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An tÚdarás Um Fhaisnéis  
agus Cáilíocht Sláinte

Health technology assessment  
(HTA) of a population-based  
colorectal cancer screening  
programme in Ireland

25 March 2009

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**Outline Report**

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# Outline Report

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## 1 Introduction

In November 2007, the Health Information and Quality Authority (the Authority) agreed to carry out a health technology assessment (HTA) of a population-based colorectal cancer screening programme in Ireland, in response to a request by the National Cancer Screening Service (NCSS) Board.

The purpose of this assessment was to evaluate various options for a population-based colorectal cancer screening programme in Ireland with a view to establishing (i) the cost-effectiveness of these options compared to the current policy of no screening and relative to each other, (ii) the key additional resource implications and health outcomes associated with these options in the first ten years of a screening programme and (iii) the ethical considerations arising from these findings.

In Ireland, colorectal cancer is the second most frequently diagnosed cancer in men, after prostate cancer, and the second most frequently diagnosed cancer in women, after breast cancer. An average of 2,040 new cases of colorectal cancer were diagnosed each year during the period 2002 to 2005, with an average of 925 deaths from colorectal cancer each year during the same period. Almost half of these deaths (49%) occur in people aged 75 and older, 8% in those aged 55 and under, 15% in those aged 55 to 64 years and 28% in those aged 65 to 74 years<sup>(1)</sup>.

The incidence of colorectal cancer increases with increasing age. The number of cases diagnosed each year in Ireland is therefore expected to increase as our population ages. By 2020, the number of new cases diagnosed each year in Ireland is projected to have increased by 79% in men and 56% in women, compared to the average annual number recorded for the period 1998 to 2002<sup>(2)</sup>. The incidence rates of colorectal cancer in Ireland rank among the highest in Western Europe for both men and women<sup>(3)</sup>, while the death rate (mortality) from colorectal cancer is higher for men in Ireland than elsewhere in Western Europe<sup>(4)</sup>.

Population-based colorectal cancer screening involves systematically inviting individuals in a defined population to participate in a programme aimed at detecting colorectal cancer and pre-cancerous lesions that may develop into colorectal cancer. The aim of a screening programme is to save lives by preventing premature deaths from colorectal cancer. Organised screening for colorectal cancer is already underway or is in the process of being rolled out in several countries, either at a regional or national level<sup>(5,6)</sup>.

The following section explains what HTA is and summarises the findings of this assessment. A more detailed description of the HTA and its findings can be read in the technical report and in the ethical commentary. A glossary of technical terms used in the report can be found at the end of the technical report.

## 2 Background

### 2.1 What is the role of the Health Information and Quality Authority in health technology assessment (HTA)?

The Health Information and Quality Authority is an independent Authority reporting to the Minister for Health and Children which was established on May 15, 2007. The Authority is the statutory organisation in Ireland with a responsibility to carry out national health technology assessments (HTAs) and to develop standards for the preparation of these and other HTAs across our health system.

### 2.2 What is HTA?

Health technology assessment is a form of health research that generates information about the clinical and cost-effectiveness of health interventions (technologies), as well as information on their wider impact. The term 'technology' includes drugs, medical equipment, diagnostic techniques, surgical procedures, and public health programmes, for example, cancer screening programmes. This information is for use by the public, service providers and policy makers. The main issues investigated as part of any HTA are:

- Does the intervention (technology) work?
- For whom does it work?
- What is the benefit to the individual?
- At what cost?
- How does it compare to the alternative options available?

### 2.3 How is a HTA carried out?

A HTA usually consists of two interlinked parts:

- i. a systematic review of the available published and unpublished literature
- ii. an economic evaluation to see whether an intervention is cost-effective compared with the current situation (or another comparator).

However, a HTA can also look at broader issues, such as resource implications and potential ethical issues associated with a technology or intervention.

The literature review is used to collect important information on the disease process that the intervention is targeting, and the efficacy and safety of the technology/ intervention (for example, how well the technology works in identifying disease and reducing deaths). In this case it included information on the relative efficacy and safety of various screening tests for colorectal cancer, as well as information on the cost-effectiveness of strategies or programmes using these screening tests in other settings. The literature review also examined the natural history of colorectal cancer, that is, how the disease is thought to develop.

The economic evaluation includes a cost-effectiveness analysis, in which alternative courses of action are compared. In this case, proposed options for a colorectal screening programme were individually compared with a policy of no screening. Subsequently, these options for a screening programme were compared directly to each other. As in this assessment, an evaluation of the resources that may be required to implement the intervention may be undertaken as part of an HTA.

## 2.4 What measurements are used?

In a cost-effectiveness analysis, the costs and effects (health benefits) of each intervention being evaluated must be measured. In this instance, the total costs incurred by the health services to provide the different screening options were estimated (for example, the cost of the screening test and the cost of diagnosing and treating the disease). The health benefit of the intervention or programme may be measured in a number of ways. Life years gained (LYG) measures the impact of an intervention on patient length of life (survival). If the effects of an intervention on the health-related quality of life of a patient, as well as on survival, are to be considered, both are combined into a single common unit of measure called the Quality Adjusted Life Year (QALY). Both LYG and QALYs are widely used in HTAs in other countries.

In this HTA, both LYG and QALYs gained were calculated while costs were measured in euro. The advantage of calculating health benefits in terms of QALYs gained is that it allows the effect of screening on both the quality of life of patients (morbidity) as well as on survival (mortality) to be estimated, rather than estimating the effect on mortality alone.

When comparing two or more interventions, the question is then, what is the additional cost involved for the additional benefit achieved. To answer this question, the incremental cost-effectiveness of one therapy over the other is calculated, with the results presented as an incremental cost-effectiveness ratio (ICER)<sup>(7)</sup>.

The ICER for two healthcare interventions A and B can be calculated as follows:

$$\text{ICER} = (\text{Cost A} - \text{Cost B}) / (\text{Effect A} - \text{Effect B})$$

One of the implications of making comparisons between the cost-effectiveness of different interventions is that there is a threshold ratio above which a programme would not be considered cost-effective. In practice, there is no fixed threshold above which an ICER would not be considered cost-effective. However, if an intervention has an ICER that is significantly higher than other healthcare interventions that are already reimbursed, other factors such as the innovative nature of the technology, or the wider costs and benefits to patients and society, would need to be taken into consideration.

The ICER is a measurement that allows the cost-effectiveness of different technologies to be compared and should not be considered as putting a monetary value on a year of life.

### 3 Natural History of Colorectal Cancer

Colorectal cancer refers to cancer of the lower bowel, that is, the colon and rectum. Evidence suggests that most colorectal cancers develop from benign polyps (non-cancerous tumours) in the lining of the bowel described medically as 'adenomas' or 'adenomatous polyps.' This is known as the adenoma-carcinoma sequence<sup>(8, 9)</sup>.

Adenomas are classified as low, intermediate or high risk in terms of their ability to cause cancer<sup>(10)</sup>. Most adenomas do not cause severe symptoms and although they can produce blood in the stools, this can go undetected, that is, occult (hidden) blood. The true prevalence of adenomatous polyps in the population is unknown<sup>(9)</sup>. The progression from pre-cancerous adenoma to cancer is generally considered to be slow and may take 10 to 15 years to occur<sup>(9)</sup>.

