



Facultad de Ciencias Económicas y Empresariales

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ECONOMIC EVALUATION OF THE PROGRAM OF EARLY DETECTION OF  
COLORECTAL CANCER

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## **ABSTRACT**

Colorectal cancer is an important public health problem which fulfills the characteristics of the World Health Organization for population-based screening. The Health Provider System (Servicio Navarro de Salud) has started to implement this screening through a Fecal Occult Blood Test (FOBT). The overview of the literature concludes that this type of test is cost-effective under the threshold of 30,000 €/QALY for efficiency and so is the cost-utility analysis. In the case of Navarra, the economic analysis has also proved that the FOBT is cost-effective. This screening program also provides health benefits and a reduction in the incidence and mortality rate of colorectal cancer which has become increasingly important as the mortality rate has risen.

## **KEYWORDS**

Population-based screening; colorectal cancer; cost-utility; Quality Adjusted Life Years, QALY.

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## 1. INTRODUCTION

Nowadays, colorectal cancer (CRC) is one of the most important health problems in the developed countries due to its high incidence and mortality rates. In Spain, around 19,000 new cases are diagnosed annually, ranking first in incidence and second in cancer mortality (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012). In Navarra, colorectal cancer ranks third in incidence in men and second in women; and is the second leading cause of overall cancer deaths in men (130 died in 2010 after lung) and first in women (75 in 2010). The mortality ratio has caught up to the breast cancer in women, which incidence has fallen by the existence of the program of early detection of breast cancer.

The colorectal cancer screening is a population-based program which aims to reduce the incidence and mortality from colorectal cancer, because in recent years it has experienced an increase in incidence. This change can be explained due to the increase in life expectancy and changes in lifestyle (diet, sedentary lifestyle, obesity). Therefore, the program of early detection of colorectal cancer is focused on the reduction of incidence and mortality and, it has been proved in other countries that there is an improvement in the quality of life of the patients who have had an early diagnose. This program has been implemented in 19 member states of the European Union and in some autonomous communities inside Spain. This program is worldwide implemented. Canada, Australia, Japan or United States are examples besides these European countries.

A report published in 2008 about the recommendations of colorectal cancer screening in the European Union, concludes that 19 of the 28 member states already have implemented (or are implementing) screening programs for colorectal cancer. 12 of them are population-based (Cyprus, Finland, France, Hungary, Italy, Poland, Portugal, Romania, Slovenia, Spain, Sweden and the UK). 7 are programs that are not population based (Austria, Bulgaria, the Czech Republic, Germany, Greece, Latvia and the Slovak Republic) (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012).

According to the latest report of the Spanish Screening Network (Red de Programas Españoles de Cribado), 14 regions out of the 17 have realized in 2012 a colorectal cancer screening program. 9 are already developing CRC screening programs (Aragon, Valencia Community, Canarias, Cantabria, Catalonia, Castilla-Leon, Murcia, the Basque Country and La Rioja). Catalonia was the first to initiate this activity in 2000 (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012).

Nowadays, if colorectal cancer is diagnosed on time, the disease can be healed in 90% of the cases. However, the percentage drops below 50% if detected at advanced stages (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012).

In Navarra, the colorectal cancer screening is population-based. The target people are women and men between 50-69 years old (population at average risk of developing the disease, around 160,000 inhabitants in Navarra). This implies that the target is the 24% of the population of Navarra (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012).

Screening for colorectal cancer has been proved in the literature to be cost-effective (Telford MD, et al., 2010; Lansdorp-Vogelaar, et al., 2010; Heitman, et al., 2010; Tran, et al., 2010; Jeong, et al., 2013). So, the key point for the Health Service Provider is the coordination with other health or non-health groups that can collaborate in promoting the participation of the screening (pharmacies, municipalities, mutual aid groups, neighborhood associations, associations...), leading to a higher percentage of the participation of the population targeted.

Along this report, an analysis of costs and effectiveness of the program in Navarra is presented. The program consists of a screening test for Fecal Occult Blood offered to all population between 50 and 69 years.

Implementing this screening increases the welfare of the people being tested because if the disease is detected early, it can dramatically change the course of the illness. And the cure rate can also increase. Moreover, an appealing fact to do this screening is that a colonoscopy (a further test of the screening) can detect polyps. These precursor lesions can be removed and can prevent the cancer cycle from beginning in the first place.

## **2. COLORECTAL CANCER**

### **2.1. Colorectal cancer: definition and types**

As the American Cancer Society defines, the colorectal cancer is a cancer that begins in either the colon or the rectum (Colorectal Cancer, 2014).

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new and abnormal cells. Cancer cells can also invade other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell to become cancerous.

#### *2.1.1. Abnormal growths in the colon or rectum*

Most colorectal cancers start as a polyp which is a growth that begins in the inner lining of the colon or rectum. Most polyps are not cancerous. Only certain types of polyps such as adenomas can become cancerous. Taking out a polyp early, may prevent the cancer to appear by not allowing the polyp to become cancerous.

Over 95% of colon and rectal cancers are adenocarcinomas. These types of cancers start in gland cells, like the cells that line the inside of the colon and rectum. There are other types of tumors in the colon and rectum (carcinoid tumors, gastrointestinal stromal tumors-GISTs, lymphomas and sarcomas) (Colorectal Cancer, 2014).

### **2.2. Etiology of colorectal cancer**

In the medical literature is found that some risk factors might increase the probabilities of getting polyps or colorectal cancer. Some of them can be changed; others cannot (Colorectal Cancer, 2014).

#### *2.2.1. Risk factors that cannot be changed*

- Age: the risk increases when a person is over 50 years. 90% of the patients diagnosed are above 50 years old.
- Having had colorectal cancer or certain kinds of polyps before.
- Having a history of ulcerative colitis or Crohn's disease.
- Family history of colorectal cancer.

- Type 2 diabetes.
- Certain family syndromes, like adenomatous polyposis (FAP) or hereditary non-polyposis colon cancer (HNPCC, also called Lynch syndrome).

