030	1,088	1,099	1,078	1,133	1,151	1,115
	2-yearly	1,035	1,041	1,030	1,085	1,095	1,075	1,141	1,159	1,123
	Comparator	1,029	1,035	1,024	1,077	1,087	1,067	1,144	1,162	1,126
Resource: Treatments (stage IV)	Immediate	645	649	642	653	660	647	679	689	668
	1-yearly	641	645	638	660	666	653	682	692	671
	2-yearly	641	645	638	661	667	655	686	697	676
	Comparator	640	643	637	662	669	656	697	708	686
Cost: Total	Immediate	185	186	184	194	196	192	204	208	201
	1-yearly	178	179	177	195	197	193	205	208	202
	2-yearly	178	179	177	192	194	190	206	210	203
	Comparator	176	177	175	187	189	185	200	204	197

Key: CRC – colorectal cancer; FIT – faecal immunochemical test; H & E – haematoxylin and eosin stain.

Note: Adenoma numbers are those detected from screening only as the model assumes no incidental or symptomatic adenoma detection. For resource, shown are most influential items which collectively account for over 95% of the total absolute incremental costs. The unit numbers related to FIT and colonoscopy are provided in thousands. The unit numbers related to histopathology refer to the number of people requiring the tests. Costs are in millions of euros. The values are rounded to the nearest whole number.

E.4 Assessment of model fit

The goodness of fit of the model outputs were assessed using standardised residuals, computed as raw residuals (that is, difference between data and model prediction) divided by the standard deviation of the residuals. Standardised residuals help identify how far each observation deviates from the model's prediction in terms of standard deviation units. Typically, a standardised residual greater than the absolute value of two to three is considered a considerable deviation, indicating potential outliers or areas where the model may not fit well. To visualise the spread of residuals, histograms were used. A well-fitting model will have most of its standardised residuals centred around zero, meaning that the observation (indicated by the residual of zero) falls within the 95% quantiles of the standardised residuals.

Figure E.3 Goodness of model fit to incidence of colorectal cancer data assessed by standardised residuals: number (top) and rate per 100,000 (bottom). Histograms display the distribution of residuals for number (top) and rate per 100,000 (bottom), respectively