When a cancer is diagnosed, it is usually 'staged.' That is, a series of tests are carried out that measure the size and spread of the cancer at that point. Like other cancers, colorectal cancer can spread into the surrounding lymph nodes (stage III) and to other parts of the body (stage IV). Stages I and II refer to more localised disease<sup>(11)</sup>. Data from the National Cancer Registry show that during the period 2002 to 2005 in Ireland, 11% of colorectal cancer cases were stage I at diagnosis, 24% were stage II, 26% stage III and 22% at stage IV. Seventeen percent of the cancers were not staged<sup>(1)</sup>.

Cancer that has advanced to stages III and IV is more complex to treat and usually requires additional treatments. In addition, patients diagnosed at these later stages have a lower chance of survival. Data from the National Cancer Registry show that for patients diagnosed with colon cancer between 1997 and 2001 in Ireland, approximately three-quarters of those with stage I disease were still alive five years after diagnosis, compared to just over 60% with stage II, around half with stage III and less than 10% with stage IV<sup>(12)</sup>.

Adenomas and colorectal cancer can be detected by a variety of screening tests and are removed by colonoscopy or surgery. In this way a cancer may either be prevented from occurring in the first place or it can be diagnosed and treated at an earlier stage where it is associated with a better chance of survival.

## 4 Screening for Colorectal Cancer

As noted, the purpose of a screening programme for cancer is to save lives by preventing the disease from occurring or by detecting the disease at an earlier stage. The existence of the adenoma-carcinoma sequence, and the strong association between the stage of disease at diagnosis and survival, provides the rationale for colorectal cancer screening.

A population-based screening programme for colorectal cancer involves inviting a defined population who are at average risk for the disease (that is, do not have medical conditions that put them at higher risk of developing colorectal cancer or a strong family history of colorectal cancer) to attend for screening. Such a programme would not only identify individuals with colorectal cancer at an earlier stage, but would also identify people who have pre-cancerous adenomas who are at risk of developing colorectal cancer. Several countries already have organised screening programmes in place either at a national or regional level<sup>(5,6)</sup>. In the United Kingdom (UK), it is expected that full national programmes will be in place by 2010.

A range of potential screening tests are available for colorectal cancer. Options include invasive diagnostic tests such as colonoscopy and flexible sigmoidoscopy that involve an examination of the bowel by a medical professional. There are also various non-invasive tests that can detect occult (hidden) blood in stool, which may indicate the presence of cancer or adenomas. These tests are known as faecal occult blood tests and can be completed by the individual in their home. Individuals who have a positive test are then referred for further screening, usually involving a direct examination of the bowel by colonoscopy.

The World Health Organisation (WHO) criteria for screening state that screening tests should be effective, safe and acceptable to the population and that the economic costs to the health service should be acceptable<sup>(13)</sup>. Therefore, a screening programme for colorectal cancer not only needs to be cost-effective, but its implementation also must be feasible, in terms of having sufficient resources available to deal with the new cancers and adenomas detected.

Screening tests can result in false positive results and false negative results. The ability of a test to accurately identify persons who truly have a disease and those who truly do not have a disease is called its sensitivity and specificity<sup>(14)</sup>. Sensitivity is the proportion of persons with disease in a screened population who are identified as having the disease by the screening test. Tests with a high sensitivity have a better chance of detecting disease. Specificity is the proportion of persons without disease in a screened population who are identified as being disease-free by a screening test. Tests with a high specificity limit the numbers of people with false positive screening test results.

## 4.1 Description of selected screening tests

A brief description of three screening tests frequently used in colorectal screening programmes (and that are evaluated in this HTA) is given below:

### 4.1.1 Guaiac-Based Faecal Occult Blood Test (gFOBT)

The faecal occult blood test (FOBT) is a test for blood in the stool (faeces)<sup>(15)</sup>. The presence of blood may be an indicator for cancer or adenomas. The test is based on a reaction between guaiac, which is present in the test, and the enzyme peroxidase which is found in blood. Peroxidase is not however specific to human blood and high peroxidase-containing foods such as red meat and certain raw plant foods can result in a false-positive result<sup>(16)</sup>. In addition, the gFOBT test can detect blood from the stomach and small intestine that may be due to bleeding associated with certain drugs, such as non-steroidal anti-inflammatory drugs like aspirin. Therefore, it is not selective for blood of colorectal origin. To minimise the effect of these interactions, those completing the test may have to restrict their diet or the use of certain drugs for several days prior to using the test<sup>(17)</sup>.

The test is relatively easy for individuals to carry out in their own homes. Testing kits are readily available in a format that is suitable for outward and return posting<sup>(18)</sup>. The test involves taking samples from a number of stools using a sampler and placing these samples on cards. The test kit is returned by mail and is processed in a laboratory to determine if the card samples are positive or negative for blood.

The analysis of the samples in the laboratory is not always straightforward and can be subjective<sup>(15)</sup>. Equivocal results can arise when some, but not all, of the test samples are positive. Repeat testing is required usually every two years in screening programmes as a once-off test is not sufficiently sensitive.

Programmes based on guaiac-based tests usually use a second round of testing in positive cases, with either the same guaiac-based test or another type of faecal test. This is known as 'reflex testing.' Reflex testing has been shown to reduce the number of false positive results arising from screening, thus reducing the number of further diagnostic tests required<sup>(19)</sup>. In this HTA, the gFOBT-based screening programme that was evaluated used a reflex FIT test (see below) in all those who had an equivocal or positive test with gFOBT.

A range of gFOBT tests are available<sup>(20)</sup>. Some more recently developed tests seem to have a higher sensitivity than the older tests, but may be more susceptible to the effects of diet<sup>(15)</sup>.

Four randomised controlled trials have been conducted to assess the efficacy of gFOBT-based colorectal cancer screening programmes. A 2008 Cochrane review that included a meta-analysis of these trials showed that repeat gFOBT testing is associated with a 25% reduction in mortality compared with no screening<sup>(21)</sup>. In other words, a screening programme based on regular gFOBT has been proven to be effective in reducing the number of deaths from colorectal cancer.

Numerous national and regional screening programmes are based on gFOBT, including those in the UK<sup>(19)</sup>, Ontario<sup>(22)</sup>, France<sup>(23)</sup>, Spain<sup>(24)</sup> and Italy<sup>(25)</sup>.

### 4.1.2 Faecal Immunochemical Test (FIT)

The faecal immunochemical test (FIT) is also based on the detection of occult blood in the stool. It depends on antibodies specific for human haemoglobin to react with blood<sup>(15,16)</sup>. It is more selective for blood originating from the colon and rectum than the gFOBT test. Therefore, dietary and drug restrictions are not required with FIT. In theory, this should cut down on the number of false positive results<sup>(16)</sup>. An advantage of FIT is that the processing and reading of FIT tests can be automated, allowing for more objective interpretation of the results. However, FIT test kits are more expensive than gFOBT test kits. As with gFOBT, repeat testing is likely to be required in a screening programme for colorectal cancer.

Several randomised controlled trials are underway to evaluate the efficacy of FIT-based screening programmes, but as yet they have not been reported. This means that there is currently no evidence that screening by FIT would be effective in reducing colorectal cancer mortality in the population. Nevertheless, screening programmes based on FIT have been adopted in Australia<sup>(26)</sup> and parts of Italy<sup>(5, 27)</sup> and a change from gFOBT to FIT testing has been recently recommended in the French screening programme<sup>(28)</sup>. It has been argued that it is not necessary to demonstrate in trials that FIT reduces mortality as it has already been proven from the gFOBT trials that faecal occult blood testing is effective<sup>(15)</sup>. Despite the absence of conclusive evidence, FIT has been adopted in a number of screening programmes on the basis that the tests may have better performance characteristics such as sensitivity and specificity and because they may be more acceptable to screening participants because there are no dietary or drugs restrictions.