### *2.2.2. Risk factors that can be changed*

Some lifestyle-related factors have been linked to a higher risk of having colorectal cancer:

- Certain types of diets: a diet that is high in red meats (beef, lamb, or liver) and processed meats (like hot dogs, bologna, and lunch meat). Cooking meats at very high heat (frying, broiling, or grilling) can create chemicals that might increase cancer risk.
- Lack of exercise.
- Being extremely overweight.
- Smoking.
- Heavy alcohol consumption.

## **2.3. Prevention of colorectal cancer**

### *2.3.1. Screening tests*

Screening is the process of searching for cancer in people who are asymptomatic. Some polyps, or cell growth, can be found and removed before they have the chance to turn into cancer. Screening can also help find colorectal cancer early, when it is small and more likely to be cured.

### *2.3.2. Diet and exercise*

Most studies agree that being overweight or obese increases the risk of colorectal cancer in both men and women. Having more belly fat which implies a larger waistline, has also been linked to colorectal cancer (Colorectal Cancer, 2014).

In general, diets that are high in vegetables, fruits, and whole grains (and low in red and processed meats) have been linked with lower colorectal cancer risk, although it is not exactly clear which factors are main leading cause of colorectal cancer.



## 2.4. Finding early colorectal polyps and cancer

### 2.4.1. Colorectal cancer screening tests

Screening tests are used to look for a disease in people who do not have symptoms. In many cases, these tests can find colorectal cancers at an early stage and improve treatment outcomes. Screening tests can also help preventing some cancers by allowing doctors to find and remove polyps that may become cancerous. These tests can be divided into two broad groups:

Test that can find both colorectal polyps and cancer: These tests look at the structure of the colon itself to find any abnormal areas. This is done either when a scope is put into the rectum or with special imaging (x-ray) tests. The period between tests are suggested by the American Cancer Society:

- **Flexible sigmoidoscopy** (every 5 years): A flexible, lighted tube is inserted into the rectum and lower colon to check for polyps and cancer.
- **Colonoscopy** (every 5 years): A longer, flexible tube is used to look at the entire colon and rectum.
- **Double-contrast barium enema** (every 5 years): This is an x-ray test of the colon and rectum.
- **CT colonography - virtual colonoscopy** (every 5 years): This is a type of CT scan of the colon and rectum.

Tests that mainly find cancer: These tests examine the stools for signs of colorectal cancer. These tests are less invasive and easier to be done than the first type of tests mentioned. However, they are less likely to detect polyps.

- **Stool DNA test (sDNA)**. These tests analyze the stools sample in order to look for abnormal sections on DNA from cancer of polyp cells.
- **Fecal Occult Blood Test (FOBT) and Fecal Immunochemical Test (FIT)**, both preferably be made yearly, are samples of stools which are later analyzed for blood, which may be a sign of a polyp or cancer. Fecal Occult Blood Test is being implemented by the Health Service of Navarra. Specifically, the one with quantitative immunological with a cut-off point of 100ng/ml. A single sample is collected without dietary restriction.

### **3. ECONOMIC EVALUATION IN HEALTH SERVICES**

#### **3.1. Introduction**

Economic studies establish the most efficient ways to allocate the limited resources a society has so the output can be maximized. If the concerning output is health, its inputs (factors that are involved in the production of health) must be allocated in the right combination so the Pareto optimum can be reached. The inputs that are taken into account are, for example, health professionals, time, equipment, buildings, knowledge... Politicians or administrative personnel of the health system are the ones who should decide on the allocation of these resources. In order to carry out the decision-making, economic evaluations are shown as a useful tool because they provide information about the costs and benefits a services or a program has. But they will not be the only factor to base the decision on, because equity is another factor that should be considered. As Lansdorp-Vogelaar et al. (2010) say: “Cost-effectiveness analysis, a form of decision analysis, is an analytic tool that formally compares the health and economic consequences of different interventions, thereby assisting decision makers to identify the interventions that will yield the greatest health benefits, given their resource constraints.”

The economic evaluation of health technologies is to measure the efficiency of different alternatives; for instance, implementing a screening program, a surgical instrument or the authorization of a new drug. The economic evaluation is comparing the value of the resources consumed by an activity or program versus the value of the results provided by that activity or program. These studies give the information that the prices provide in a competitive economy. They give information in order to allocate efficiently the resources in areas such as the public health care system, where there is no market (or it is influenced by the government: subsidies, prioritization between health care technologies...). As previously mentioned, economic evaluations exist to help to make a decision between several options, considering other criteria such as equity and political and social sensitivity.

#### **3.2. Principles of economic evaluation of health technologies**

The aim of an economic evaluation is to measure the outcomes of a technology or a program in order to compare the value of the resources consumed in the process and the corresponding results. By applying this principle, some tools are available:

- **Cost-benefit analysis (CBA):** compares the incremental cost of a program with its incremental benefits in monetary bases.
- **Cost-effectiveness analysis (CEA):** is characterized by the use of "natural" outcomes, that is, define the outcome depending on the immediate goal of health spending. These outcomes can be detected cases, cases of illness avoided, lives saved or life-years gained.
- **Cost-utility analysis (CUA):** is the most widely used in health economics and where results are measured in homogeneous units. This analysis is considered as a specific case of CEA, which has as main feature the measuring health outcomes in quality-adjusted life year (QALYs).

### Cost-effectiveness analysis

Cost-effectiveness analysis provides a tool to calculate and summarizes benefits, costs and harms of a service or a program. That is the reason why this type of analysis can inform the decision makers. A mathematical model is used to analyze benefits and costs.