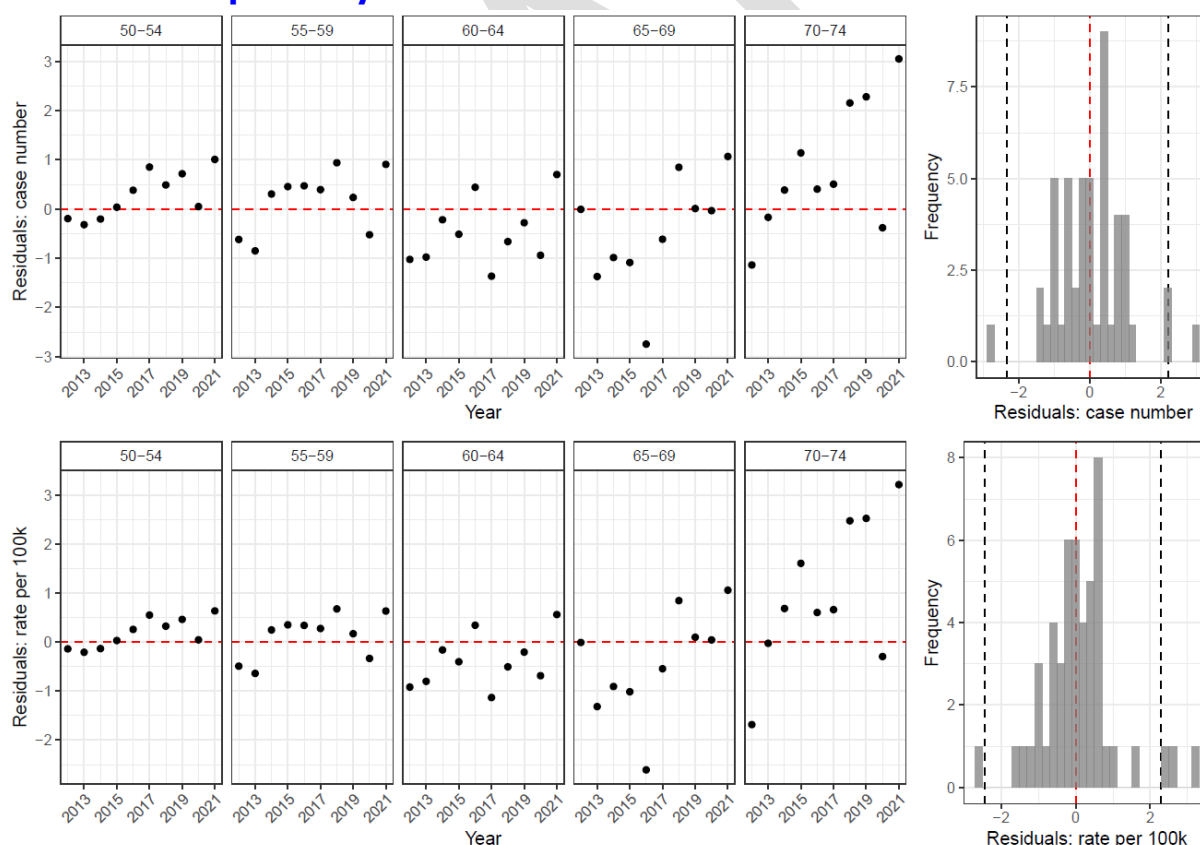
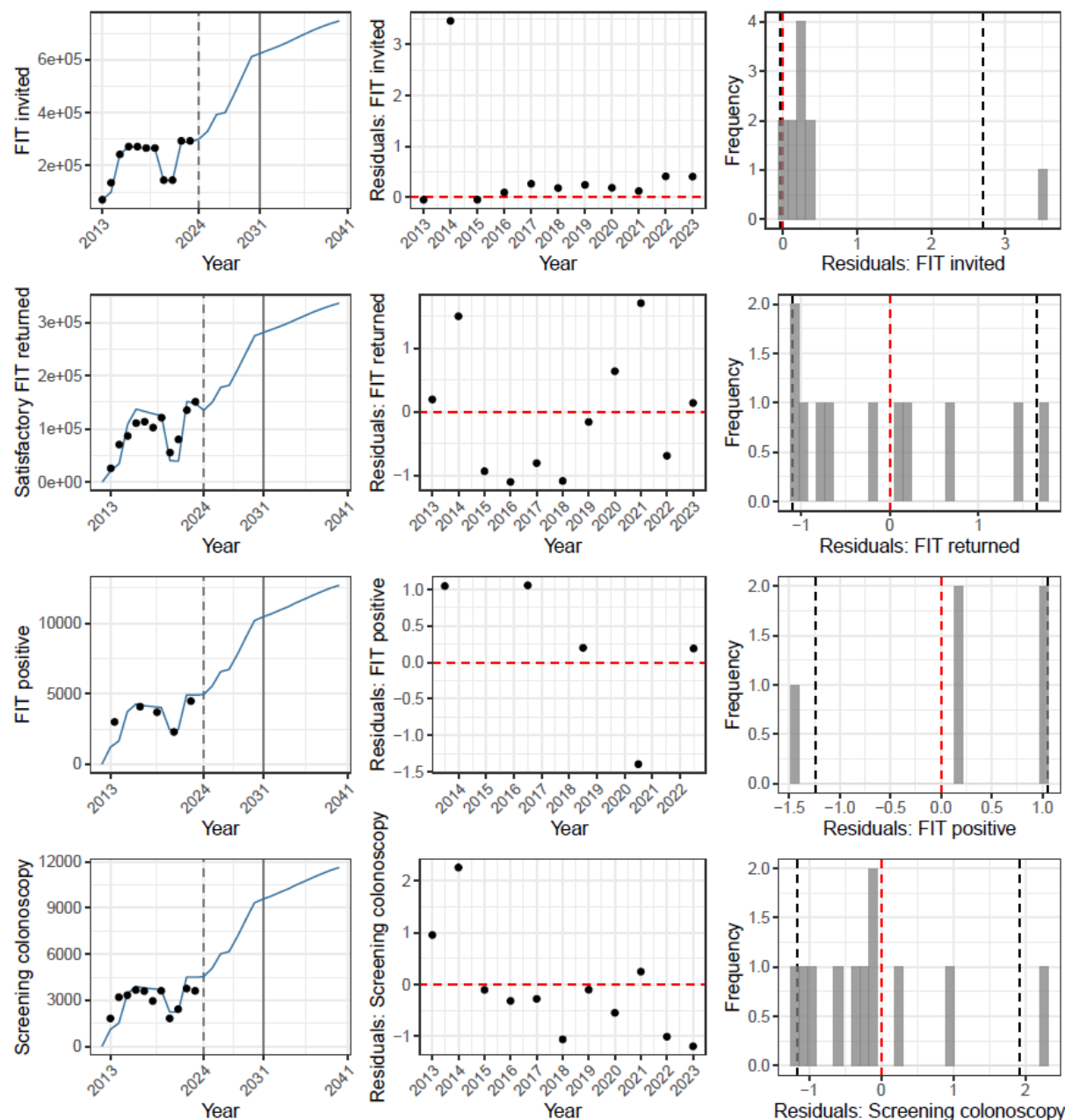