There is no clear evidence whether gFOBT or FIT has better sensitivity or specificity<sup>(20, 29)</sup>. Newer tests tend to perform better than the older tests, so the performance of gFOBT or FIT very much depends on the type of test chosen.

### 4.1.3 Flexible Sigmoidoscopy (FSIG)

Flexible sigmoidoscopy is a procedure in which a slender, hollow, flexible, lighted tube is placed into the rectum to help find polyps or cancers in the rectum and lower part of the colon. The rationale for the use of FSIG as a screening tool for colorectal cancer is the observation that 50 to 75% of adenomatous polyps are within reach of the 60cm instrument<sup>(30)</sup>. An advantage of FSIG as a screening test is that screening and diagnosis can be combined, that is, for the majority of those with adenomas, the lesion can be removed at the time of testing. Another advantage is that a single screening examination (once-off with no repeat testing) may be sufficient to provide protection against colorectal cancer, unlike the requirement for biennial testing with the faecal tests<sup>(31)</sup>.

No randomised controlled trials of flexible sigmoidoscopy demonstrating reduced mortality have been published in full yet. Results from a number of trials are awaited including that of a large UK population-based trial in 40,674 individuals with results relating to colorectal mortality expected in 2010<sup>(32)</sup>.

Flexible sigmoidoscopy (FSIG) is used for colorectal screening in parts of Italy, Australia, Canada and the USA<sup>(5)</sup>.

## 4.2 Screening and resource implications

Following an initial screening test, a screening programme will require resources to follow up those individuals who have a positive test. Pathology (including biopsy and/or relevant blood tests) will be required to categorise adenomas removed during colonoscopy or flexible sigmoidoscopy and to stage the cancers detected. Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scans, Positron Emission Tomography (PET) scans and transrectal ultrasound (TUS) will be required for the diagnosis and staging of cancers detected to varying degrees. For example, all colorectal cancers are likely to require a CT scan, but only 10% of colorectal cancers are likely to require a PET scan<sup>(33)</sup>.

Surgery and treatment with post-operative chemotherapy and/or radiotherapy will be required for most colorectal cancers that are diagnosed. All cancers will require follow-up after treatment to detect recurrence or spread of the cancer.

Some individuals with adenomas diagnosed during the screening process will require ongoing surveillance, usually by colonoscopy, the frequency of which depends on the size, nature and number of adenomas detected. Current UK surveillance guidelines recommend annual colonoscopy for those classified as high risk and colonoscopy every three years for those that are at an intermediate risk<sup>(10)</sup>. Individuals that are classified as low risk return to routine screening.

It is important to consider the resource implications for existing services (cancer treatment, surveillance) as well as the costs of conducting screening when evaluating screening programmes. Establishing a screening service requires investment in new and existing resources. However, in time, screening programmes are expected to reduce the number of cancers occurring in the population or to allow these cancers to be diagnosed at an earlier stage and therefore have the potential to reduce overall cancer resource requirements in the future.

## 4.3 Screening and health outcomes

Studies investigating screening programmes usually measure health outcomes in terms of LYG or QALYs gained in the main analysis. Health outcomes may also be evaluated in other ways including: reduction in colorectal cancer cases, reduction in colorectal cancer deaths, stage–distribution of screen-detected cancers, and rates of complications.

Complications of screening can arise at the screening or diagnostic stages and include bowel perforation, bleeding and rarely, death<sup>(32, 34, 35, 36)</sup>. While the risk to an individual of complications occurring may be low, it is important to consider potential negative and positive outcomes when evaluating any screening programme.

## 5 Health Technology Assessment on a Population Based Colorectal Cancer Screening Programme

Colorectal cancer screening presents an opportunity to reduce the risk of developing colorectal cancer and dying from the disease in Ireland. Currently, there is no nationally organised or 'population-based' screening programme for individuals that are at an average risk of developing colorectal cancer in Ireland. That is not to say that screening does not take place. Screening for colorectal cancer is conducted within research programmes and on a case by case basis for individual patients identified by their doctors. Hereafter, this situation is referred to as 'no screening' in relation to this HTA.

### 5.1 Objectives

The objectives were to:

- evaluate the cost-effectiveness of various options for a colorectal cancer screening programme compared to a policy of no screening
- compare these options with one another in terms of their relative cost-effectiveness
- estimate the key additional resource requirements (for example, colonoscopy capacity) and key health outcomes (for example, numbers of cases of adenomas and cancer detected) in the initial ten years of the programme.

The ethical considerations arising from these findings were also evaluated separately as part of the HTA.

**It should be noted that it was not within the remit of this HTA to estimate the budgetary impact of establishing a population-based screening programme in Ireland. This process was undertaken by the NCSS, the body responsible for the implementation of population-based screening programmes, and is described in a business implementation plan issued as part of a December 2008 report from the NCSS that outlined their recommendations for a colorectal cancer screening programme in Ireland.**

### 5.2 Evaluation process

Following a request from the NCSS in November 2007, the Board of the Authority agreed to undertake the HTA and a competitive tender process was initiated to select an evaluation team. To lead and oversee the process, and to advise the Authority, a multidisciplinary Expert Advisory Group was convened. This group included clinical experts, experts in public health, international experts in HTA, key stakeholders, patient and public representatives.

The scope of the HTA was refined following consultation with the Expert Advisory Group and a multi-disciplinary team, led by the National Cancer Registry Ireland, was subsequently appointed in May 2008 to conduct the HTA on its behalf. The team included groups from the National Centre for Pharmacoeconomics in Dublin, the School of Health and Related Research (ScHARR) at the University of Sheffield, and Dublin City University. These groups had extensive experience in economic modelling, health technology assessment, health services research and expertise in the epidemiology of colorectal cancer. This project was managed by the HTA directorate within the Authority.

Dr Deirdre Madden from the Faculty of Law, University College Cork provided the ethical commentary.

### 5.3 Screening options

The advice of the Expert Advisory Group was taken in selecting the screening options to be evaluated as part of this HTA. There are several screening options for colorectal cancer – evaluation of all of which would be a time consuming, resource intensive exercise. In selecting the screening options to be evaluated, consideration was given to the timeframe within which the HTA needed to be completed, the volume and strength of the scientific evidence supporting the different options, screening practices in other countries, and factors such as the acceptability, feasibility and risk of serious adverse events associated with different screening options. The appropriate age-range for a programme based on faecal testing was agreed by the Expert Advisory Group to be 55 to 74 years and is in line with international recommendations and screening programmes implemented in other countries. Three core screening options were recommended by the Group:

- Biennial immunochemical faecal testing (FIT) at ages 55 to 74 years to be fully implemented over two consecutive years, hereafter, referred to as ('Biennial FIT at ages 55 to 74 years')
- Biennial guaiac-based faecal occult blood test (gFOBT) at ages 55 to 74 years (with reflex FIT testing) to be fully implemented over two consecutive years, (hereafter referred to as 'Biennial gFOBT at ages 55 to 74 years')
- Flexible sigmoidoscopy (FSIG) once only at age 60 (hereafter, referred to as once-off FSIG at age 60').