In order to do a cost-effectiveness analysis, the ICER ratio is commonly used. It is a ratio whose numerator is the cost difference of implementing the program which is being tested or not implementing a program at all ( $C_0$  and  $C_1$ , respectively), and the denominator is the difference between the effectiveness of having or not a program ( $E_0$  and  $E_1$ , respectively). This ratio is called Incremental Cost Effectiveness Ratio (ICER):

$$ICER = \frac{C1 - C0}{E1 - E0}$$

As Lansdorp-Vogelaar et al. (2010) say: “The (quality-adjusted) life-years gained with a particular strategy (compared with an alternative) are included in the denominator, and the additional costs of that strategy (compared with the same alternative) are included in the numerator, yielding an incremental cost per (quality adjusted) life-year gained.”

In order to maximize the welfare of the health system, a program that provides a lower ICER, would be the one whose cost per unit of output compared to the option of not implementing the program are lower. Such analysis can guide policy makers in the distribution of funding between different programs in order to achieve a higher level of health for the society given the limited resources. The program with lower ICER would be

the one providing the greatest health benefits. Policy makers while making a decision will also take into account factors such as equity.

The Incremental Cost-Effectiveness Ratio can compare a program with the alternative of not implementing it or with the most efficient technique which has been found so far. A program is said to be dominated when its costs are higher and/or its effectiveness is lower in comparison to a program whose costs are lower and/or its effectiveness is higher. A program is defined as weakly dominated if the opposite situation occurs. Figure 1 helps define if a program is dominated by others.

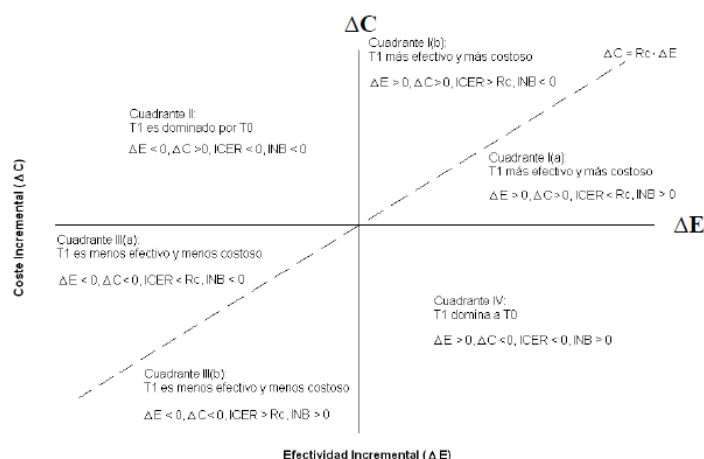


Figure 1. Cost-effectiveness plane. (Source: Drummond; M.F., 2001)

### Health care costs. The economic management and clinical management: analytical accounting for health care organizations

The health care institutions are supposed to achieve an appropriate match between the resources they use, between the costs and the services they provide. They should try to be efficient in their allocation of resources, because by not doing so, it would mean sacrificing resources that could be used in alternative activities.

The financial information these organizations have, can be used to be presented for external agents or for internal management. For managers this information is insufficient, they need to know the economic and financial aspects of the transformation of resource while providing a service. This is what is called analytical, internal management or accounting. The techniques used in accounting general ledger intended to decompose into useful components for making decisions to answer the questions of where and by whom, for what and when.

Analytic accounting provides different techniques depending on the cost objectives settle by a department and also propose different cost systems. There are several types of analytical accounting. Full cost systems are based on the distinction between direct and indirect costs; controllable systems distinguishing between controllable and uncontrollable costs; variable costs systems distinguishing variables with fixed costs and, finally, relevant costs systems against irrelevant costs.

Probably the most widespread system in health care organizations are the systems whose aim is to find the full costs of the total monetary value of resources used to provide a service, including both direct and indirect costs.

Controllable costs systems exist to evaluate the costs over which the personal studied have influence in, against those who are out of their control.

### **3.3. Quality Adjusted of Life Years (QALYs)**

The QALYs are a measure of the outcome of preferences for health states. There are tests which establish the utility the individuals have throughout their lives. The result of these changes in the health profiles is a measure of the effectiveness of the health interventions for these individuals. The QALYs is a health measure combining basic components defining health, that is, the quantity and quality of life. The QALYs are calculated by multiplying the life expectancy by a weight that reflects quality. The concept which lies behind the QALY is that years of life should not be calculated without weighting the health benefits, but must be adjusted or weighted by the quality of those years the patient is alive due to the program.

The QALYs are a measure of the state of health provided by the quality of life of the difference of having a program against the possibility of not having it. This measure is ranged from 0 to 1, where 1 represents perfect health and 0 corresponds to a state of health corresponding to death. There is a possibility in which this measure can take negative values, implying a stage where the patient is worse than being death.

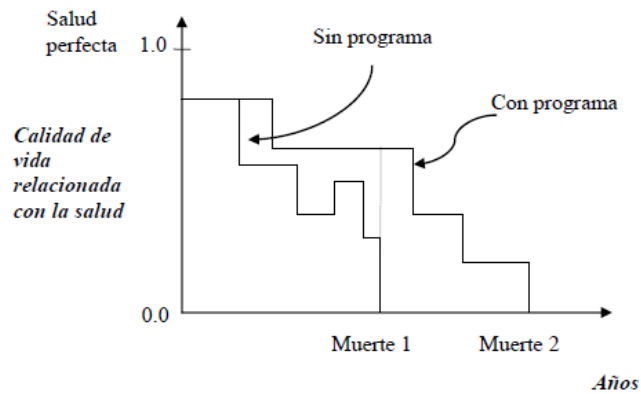


Figure 2. QALYs gained with the intervention of the program. (Source: Drummond; M.F., 2001)

In Figure 2 can be observed two programs corresponding to variations in health of an individual due to a health program (the existence of a program versus the non-existence of it). The area between the two programs is the health gain produced due to the program.

There are several instruments for measuring quality of life associated with health that serve developing the QALY, such as the EQ-5D. The EQ-5D is an instrument that has been developed by the EuroQol group. This group was founded in 1987 and was the first to make a test of the feasibility of a standardized instrument to describe and value health on quality of life, without referring the test to any specific disease. The existence of standardized tools holds a great importance because these standardized instruments are the ones which allow comparing the cost-utility of different programs.