Figure E.4 Goodness of model fit to screening resources data (FIT invitations, FIT returned, FIT positive and BowelScreen colonoscopy), assessed by overlaying model outputs with data (left), standardised residuals (middle) and their distributions (right)



Note: The number of screening colonoscopies include both index colonoscopies and additional procedures due to inadequate bowel preparation and other complications.

Key: FIT – faecal immunochemical test.

Appendix F Organisational considerations

Table F.1 Estimated number of invitations and screening outcomes following BowelScreen extension: Scenario analysis for two-yearly expansion

Parameter	Year 1 ^{\$}		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
Invitations distributed [¥] (N)	624,217	663,186	679,925	814,364	746,138	948,132
FIT kits distributed (N)	281,311	293,470	306,674	348,593	336,833	399,787
FIT uptake rate (%)	45.1%	44.3%	45.1%	42.8%	45.1%	42.2%
FIT positive (N)	10,453	10,880	11,483	12,880	12,697	14,694
FIT positivity rate (%)	3.7%	3.7%	3.7%	3.7%	3.8%	3.7%
Index colonoscopy (N)	8,249	8,585	9,061	10,163	10,019	11,595
CT colonography (N)	177	184	194	218	215	249
Participants with adenomas (total) (N)	3,630	3,773	4,039	4,480	4,508	5,098
Adenoma detection rate (%)	44.0%	43.9%	44.6%	44.1%	45.0%	44.0%
Participants with CRC (N)	707	726	786	837	879	938
Cancer detection rate (per 1,000 screened)	2.51	2.47	2.56	2.40	2.61	2.35

Key: CRC – colorectal cancer. CSO – Central Statistics Office. CT – computed tomography. FIT – faecal immunochemical test.

¥Two-yearly scenario expansion scenario. Based on CSO population projections assuming moderate net migration.

\$ Base year: 2031.

Note: Adenoma detection rate excludes participants who also have CRC.

Table F.2 Estimated healthcare resource use required for expansion: Two-yearly expansion scenario

Number of participants [‡]	Year 1		Year 5		Year 10	
	55–74	50–74	55–74	50–74	55–74	50–74
Index colonoscopy	8,249	8,585	9,061	10,163	10,019	11,595
Additional planned procedures [±]	1,129	1,175	1,240	1,391	1,372	1,587
Surveillance colonoscopy	2,374	2,374	3,389	3,491	4,026	4,470
N participants requiring histopathology [§]	4,328	4,489	4,811	5,302	5,372	6,018
CT colonography	177	184	194	218	215	249
CT scan	697	716	772	822	864	920
MRI (pelvis)	233	240	259	275	289	308
PET	105	107	116	123	130	138
Surgery	677	695	753	801	842	899
Chemotherapy	315	324	350	373	392	418
Radiotherapy	98	101	109	116	122	130
Stage I treatment	290	298	322	343	361	385
Stage II treatment	156	160	173	184	193	206
Stage III treatment	212	218	236	251	264	281
Stage IV treatment	49	51	55	59	62	66

[‡] BIA estimates based on CSO population projections (moderate net migration scenario) and empirically-derived screening uptake rates under the two-yearly expansion scenario analysis. Base year: 2031.

[±] Reasons for additional planned procedures include incomplete index colonoscopy due to poor bowel preparation, the participant's level of tolerance of the first procedure, the requirement to have a second colonoscopy to check a site previously examined or resected, or a clinical decision to perform colonoscopy over two visits instead of surgery.

[§] Participants may have multiple specimens requiring histopathology.

Key: BIA – budget impact analysis. CSO – Central Statistics Office.

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