The cost-effectiveness of age-related variations of the three core scenarios were also evaluated by the Evaluation Team to aid decision making and included:

- Biennial FIT at ages 55 to 64 years
- Biennial FIT at ages 65 to 74 years
- Biennial gFOBT at ages 55 to 64 years
- Biennial gFOBT at ages 65 to 74 years
- FSIG once only at age 55 years.

The HTA also investigated a staggered implementation of the FIT-based screening option (55 to 74 years) incorporating different ages over several years to determine the impact on resources and health outcomes.

## 5.4 Outcomes evaluated

The main analysis in this HTA (the cost-effectiveness analysis) examined health outcomes in terms of QALYs gained and LYG for each of the three main screening options. Secondary health outcomes evaluated in this analysis included:

- Reduction in the lifetime incidence of colorectal cancer (that is, the number of new cases of colorectal cancer occurring)
- Reduction in the lifetime number of deaths due to colorectal cancer
- Percentage of all cases of colorectal cancer that would be detected by screening
- Stage distribution of cancers detected in the screening programme compared with stage distribution of cancers detected without screening (henceforth referred to as 'symptomatically-detected cancers')
- Rates of complications (major bleeding, bowel perforation, deaths due to perforation)
- Lifetime rates of endoscopy procedures.

In a separate analysis on resources and health outcomes in the first ten years of a screening programme, the following health outcomes were examined:

- The number of deaths due to colorectal cancer in the first ten years of a screening programme
- The number of cases of colorectal cancer occurring in the first ten years of a screening programme.

Costs involved for each screening option, as well as the costs involved in managing colorectal cancers and surveillance of intermediate and high-risk adenomas, were evaluated in this HTA. Costs were measured in euro and were examined from the perspective of the Health Service Executive (HSE). This means that only direct costs to the HSE were taken into account. Costs incurred by the patient (for example, travel expenses, time off work) or costs to society (for example, carers' time, loss of productivity) were not taken into account. ICERs were computed for each option compared to no screening and subsequently were calculated for the various screening options compared to each other.

## 5.5 Economic modelling approach

As the HTA required the prediction of outcomes and costs occurring in the future, it was necessary to use economic modelling in the evaluation. An independent economic model, the ScHARR colorectal cancer screening model that was previously used to conduct an economic evaluation of screening in England, was updated and modified to the Irish setting<sup>(37)</sup>. Estimates and data on the efficacy of the screening tests, likely uptake of screening, frequency of disease, treatment patterns and resource use were incorporated into the model. These data were mainly obtained by literature review as described earlier and came from published trials and studies, other population-based screening programmes, Irish databases, and where relevant data was not available in the literature, from expert opinion. All estimates were approved by the Expert Advisory Group.

Within the timeframe of the HTA it was not possible to conduct specific micro-costing exercises. Therefore, cost estimates were compiled from a range of sources, including from single hospitals and pharmacies in Ireland, from the Diagnostic Related Group (DRG) costs (HSE Casemix unit), and from other studies.

The base-case analysis refers to the evaluation conducted using a set of agreed parameters. To deal with uncertainty in the true values of the parameters and to assess the robustness of the results, extensive sensitivity analysis was conducted. This involved repeating each evaluation using a range of parameter values in order to see whether the results were significantly affected by changing any particular parameter or all parameters simultaneously.

Following consultation with the National Cancer Screening Service (NCSS) and the National Cancer Control Programme, and with the agreement of the Expert Advisory Group, it was decided that the definition of a colorectal screening programme would encompass all procedures up to and including the completion of primary treatment. Thus for individuals with:

- Adenomas, screening would include everything up to and including removal of the polyp
- Colon cancer, screening would include everything up to and including removal of the cancer by surgery
- Rectal cancer, screening would include everything up to and including removal of the cancer by surgery. Since pre-operative radiotherapy is the standard of care, this would also be included in the screening programme.

Thereafter, the individual would enter the symptomatic services for further treatment or follow-up. This would include surveillance of individuals who had adenomas removed, with the frequency of follow-up depending on whether the individual was considered as low, intermediate or high risk.

Once individuals left the screening programme, they would return to the care of their General Practitioner (GP) or routine clinical services.

The impact of screening versus a policy of no population-based screening on health service resources was calculated for the ten years following commencement of a screening programme. These resources were agreed with the Expert Advisory Group and included:

- Colonoscopy resources (diagnosis and ongoing surveillance)
- Pathology for diagnosis and staging/risk classification
- Surgery for colon and rectal resection
- Radiology procedures (PET, CT scan, TUS, MRI) for work-up of cancers.

## 5.6 Assumptions

In conducting the HTA the following assumptions were made:

- Under the gFOBT and FIT options, test kits would be dispatched by post to screening invitees and returned by post for laboratory processing and analysis
- All lesions (cancers and adenomas) would be removed at detection by FSIG or colonoscopy
- No further surveillance would occur beyond 80 years of age
- Because of a lack of data on the performance characteristics (sensitivity and specificity) of combinations of screening tests (gFOBT with reflex FIT), it was assumed that the performance characteristics of gFOBT and reflex FIT are independent
- All those who have a positive gFOBT test will complete a FIT test
- All individuals in whom colonoscopy was incomplete or unsuitable will undergo CT colonography.

The resource model was structured to predict resource requirements if a screening programme were implemented immediately. That is, for biennial FIT- and gFOBT-based programmes, 50% of the eligible population (55 to 74 year olds) would be offered screening in year one (equating to 357,812 individuals) and the remaining 50% in year two (362,535 individuals).

Costs and outcomes occurring in the future were discounted (that is, adjusted for time-preference for costs (later) and benefits (now)) at a rate of 4% in accordance with recommendations of the Department of Finance.

## 6 Findings

### 6.1 Cost-effectiveness of possible screening options for a population-based screening programme in Ireland

As outlined in further detail below, the key finding of the economic evaluation in the primary analysis was that a population-based colorectal cancer screening programme based on, (i) biennial FIT at ages 55 to 74 years, (ii) biennial gFOBT at ages 55 to 74 years or (iii) once-off FSIG at age 60 would be highly cost-effective compared to the current policy of no screening.

Secondary analysis demonstrated that a screening programme based on biennial FIT at ages 55 to 74 years (i) provided the greatest health gain (measured as QALYs gained) compared with no screening and (ii) was highly cost-effective when compared with all other screening options evaluated. It therefore represents the optimal screening strategy for a population-based colorectal screening programme.

#### 6.1.1 Cost-effectiveness of core screening options compared to no screening

Each of the three screening options proposed by the Expert Advisory Group was compared to the current standard of care, that is, no population-based screening (Table 1).

**Table 1:** Cost-Effectiveness of Core Screening Options Compared to No Screening

Screening Option	ICER (€ / QALY)
Biennial FIT at ages 55 to 74 years	€1,696
Biennial gFOBT at ages 55 to 74 years	€4,428
Once-off FSIG at age 60 years	€589

When the analysis was repeated with LYG as the outcome, the above results changed little. This means that any of these options would be considered highly cost-effective in the Irish healthcare setting and compare favourably with recent economic evaluations of other interventions that have been recommended and approved for reimbursement. These include evaluations of universal infant pneumococcal conjugate vaccination (€5,997/LYG) and universal infant hepatitis B vaccination (€37,018/LYG)<sup>(38,39)</sup>. Internationally, screening for colorectal cancer has been considered to be cost-effective, and occasionally cost-saving, in most of the settings in which it has been evaluated.