## 4. PROGRAM FOR EARLY DETECTION OF COLORECTAL CANCER IN NAVARRA

### 4.1. Situation of colorectal cancer in Navarra

#### 4.1.1. Incidence rate

According to the Cancer Record of Navarra (Registro de Cancer de Navarra) (2003-2007), the colorectal cancer is the third most common tumor in men (15.1% of total cancers), behind lung and prostate; and the second in females (14.46% of all cancers), behind breast cancer. If both genders are considered, the colorectal cancer is the most common. These rates cannot be generalized to the whole Spanish population because each autonomous community has different incidence rates.

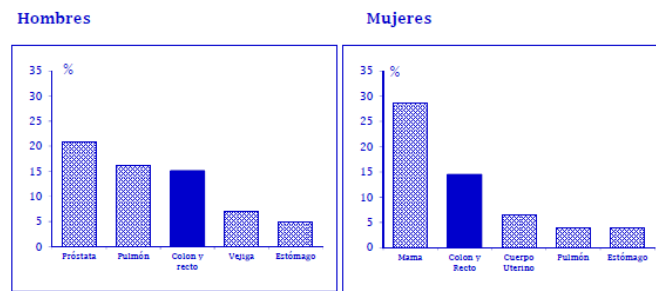


Figure 3. Incidence rate of cancers in men and women in Navarra.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

According to the latest data of the Cancer Record of Navarra (2003-2007), the tumor is more likely to appear at 50 years, increasing with the age. The incidence is very low when a person is below the 50 years.

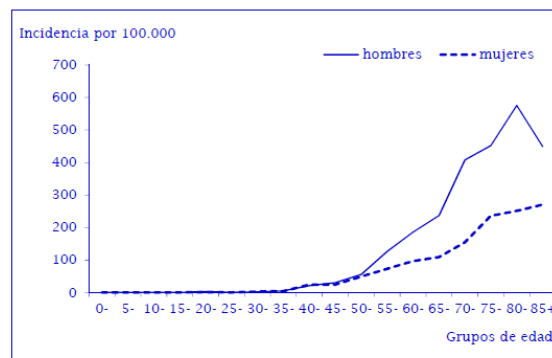


Figure 4. Incidence of colorectal cancer in men and women in Navarra through the life time.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

CRC incidence shows an increasing trend since 1973, for both men and women, with a greater increase among men.

#### 4.1.2. Survival rate

According to data from EUROCORE 46 study, the five-year relative survival of patients diagnosed with colorectal cancer in Europe, during the period 1995-1999 was 54%.

According to the same source, the survival rate of colorectal cancer during the same period in Spain was 53,65%.

#### 4.1.3. Mortality rate

Colorectal cancer is the second tumor that causes more cancer deaths for men in Navarra, behind lung cancer. For women in Navarra, colorectal cancer is the first cancer that causes more deaths, being the second breast cancer and third lung cancer.

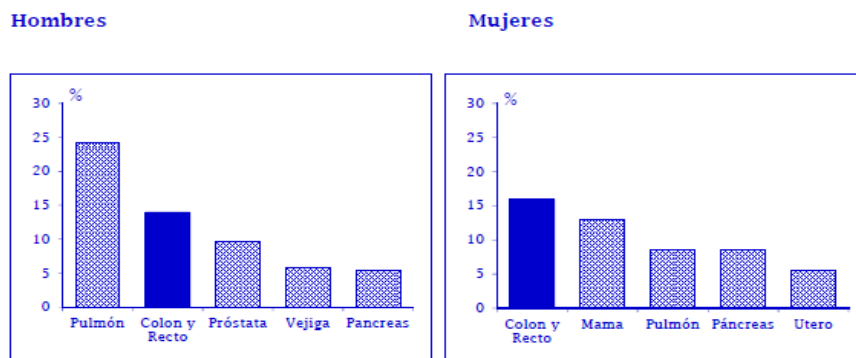


Figure 5. Mortality rate of cancers in men and women in Navarra.  
(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)



## 4.2. Early detection program

### 4.2.1. Justification

Screening for early detection of colorectal cancer has proved to be effective through all the literature. These articles also state that this screening program also reduce the mortality rate significantly.

The benefit of a screening test is obtained by applying an early treatment for malignant lesions detected in early stages. If a screening is performed, there is a likelihood of decreasing the colorectal cancer incidence because benign polyps can be detected (before they become cancerous) and can be removed, so the appearance of illness is prevented.

### 4.2.2. Objectives

#### Main objective

- Reduce the incidence of colorectal cancer.
- Reduce mortality from colorectal cancer.
- Improve the quality of life of patients who are diagnosed colorectal cancer.

#### Secondary objectives

- Achieve at least 60% of participation (willingness to participate in the program) of the people who are invited to the program for the first time and 80% of adherence (willingness to remain in the program once the screening test has been delivered to the patient's home).
- Ensure a track and continuity of care for all participants, ensuring proper coordination between different services and levels of care involved, in order to achieve an early diagnosis and as early treatment as possible.
- Establish a plan that would ensure an optimal quality level and adequate quality in the performance of the test screening and diagnostic confirmation phase and treatment.

### 4.2.3. Basis of the program

#### Target population

The target of the program for the early detection of colorectal cancer are asymptomatic men and women living in Navarra, between 50 and 69 years with an average risk of developing the disease. People with family risk factors and/ or factors determining high risk are not a target; they will be included in specific programs.

According to the 2012 Census, 165,934 people reside in Navarra aged between 50 and 69 years, almost half men and half women.

124,017 people in the target age (75%) live in the health area of Pamplona, 24,237 (14%) in the health area of Tudela and 17,680 (11%) in the health area of Estella.

#### Screening test

As a screening test, a Fecal Occult Blood Test (FOBT) will be used. It is a quantitative immunological test with a cut-off point of 100 ng/ml. A single sample is collected without dietary restriction.

As the American Cancer Society describes, “The Fecal Occult Blood Test (FOBT) is used to find occult blood (blood that can't be seen with the naked eye) in feces. The idea behind this test is that blood vessels at the surface of larger colorectal polyps or cancers are often fragile and easily damaged by the passage of feces. The damaged vessels usually release a small amount of blood into the feces, but only rarely is there enough bleeding for blood to be visible in the stool.

The FOBT detects blood in the stool through a chemical reaction. This test cannot tell whether the blood is from the colon or from other parts of the digestive tract (such as the stomach). If this test is positive, a colonoscopy is needed to find the cause of bleeding. Although cancers and polyps can cause blood in the stool, other causes of bleeding may

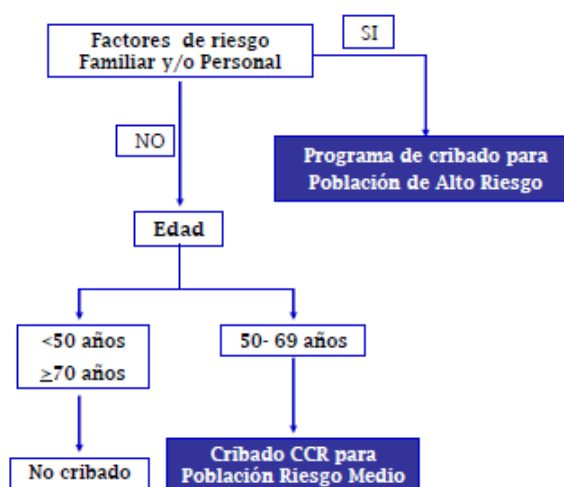


Figure 6. Target population of the screening program in Navarra.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

occur, such as ulcers, hemorrhoids, diverticulosis (tiny pouches that form at weak spots in the colon wall), or inflammatory bowel disease (colitis).” The significant gastrointestinal diseases leading to cancer are, for example, ulcerative colitis, Crohn's disease or polyposis.

#### Range of exploration

The interval between tests is set to 2 years. Depending on the detected pathology, protocols for specific trace will be established.

#### *4.2.4. Operating plan*

##### Identification of the target population

Given the nature of the program (population-based), the primary source of data used to identify the target population will be the last update of the census of Navarra.

As stated, the women and men whose residence is Navarra and are aged between 50 and 69 years.

Navarra resident population born between 1 January 1944 and 31 December 1964 will be considered for the first round of the program, November 2013 and July 2015. Those born in the years 1965 and 1966 will be included in the second round. Although in this second round the people who were born in 1944 and 1995 should leave the program because they overcome the target age. For the third round, people who reach the target age will be included and those who have overcome the target age will leave the program (Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012).

##### Identification of the eligible population

All individuals who meet the following conditions should be excluded:

- Personal history of colorectal cancer.
- Personal history of adenomas, in which specific tracks have been performed.
- History of colon pathology susceptible of being monitored with colonoscopy (ulcerative colitis, Crohn's disease, attenuated familial adenomatous polyposis...) and family-related hereditary syndromes for colorectal cancer.
- Family history of colorectal cancer with high-risk criteria:

- 2 or more relatives with first degree of relation (parents, children, siblings...)
- 1 family member of first degree-relation with lower age at diagnosis of 60.
- People who have had a colonoscopy in the last 5 years, regardless of the reason why it was performed (permanent or temporary exclusion depending on the subject if known).
- Those exhibiting symptoms suggestive of a severe coagulopathies disease that prevent the realization of a colonoscopy, or carry a total colectomy.
- Patients in palliative care programs.
- Terminal illness and serious illness or disability that contraindicates further study of the colon.

Overall planning and programming

The planning is implemented in the three health areas in Navarra: Tudela, Pamplona and Estella.

Full coverage of the target population will take place in 4 years in a 2 rounds program.

During the first round between November 2013 and July 2014, half the population is invited from each of the health areas. The second invitation for the people of the first round and the first invitation for rest are held during the second round, September 2015 to July 2017. This means, that by July 2017, all people living in Navarra identified as the population target will be invited at least once.

The health areas to be included for the rounds are:

**Tudela's health area:**

Vuelta 1	Vuelta 2
Corella Tudela Este Tudela Oeste	Buñuel Cascante Cintruénigo Valtierra-Cadreita

*Figure 7. Rounds in Tudela's health area for the screening program in Navarra.  
(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)*

In Tudela's area, 12,005 people are included.

### Pamplona's health area:

Vuelta 1	Vuelta 2
Auritz/Burguete	Altsasu/Alsasua
Azpilagaña	Ansoáin
Buztintxuri	Aoiz
C. Viejo-I Etsanhe	Artajona
Chantrea	Barañáin
Echavacoiz	Berriozar
Ermitagaña	Burlada
Huarte	Carcastillo
II Etsanhe	Doneztebe/Santesteban
Isaba	Elizondo
Iturrama	Etxarri-Aranatz
Mendillorri	Irurtzun
Milagrosa	Leitza
Rochapea	Lesaka
San Jorge	Noáin
San Juan	Olite
Sarriguren	Orcoyen
Villava	Peralta
	Puente la Reina
	Sangüesa
	Tafalla
	Ultzama
	Valle de Salazar
	Zizur

Figure 8. Rounds in Pamplona's health area for the screening program in Navarra.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

The target population Pamplona area has is 65,658 people.

### Estella's health area:

Vuelta 1	Vuelta 2
Estella	Allo
San Adrián	Ancín-Améscoa
	Lodosa
	Los Arcos
	Viana
	Villatuerta

Figure 9. Rounds in Estella's health area for the screening program in Navarra.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

In the area of Estella, 8,479 people will be invited to be part of the program.

### Population awareness

In population-based screening programs, the outcome of reducing the incidence and mortality of the disease is usually achieved in a period of ten years.

But to achieve this aim of the program, the response of the target population is essential. It is necessary to achieve at least a 60% of participation. Due to this reason, a sensitivity

campaign needs to be implemented. The objective is not only the target population (50-69 years old), but also to health professionals and the population as a whole.