Of the three core screening options evaluated, while a screening programme based on biennial FIT at ages 55 to 74 years was found to be the most costly, it was also found to be the most effective option, that is to say it would provide the greatest health gain as measured in QALYs gained compared to a policy of no screening.

### 6.1.2 Cost-effectiveness of core screening options compared to each other

In comparing the three core screening options with one another the following results were found (Table 2):

**Table 2:** Cost-Effectiveness of Core Screening Options Compared to Each Other

Screening Option	ICER (€ / QALY)
Biennial gFOBT at ages 55 to 74 years vs. Biennial FIT at ages 55 to 74 years Once-off FSIG at age 60	Dominated*
Biennial FIT at ages 55 to 74 years vs. Once-off FSIG at age 60	€2,058

\* More costly and less effective than a combination of these two screening options. An ICER was therefore not calculated for gFOBT vs FIT or FSIG.

A screening programme based on biennial gFOBT was found to be the least favourable of the three options. In technical terms it is described as “dominated,” that is more expensive and less effective than a combination of the other two options.

The ICER associated with investing in FIT compared to FSIG was €2,058 / QALY gained, which would be considered to be highly cost-effective in the context of the Irish healthcare setting.

Therefore, based on the evidence that it would provide the greatest health gain (QALYs) compared to a policy of no screening, while remaining highly cost-effective compared to the other screening options evaluated (gFOBT and FSIG), a screening programme based on biennial FIT for those aged 55 to 74 years was found to be the optimal screening option.

### 6.1.3 Cost-effectiveness of the age-related variations of the core screening options

When age-related variations of the core screening scenarios were compared to no screening, the most cost-effective strategies were biennial FIT at ages 55 to 74 years, biennial FIT at ages 55 to 64 years, and once-off FSIG at age 60. All other options were found to be dominated by these three options. When the three options were compared to each other, biennial FIT at ages 55 to 74 years:

- Provided the greatest health gain of the three screening options
- Had an ICER of €3,221 per QALY gained compared to biennial FIT at ages 55 to 64 years, that is to say, it would be considered highly cost-effective compared with restricting implementation to ages 55 to 64 years.

#### 6.1.4 Robustness of the findings

Extensive sensitivity analysis was conducted to test the robustness of the findings and to identify circumstances that may alter the results. The results were sensitive to (that is to say, were changed by) a range of factors including the discount rate, cost of the screening tests, the cost of managing colorectal cancer, utility values (measure of patient preference or desirability for a specific health outcome), and, for gFOBT and FIT, the sensitivity of the test.

However, even when these parameters were set at their most extreme values, all three core options remained cost-effective; in some instances, they became cost-saving compared to no screening. The probabilistic sensitivity analysis confirmed the ranking of the three screening options in terms of their cost-effectiveness. It was noteworthy that if one of the newer, more sensitive guaiac-based tests were to be used, instead of one of the older, less sensitive tests, this could increase the cost-effectiveness of gFOBT compared to no screening.

#### 6.1.5 Health gains

Significant improvements in health outcomes were predicted for each option compared with no screening. Biennial FIT at ages 55 to 74 years was associated with the greatest health gain (QALYs gained) in the primary analysis. Other health gains evaluated in the secondary analysis are summarised in Table 3.

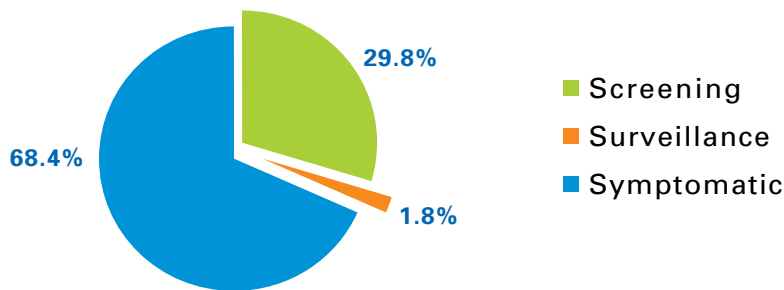
**Table 3:** Predicted Reduction in Incidence and Mortality from Colorectal Cancer with Core Screening Options Compared to No Screening

Screening Option	% Reduction in lifetime incidence rate	% Reduction in lifetime mortality rate
Biennial FIT at 55 to 74 years	14.7	36.0
Biennial gFOBT at 55 to 74 years (with reflex FIT testing)	1.0	11.8
FSIG once only at 60 years	4.9	7.5

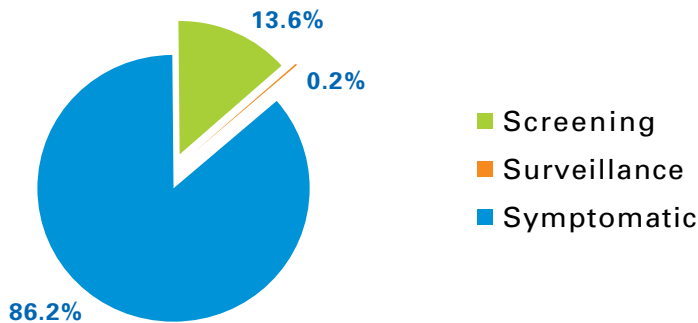
Of the three screening options, a programme based on biennial FIT at ages 55 to 74 years was associated with the largest predicted reduction in colorectal cancer incidence (-15%) and mortality rates (-36%). It was also associated with a much higher percentage of cancers detected by screening (30%) than either a programme based on biennial gFOBT (14%) or once-off FSIG (3%) (Figure 1). Screen-detected cancers are typically detected at an earlier stage than cancers detected symptomatically. For all three core screening options, over 70% of screen-detected cancers would be stage 1 or stage II.

**Figure 1:** Estimated Lifetime Percentage of Cancers Detected through Screening, Surveillance and Symptomatic Presentation for the Core Screening Options

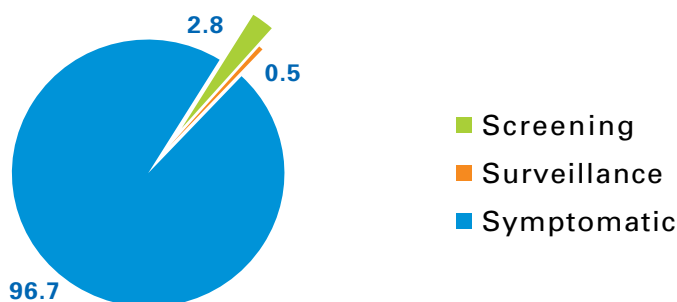
**Figure 1.1:** Biennial FIT at Ages 55 to 74 Years



**Figure 1.2:** Biennial gFOBT at Ages 55 to 74 Years



**Figure 1.3:** Once-off FSIG at Age 60



### 6.1.6 Summary of cost-effectiveness analysis

Of the three core screening options evaluated (FIT, gFOBT, FSIG), a screening programme based on biennial FIT for those aged 55 to 74 years would provide the greatest health gain (QALYs) compared to a policy of no screening while remaining cost-effective compared to the other screening options. Therefore, FIT was found to be the optimal screening option.

Consideration of the age-related variations in the core scenarios did not affect the key findings of the analysis. When the analysis was repeated with LYG as the outcome, the above results changed little. The findings remained cost-effective for all options in extensive sensitivity analysis to test the robustness of the findings.