In addition to the personalized information the eligible population will receive, there are scheduled specific information and awareness actions for the health personnel involved (primary and specialized care professionals: digestive, anesthesia, pathology, surgery, radiology, oncology...).

The Institute of Public Health and Labor is also requesting the assistance of more than 10,000 companies and entities that can encourage the participation (pharmacies, municipalities, self-help groups, associations, clubs...).

Moreover, a communication campaign with the slogan "Choose 90. A simple test can save your life" is being conducted referring to the 90% of colorectal tumors which are curable if they are detected on time. The campaign includes print ads, radio, brochures, and posters in buses shelters and in buses. There is also a web-page available, [www.cancercolon.navarra.es](http://www.cancercolon.navarra.es), with relevant information about the program and the access to the campaign.

All this measures are expected to increase the awareness of this type of cancer and the participation rate which will lead to a greater health benefit and cost-effectiveness of the screening program.

#### Detection and confirmation process

The participation in the program is developed as follows:

- **Invitation.** When the program starts in a health area, the target population belonging to that area receives a personalized invitation letter which is sent to their homes. In it, it is explained the campaign content. It includes the option to send the card to the issuer expressing the willingness to participate in the program.
- **Confirm participation.** To participate in the program, the patient can send the card by post to the address of the issuer. But the card can also be given to the health center in which the patient is enrolled, by calling to the following number: 848 42 34 98 or by sending an email to the address [precolon@navarra.es](mailto:precolon@navarra.es).

- **Reception of the Kit.** Days after showing the desire to participate, the person will receive at home a kit for sample collection and data tagged with the participant name and a letter with instructions explaining how to perform the process of sampling and where to deliver it.



Figure 10. Instructions for the sample collection.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

- **Sample delivery.** Once the test is done, the kit with the sample must be delivered to the health center. It should be deposited in a specific container identified with the program logo.
- **Reporting of results.** Once the samples are analyzed, negative results will be communicated by letter and positive results (if blood is detected in the stools) will be communicated personally and the patient will be referred to his/her health center to carry out a clinical evaluation and diagnostic confirmation.

It is estimated that the test will be positive in about 70 of every 1,000 people, but only 3 will be confirmed with colorectal cancer. In 1 out of 3 positive FOBT, the presence of blood will be due to the existence of benign polyps which should also be treated to avoid the future appearance of cancer.

To find the source of bleeding a colonoscopy will be performed. This is a scan inside the intestine that is performed with sedation to prevent it from being painful. It will help visualize, detect and remove the lesions that have caused the bleeding. Thus, there are more benefits than being able to apply an early treatment for cancerous tumor through the test. This screening program also removes precursor lesions and, consequently, avoids the appearance of the disease.

## 5. COST-EFFECTIVENESS ANALYSIS OF COLORECTAL CANCER SCREENING

In the past decades, a vast amount of articles have been published about the effectiveness of the screening for colorectal cancer. Several strategies have been tested; they have been compared using Quality Adjusted Life Years (QALYs) or Life Years Saved (LYS). Sensitivity analyses have also been implemented and the databases used to compare the different screenings are known globally.

The first article analyzed is “The cost-effectiveness of screening for colorectal cancer” which was published in CMAJ in 2010 (Telford, Levy, Sambrook, Zou, Enns).

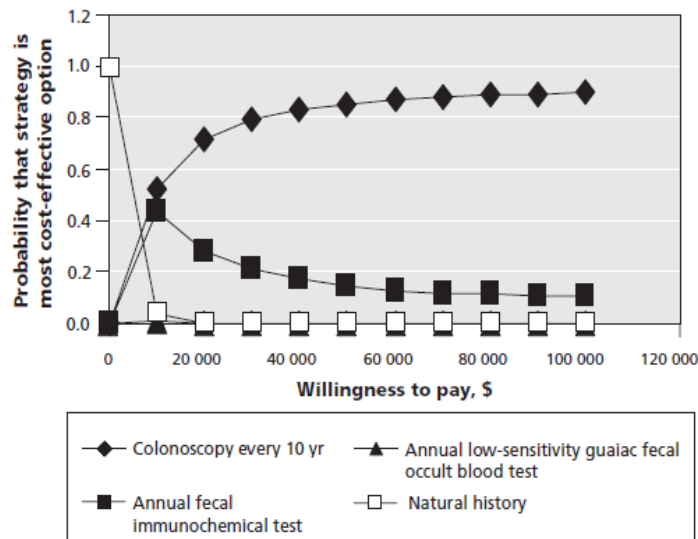
This article is an evaluation about the screening for colorectal cancer which has been proved to be cost-effective. 10 strategies have been tested for colorectal cancer screening, including no screening. In this research, incremental cost-effectiveness has been estimated, as well as quality of life and costs of each strategy.

In order to estimate the costs, the perspective of a third-party has been established. This means that the cost of the patients and the cost of those who take care of them are not taken into account. In order to calculate the QALYs (Quality-Adjusted Life Years), the strategies have been compared with the no screening alternative. The model method used is the Markov model.

This research was done to test the cost-effectiveness of screening for colorectal cancer. Even though 10 strategies are being considered, this evaluation paper has focused on those which are being implemented in the population (average-risk Canadians) screening programs in the Canadian provinces (colonoscopy – every 10 years, annual fecal immunochemical test, annual low-sensitivity guaiac fecal occult blood test). The incidence rate has been reduced by 81%, 65% and 44%, respectively, comparing with no screening; and the mortality rate has been reduced by 83%, 74% and 55%. The QALYs per each program are \$6133, \$611 and \$9159. After applying a probabilistic sensitivity analysis the data has been found to be robust (Telford MD, et al., 2010).

Screening for colorectal cancer is cost-effective taking into account the established threshold of willingness to pay 30,000 €/QALY (Sacristan, et al., 2002). Annual fecal immunochemical test and colonoscopy every 10 years offer the best value for the money in Canada.