## 6.2 Resource requirements and health outcomes

Implementation of a screening programme requires resources to (i) implement the screening programme in the first instance and (ii) to follow up individuals who test positive during screening. One of the key criteria for establishing a screening programme is that there should be sufficient facilities available for the diagnosis and treatment of individuals who have a positive screening test or disease detected through screening.

The resources evaluated in this HTA included those required for the diagnosis, treatment and follow-up surveillance of adenomas and cancers detected through the screening programme. A summary of the key screening related resource use and health outcomes is presented below. Overall, it was predicted that the resource requirements in the first ten years of screening would be greatest for a programme based on FIT compared to programmes based on gFOBT or FSIG. This would include significantly greater requirements for colonoscopies as well as the increased requirements to diagnose, treat and follow-up on the ensuing greater yield of screen-detected cancers and adenomas.

### 6.2.1 Participants in screening programme

Assuming a 53% uptake for a screening programme based on FIT or gFOBT, an estimated 189,640 test kits would be returned for processing in year one. Likewise, for a programme based on FSIG, assuming 39% uptake, an estimated 18,617 patients would present for screening in year one. These figures would increase by between 11% (FSIG) and 16 to 17% (FIT / gFOBT) by year ten of the screening programme being implemented due to projected increases in the population. (Table 4)

**Table 4:** Summary of estimated screening-related resource use and health outcomes (number) by year of programme

Screening scenario	gFOBT at 55 to 74 years		FIT at 55 to 74 years		Once-off FSIG at 60 years	
	Year 1	Year 10	Year 1	Year 10	Year 1	Year 10
<b>Participants</b>						
Invited to Screen	357,812	420,151	357,812	417,464	30,520	33,811
Screened <sup>1</sup>	189,640	222,637	189,640	220,999	18,617	20,625
<b>Endoscopy Requirements</b>						
FSIG <sup>2</sup>	0	0	0	0	18,617	20,625
Diagnostic colonoscopies <sup>3</sup>	967	1,103	11,095	12,414	381	423
Surveillance colonoscopies <sup>3</sup>	0	297	0	2,406	0	620
<b>Complications of Screening</b>						
Major bleeding following endoscopy	4	6	48	62	7	10
Perforation following endoscopy	2	2	21	27	1	2
Death following perforation	0	0	1	1	0	0
<b>Adenomas &amp; Cancers Detected</b>						
Screen-/ surveillance-detected adenomas	366	537	3,320	4,327	808	1,128
Screen- /surveillance-detected colorectal cancers	309	336	853	687	64	78
<b>Procedures Required</b>						
Colorectal resections	281	307	779	635	59	71

1 Assuming 53% uptake of FIT and gFOBT-based options and 39% uptake of FSIG

2 All individuals that attend for screening are screened using FSIG

3 Diagnostic colonoscopies would be delivered as part of the screening programme; surveillance colonoscopies would be delivered as part of the routine symptomatic services programme.

## 6.2.2 Impact on colonoscopy/CT colonography resources

The number of colonoscopies required for FIT-based screening was predicted to be ten times higher than that for screening based on gFOBT, due to the greater sensitivity of the immunochemical test. This would result in much larger numbers initially being referred for diagnostic investigation and subsequently entering surveillance for intermediate and high-risk adenomas.

For FIT in year one of the programme, resources would be required to perform over 11,000 additional diagnostic colonoscopies increasing to 12,414 colonoscopies by year ten. The diagnostic resources required for gFOBT would be one-tenth of those required for FIT. With once-off FSIG, the estimated number of diagnostic colonoscopies required ranged from 381 in year one to 423 in year ten. (Table 4) The estimated number of surveillance colonoscopies required was predicted to increase to 297, 2,406 and 620, for screening programmes based on gFOBT, FIT and once-off FSIG, respectively.

Requirements for CT colonography for the diagnostic investigation of those with a positive test would also be much greater for a screening programme based on biennial FIT (55 to 74 years) than screening based on gFOBT or FSIG. For FIT in year one of the programme, resources would be required to perform 1,442 CT colonographies; rising to 1,614 scans in year ten. The diagnostic resources required with gFOBT would be one-tenth of those required for FIT.

### **6.2.3 Impact on pathology/radiotherapy**

A screening policy based on biennial FIT in the 55 to 74 age group would result in the largest number of cancers detected and hence would have the greatest requirements for histopathology. This number would fall in time with repeated screening. In year one of the programme, capacity would be required nationally for histopathology of an additional 824 cancers. However, from year six onwards the predicted national pathology capacity for colorectal cancer would be lower with a screening programme than with the current policy of no screening. A similar pattern is predicted for other resources related to cancer diagnosis and treatment (although the impact on surgery is not predicted until year 9).

For example, in year one, increased capacity would be required to provide pre-operative radiotherapy for an additional 192 rectal cancers detected by screening, but by year ten the requirements for radiotherapy would be less than those predicted for a policy based on no screening.

### **6.2.4 Impact on surgery**

The requirement for colon and rectal resections would increase for all screening options, but would be highest for a screening programme based on FIT, as a function of the larger number of cancers detected by this screening option. (Table 4). However, by year 10, the predicted national requirement for colorectal surgery would be lower with a screening programme based on FIT than with a policy of no screening.

### **6.2.5 Overall impact on colorectal cancer resources (screening or symptomatic services)**

While a screening programme based on any of three core screening options would require an initial investment in new resources, after the first five years of a screening programme based on FIT there would be a potential to bring about reductions in overall requirements for pathology, pre-operative radiotherapy, colorectal resections, PET, MRI, CT scans and TUS (transrectal ultrasound) compared with a policy of no screening. For example, by year ten of a screening programme based on FIT, the overall requirement for surgery (patients presenting through screening or symptomatic services) would be lower than with the current policy of no screening (26 fewer colon resections and three fewer rectal resections). This effect was most notable with an FIT-based programme. It should be noted, however, that screening uptake rate was found to significantly impact on the resources required.

### **6.2.6 Health Outcomes**

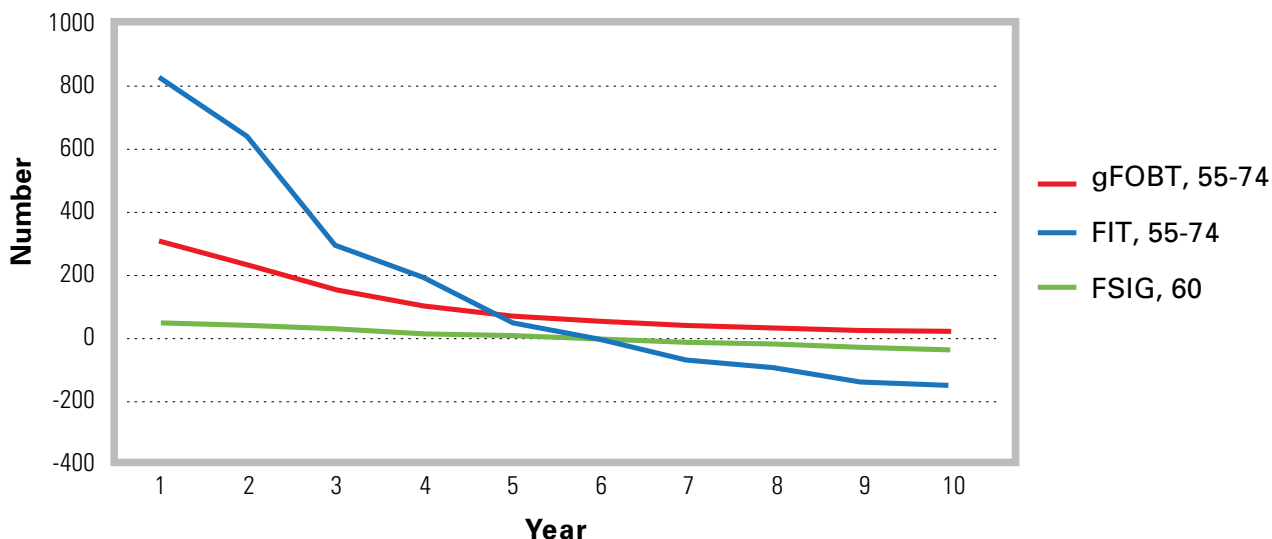
A consequence of the improved detection of cancers through a screening programme based on FIT is that over 30% of colorectal cancers diagnosed in Ireland would be expected to come from screening services rather than the symptomatic services, with in excess of 70% of these cancers diagnosed at stage I or II. However, as noted previously, colonoscopies are invasive procedures that are not without risk. While the risk to the individual patient would remain low, an important consequence of the increased number of colonoscopies associated with a screening programme based on FIT is that there would be a proportionate increase in the projected incidence of potential complications such as colonoscopy-associated major bleeding, bowel perforation and rarely, death. (Table 4) Based on international evidence from established screening programmes, the estimated risk for the individual patient would be low, nonetheless, these negative outcomes are an important consideration when evaluating population-based screening programmes.