**Figure 3:** Cost-effectiveness acceptability curve. The gain in quality-adjusted life years estimated with each strategy was adjusted for the cost and a hypothetical payer's willingness to pay. The probability that a strategy is cost-effective (y axis) relative to alternative strategies is shown for a range of willingness to pay, up to \$100 000 per quality-adjusted life-year gained (x axis).

Figure 11. Cost-effectiveness acceptability curve. (Source: Telford MD, et al., 2010)

**Table 3:** Cost and effectiveness of three strategies for screening for colorectal cancer over the lifetime of 100 000 individuals who commence screening at age 50 years, relative to not screening

Strategy	Cost, 2007 Can\$	Quality-adjusted life-years gained	Deaths prevented	Decrease in mortality rate, %	Cases of cancer prevented	Decrease in incidence, %
Low-sensitivity guaiac fecal occult blood test, performed annually	63 139 823	6 914	2113	55	2748	44
Fecal immunochemical test, performed annually	65 429 821	10 491	2834	74	4081	65
Colonoscopy, performed every 10 years	76 094 757	12 013	3157	83	5082	81

Table 1. Cost and effectiveness of three strategies for screening for colorectal cancer.

(Source: Telford MD, et al., 2010)

The second article analyzed is “Cost-effectiveness of colorectal cancer screening” which was published in Epidemiologic Reviews in 2011 (Lansdorp-Vogelaar, Knudsen, and Brenner).

This article shows that numerous colorectal cancer screenings have proved to be effective in decreasing colorectal cancer mortality. The timeline of the databases searched were between January 1993 and December 2009. After an extensive search in the literature, the

conclusions of this article are that all the screening strategies are cost-effective and some of them even cost-saving comparing with no screening.

Nevertheless, the articles differ in which is the most effective one or which one has the best incremental cost-effectiveness ratio given the willingness to pay per life-year gained. There was consensus about computed tomographic colonography, capsule endoscopy and stool DNA testing are not yet cost-effective in comparison with the established screening options.

**Table 1.** Discounted Life-years Gained, Costs, and Costs per Life-year Gained of Established Screening Strategies for Colorectal Cancer Compared With no Screening

Study: First Author, Year (Reference No.) <sup>a</sup>	Annual gFOBT			Biennial gFOBT			Flexible Sigmoidoscopy Every 5 Years			Flexible Sigmoidoscopy Every 5 Years + Annual gFOBT			Colonoscopy Every 10 Years		
	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG
Flanagan, 2003 (34)	0.025	328	13,100	0.016	185	11,600									
Frazier, 2000 (35)	0.042	825	19,600				0.039	751	19,500	0.059	1,523	26,000	0.048	1,514	31,700
Gyrd-Hansen, 1998 (28)	0.006	36	6,400	0.004	20	5,300									
Hassan, 2007 (44)													0.036	-10	CS
Helm, 2000 (36)				0.014	72	4,000									
Khandker, 2000 (37)	0.100	2,519	25,600				0.090	1,904	22,500	0.110	3,553	32,400	0.110	3,487	31,500
Lejeune, 2004 (38)				0.029	126	4,400									
Leshno, 2003 (39)	0.160	-158	CS							0.182	-324	CS	0.180	-26	CS
Macafee, 2008 (45)				0.009	30	3,400									
O'Leary, 2004 (40)													0.021	2,883	9,800
Pickhardt, 2007 (19)													0.046	495	10,700
Shimbo, 1994 (32)	0.013	750	56,300												
Song, 2004 (20)	0.056	508	9,100				0.048	940	19,600	0.063	1,347	21,500	0.062	1,330	21,500
Sonnenberg, 2000 (41)	0.019	285	15,100				0.036	2,059	56,600				0.080	1,355	17,000
Steele, 2004 (42)	0.008	94	11,700				0.012	132	11,400				0.019	515	26,800
Stone, 2004 (27)				0.001	23	15,500									
Tappenden, 2007 (26)				0.026	147	5,700									
Tsoi, 2008 (46)	0.094	651	7,000				0.110	989	9,000				0.159	1,281	8,100
Vijan, 2007 (23)	0.029	202	6,800				0.031	948	30,100	0.050	1,138	22,800	0.053	544	10,200
Wagner, 1995 (18)	0.059	1,086	18,500				0.036	705	19,700	0.067	1,461	21,700	0.059	1,028	17,300
Whynes, 1998 (25)				0.017	76	4,600									
Wu, 2006 (47)	0.025	-27	CS				0.014	35	2,500				0.025	-2	CS
Zauber (MISCAN), 2009 (22)	0.066	-88	CS				0.077	102	1,300	0.085	133	1,600	0.087	205	2,400
Zauber (SimCRC), 2009 (22)	0.060	-305	CS				0.069	-231	CS	0.087	-315	CS	0.094	-207	CS
Zauber (CRC-SPIN), 2009 (22)	0.064	-471	CS				0.080	-375	CS	0.095	-413	CS	0.106	-403	CS

*Table 2. Cost and effectiveness of the strategies for screening for colorectal cancer.*

*(Source: Lansdorp-Vogelaar, et al., 2011)*

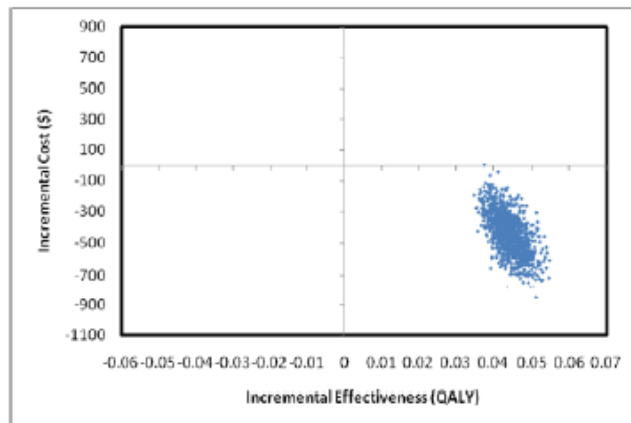
The third article analyzed is “Colorectal cancer screening for average-risk North Americans: an economic evaluation” which was published in PLOS Medicine in 2010 (Heitman, Hilsden, Au, Dowden, Manns).