Compared to a policy of no screening, screening based on biennial FIT in the 55-74 age group would be expected to bring about a greater reduction in the number of cases of colorectal cancers occurring and the numbers of deaths from colorectal cancer than the other two core options. The model predicted that, with an FIT-based programme, a reduction in the total number of colorectal cancers in Ireland would be expected from year six of the programme onwards, with approximately 160 cases averted in year ten. A reduction in mortality would be expected from year two onwards, with approximately 270 deaths from colorectal cancer avoided in year ten. (Figure 2) As noted previously, the potential to realise these benefits will depend greatly on the uptake of screening in the population.

**Figure 2:** Estimated difference in numbers of cases of, and deaths from, colorectal cancer in the population with screening versus a policy of no screening, over years 1-10, core screening scenarios

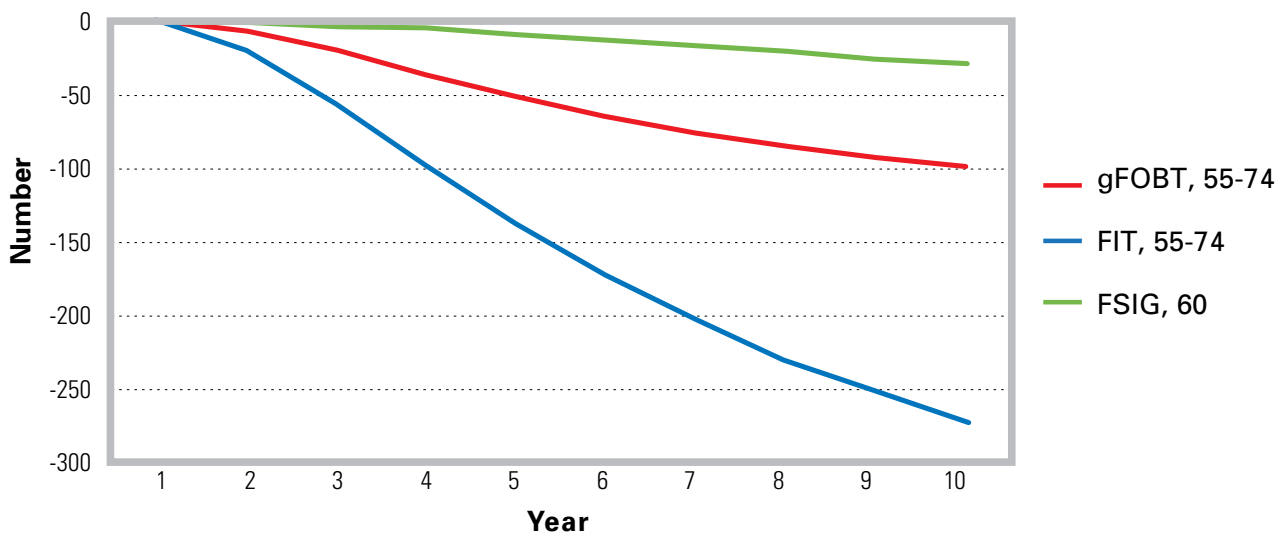
**(a) Colorectal cancer cases**

Difference between total colorectal cancers detected in the population with screening versus no screening, by year and scenario



**(b) Deaths from colorectal cancer**

Difference between total colorectal cancer deaths in the population with screening versus no screening, by year and scenario



### **6.3 Alternatives to an immediate and full implementation of a biennial FIT (ages 55 to 74 years) programme**

There are various options for reducing the initial resource requirements associated with implementing biennial FIT-based screening. Rather than screening the full age-group immediately in the first two years of the programme, different implementation options could be considered, such as restricting screening to those aged 55 to 64 years, or staggered implementation of screening across the 55 to 74 year age-group.

The advantage of the options based on staggered implementation is that they would allow for capacity to be built-up gradually over the initial years of the programme. The details of the staggered implementation (for example, the number of years it would take to encompass the entire 55 to 74 age group in the programme) could be designed to match the speed at which capacity could be made available.

In considering the different implementation options, a staggered implementation of screening in the 55 to 74 age group would be preferable to immediate implementation in the 55 to 64 age group. This is because the cost-effectiveness results indicate that, in future years, when a programme based on the 55 to 74 age group was fully operational, it would result in a greater overall health gain than a programme limited to the 55 to 64 age group.

A screening programme based on biennial gFOBT, with reflex FIT, in the 55 to 74 age group, or FSIG once at age 60, would also remain highly cost-effective compared to a policy of no screening. However, it should be borne in mind that neither of these programmes would achieve the same health gains as a programme based on FIT.

### **6.4 Limitations**

As with any HTA, the findings of this type of economic analysis are dependent on the quality of the data on which the model is based. There were important limitations in the evidence-base. The evidence relating to the performance characteristics of the screening and diagnostic tests was of particular concern.

In addition, there is a lack of robust Irish cost data. However, extensive sensitivity analysis has been conducted as part of the HTA and the key findings were not found to be altered.

### **6.5 Ethical Commentary**

The ethical commentary highlighted the importance of an effective and comprehensive informed consent process, appropriately trained personnel, and robust quality assurance procedures in relation to the handling and communication of risks associated with implementation of screening in asymptomatic individuals.

## 7 Conclusions

The following conclusions arise from this HTA:

- 1 Compared to a current policy of no screening, a population-based screening programme for colorectal cancer in Ireland based on biennial FIT or gFOBT in individuals aged 55 to 74 years old or once-off FSIG in individuals aged 60 years old would be highly cost-effective.
- 2 Of the three core screening options evaluated (FIT, gFOBT, FSIG), a screening programme based on biennial FIT for those aged 55 to 74 years would provide the greatest health gain (QALYs) compared to a policy of no screening. This strategy would also result in:
  - a. The highest estimated lifetime reduction in the incidence (14.7%) and mortality (36.0%) from colorectal cancer
  - b. The highest percentage of screen-detected cancers.
- 3 A screening programme based on FIT would cost most more than programmes based on gFOBT or FSIG, however, it would provide the greatest health gain (QALYs) compared to a policy of no screening, while remaining highly cost-effective relative to the other screening options, and was therefore determined to be the optimal screening option.
- 4 In the first ten years of programme implementation, a screening programme based on FIT at ages 55 to 74 would detect the highest number of adenomas and cancers. In addition, compared to a policy of no screening, it would result in more colorectal cancer cases and deaths averted in the population than either of the other screening options evaluated. These gains would be seen within this ten-year window. In the cases of deaths averted, the benefit would be seen by the second year of programme implementation.
- 5 All screening options would be associated with increased resource requirements in the first ten years of a programme, with FIT placing the greatest demand on resources due to the large number of colonoscopies and the additional resources required to diagnose, treat and provide follow-up for cancers and adenomas detected during screening and surveillance.
- 6 In considering alternative options to full and immediate implementation of biennial FIT (ages 55 to 74 years), staggered implementation of screening in the 55 to 74 year age group over several years would be cost-effective once fully implemented and would allow screening capacity to be built gradually in the system.
- 7 Notwithstanding the fact that a programme based on FIT would be the optimal strategy in terms of cost-effectiveness, a screening programme based on biennial gFOBT with reflex FIT in the 55 to 74 age group, or FSIG once at age 60, would also be considered highly cost-effective compared to a policy of no screening.
- 8 The Ethical Commentary highlighted the importance of an effective and comprehensive informed consent process, appropriately trained personnel, and robust quality assurance procedures in relation to the handling and communication of risks associated with implementation of screening in asymptomatic individuals.

# Advice to the Minister for Health and Children

The Health Act 2007 states that one of the functions of the Health Information and Quality Authority is 'to evaluate the clinical and cost-effectiveness of health technologies including drugs and provide advice arising out of the evaluation to the Minister and the Executive.'

The advice to the Minister for Health and Children on a population-based colorectal cancer screening programme is outlined below.

As economic models incorporate a number of assumptions and are dependent on the quality of data available, the results are subject to a degree of uncertainty. Bearing in mind the estimates and assumptions that were used in this analysis, the following conclusions can be drawn:

- 1 Each of the three screening options (biennial FIT (55 to 74 years), biennial gFOBT (55 to 74 years) or once-off FSIG at age 60) proposed by the Expert Advisory Group would be considered highly cost-effective compared to a policy of no screening in the Irish healthcare setting and would compare very favourably with recent economic evaluations of other interventions that have been recommended and approved for reimbursement. These include evaluations of universal infant pneumococcal conjugate vaccination (€5,997/LYG) and universal infant hepatitis B vaccination (€37,018/LYG).
- 2 Compared to no screening, the following ICERs were obtained for the core screening scenarios:
  - Biennial FIT (55 to 74 years): €1,696/QALY
  - Biennial gFOBT (55 to 74 years): €4,428/QALY
  - Once-off FSIG at age 60 years: €589/QALY.
- 3 Of the three core screening options evaluated (FIT, gFOBT, FSIG), a screening programme based on biennial FIT for those aged 55 to 74 years would provide the greatest health gain (QALYS or LYG) compared to a policy of no screening. This strategy would also result in:
  - The highest estimated lifetime reduction in the incidence (14.7%) and mortality (36.0%) from colorectal cancer;
  - The highest percentage of lifetime cases of screen or surveillance-detected cancers (31.6% of all cancers versus 13.8% for gFOBT and 3.3% for FSIG) and adenomas. Screen-detected cancers are more likely to be detected at an earlier stage (stage I or II) than those detected symptomatically and therefore would be associated with improved survival rates.

- 4 In comparing the three screening options with one another:
  - Biennial FIT at ages 55 to 74 years would be the most effective screening option providing the greatest health gain (QALYs and LYG gained).
  - Biennial FIT at ages 55 to 74 would be more costly than once-off FSIG at 60 years. However, at an ICER of €2,058 per additional QALY, investing in FIT compared to FSIG would be considered highly cost-effective in the Irish healthcare setting.
  - A screening programme based on biennial gFOBT was found to be the least favourable option in the cost-effectiveness analysis, as it would be more costly and less effective than a combination of the other two options.
- 5 In summary, the results of the cost-effectiveness analysis show that a screening programme based on FIT would cost most more than programmes based on gFOBT or FSIG, however, it would provide the greatest health gain (QALYs or LYG) compared to a policy of no screening, while remaining highly cost-effective relative to the other screening options, and is therefore recommended as the optimal screening option.
- 6 The resource analysis showed that the resource requirements in the first ten years of programme based on biennial FIT at ages 55 to 74 years would be greater than those required for the other screening options. This includes resources for the diagnosis, management and surveillance of screen-detected adenomas and cancers.
- 7 In the first ten years of programme implementation and compared to a policy of no screening, a screening programme based on FIT at ages 55 to 74 years would:
  - Detect the highest number of adenomas and cancers
  - Avert more colorectal cancer cases and deaths in the population than either of the other screening options evaluated. Approximately 160 cases of cancer and 270 deaths from colorectal cancer would be avoided in year ten of a screening programme based on FIT. In the case of deaths averted, the benefit would be seen by the second year of programme implementation
  - Have the highest endoscopy requirement with an additional 11,000 to 15,000 colonoscopies being required each year
  - Result in the highest number of individuals suffering adverse consequences of screening (for example, major bleeding, bowel perforation or rarely, death from perforation) as a consequence of the higher number of colonoscopies
  - Require the largest number of resources to manage and treat screen-detected adenomas and cancers (for example, histopathology, radiology, radiotherapy and surgery) due to the higher yield of adenomas and cancers detected.

- 8 These resource requirements for a programme based on FIT, are based on an assumed screening uptake rate of 53%. Should uptake be considerably higher or lower than this, then, the resources required, yield of screen-detected cancers and adenomas, health outcomes gained (cases and deaths of colorectal cancer averted) and number of screening-related adverse events suffered would vary accordingly. However, in the context of all the resources examined as part of this evaluation, only a screening programme based on FIT has the potential to reduce several of these cancer resource requirements from year six onwards compared to continuing a policy of no screening.
- 9 A number of options were evaluated that would reduce the initial resource requirements associated with implementing population-based screening and to allow capacity to build gradually in the system. Of the options considered, a programme based on staggered implementation of FIT for those in the 55 to 74 year age group was found to be the optimal strategy and preferable to limiting screening to a restricted age group (such as 55 to 64-year-olds), as once fully operational, this option would provide the greatest overall health gain. The details of the staggered implementation (how many years it would take to encompass the entire 55 to 74 year age group) could be designed to match the speed at which capacity could be made available in the system.
- 10 Notwithstanding the fact that a programme based on FIT would be the optimal strategy in terms of cost-effectiveness, a screening programme based on biennial gFOBT in the 55 to 74 age group, or FSIG once at age 60, would still be considered highly cost-effective compared to a policy of no screening.
- 11 No particular areas of concern were noted in the ethical commentary when colorectal cancer screening was compared to other population-based screening programmes. It was noted, however, that while the absolute risk of screening-related adverse events for the individual is low, the risk of death from perforation of the bowel under a policy of biennial FIT at ages 55 to 74 at a population level, emphasises the importance of informed consent, the availability of trained personnel to assist with the informed consent process and the requirement for appropriate quality assurance in the governance and running of a screening programme to mitigate some of the risks that may be associated with implementation of screening in asymptomatic individuals.

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