The aim of this article was to do an economic analysis of colorectal screening in average risk North American individuals considering all screening alternatives and current colorectal treatment costs.

Incremental cost-utility analyses were made using the Markov model. Fecal Immunochemical Test (FIT) annually (divided by *low*, *mid* and *high* test performance), guaiac-based Fecal Occult Blood Test (FOBT), fecal DNA every 3 years, flexible

sigmoidoscopy or computed tomographic colonography every 5 years, and colonoscopy every 10 years were strategies tested for this economic analysis. All programs were compared to the alternative of a no screening program. Annual FIT (*mid* test performance) was more effective and less costly compared to the rest of strategies (including no screening) except the alternative of FIT-high. The percentage of cancers that could be reduced is from 4.857% to 1.782% and the percentage of CRC deaths is from 1.393% to 0.457% (Heitman, et al., 2010).

CRC screening with FIT decreases the probability of CRC and deaths related to colorectal cancer, and reduces health care costs if it is compared with no screening and to other existing screening strategies.



**Figure 2. Probabilistic sensitivity analysis.** An incremental cost-effectiveness scatterplot comparing FIT-mid with no screening in which the uncertainty in all model inputs has been tested simultaneously. Data points in the lower right quadrant reflect situations where FIT-mid is more effective and less costly than no screening.  
doi:10.1371/journal.pmed.1000370.g002

Figure 12. Probabilistic sensitivity analysis. (Source: Heitman, et al., 2010)

**Table 4.** Base case incremental cost per QALY gained for average risk patients (reported value compares strategy reported in the column with the strategy reported in the row).

Screening	Average Costs (CANS) (95% CI) <sup>a</sup>	Average QALYs (95% CI) <sup>a</sup>	Incremental Cost Per QALY Gained										
			FIT-Mid	No Screening	FIT-High (CANS)	FIT-Low (CANS)	FOBT-High (CANS)	Colonoscopy (CANS)	FOBT-Low (CANS)	Flex Sig (CANS)	CTC (CANS)	FDNA-SDT 2 (CANS)	FDNA-SDT1 (CANS)
FIT-mid	1,833 (1,275-1,924)	11.300 (11.29-11.30)	—	Dominated <sup>b</sup>	85,150	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>
No screening	1,901 (1,641-2,226)	11.255 (11.24-11.26)	—	—	2,219	3,883	15,991	4,870	18,595	10,008	12,500	25,974	82,747
FIT-high	2,004 (1,353-2,207)	11.302 (11.29-11.31)	—	—	—	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>
FIT-low	2,005 (1,519-2,020)	11.282 (11.27-11.29)	—	—	—	—	Dominated <sup>b</sup>	6,706	Dominated <sup>b</sup>	27,158	28,871	Dominated <sup>b</sup>	Dominated <sup>b</sup>
FOBT-high	2,084 (1,820-2,301)	11.267 (11.25-11.27)	—	—	—	—	—	573	25,341	7,247	11,137	36,044	Dominated <sup>b</sup>
Colonoscopy	2,100 (1,536-2,120)	11.296 (11.29-11.30)	—	—	—	—	—	—	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>	Dominated <sup>b</sup>
FOBT-low	2,195 (1,892-3,375)	11.271 (11.26-11.28)	—	—	—	—	—	—	—	3,325	8,617	42,870	Dominated <sup>b</sup>
Flex sig	2,263 (2,136-2,433)	11.291 (11.28-11.30)	—	—	—	—	—	—	—	—	32,489	200	Dominated <sup>b</sup>
CTC	2,409 (2,124-2,508)	11.296 (11.27-11.28)	—	—	—	—	—	—	—	—	—	Dominated <sup>b</sup>	Dominated <sup>b</sup>
FDNA-SDT2	2,491 (2,187-2,644)	11.278 (11.27-11.28)	—	—	—	—	—	—	—	—	—	—	Dominated <sup>b</sup>
FDNA-SDT1	2,720 (2,422-2,937)	11.265 (11.25-11.27)	—	—	—	—	—	—	—	—	—	—	—

<sup>a</sup>95% confidence intervals (CIs) based on probabilistic sensitivity analysis using baseline statistical distributions around all uncertain variables.  
<sup>b</sup>Dominated is defined as more costly and fewer QALYs compared with the strategy reported in the row.  
doi:10.1371/journal.pmed.1000370.t004

Table 3. Base case incremental cost per QALY gained for average risk patients. (Source: Heitman, et al., 2010)

The fourth article analyzed is “Preliminary analysis of the cost-effectiveness of the National Bowel Cancer Screening Program; demonstrating the potential value of comprehensive real world data” which was published in Internal Medicine Journal in 2011 (Tran, Keating, Ananda, Kosmider, Jones, Croxford, Field, Carter and Gibbs).

An economic analysis was made by the government health care point of view. Specially, an incremental cost-effectiveness analysis, comparing the Australian database of the National Bowel Cancer Screening Program (NBCSP) with the alternative of no screening. The effectiveness was expressed as CRC-related life years saved (LYS).

The conclusion of this article is that along the lifetime of the people tested in the sample and the program being compared with the alternative of no screening, the effectiveness of the NBCSP was 1,265 life years saved; avoid 225 CRC cases and a cost-effectiveness ratio of \$38,217 per LYS. If the 100% had been participated in the program the cost-effectiveness ratio would have improved up to \$23,395 (Tran, et al., 2010).

The fifth article analyzed is “Review of economic evidence in the prevention and early detection of colorectal cancer” which was published in Health Economics Review in 2013 (Jeong and Cairns).

This article shows the economic conclusions of the colorectal cancer screenings published from 1999 to 2012. The databases used were MEDLINE, EMBASE, National Health Service Economic Evaluation (NHS EED), EconLit, and HTA. Different combinations of screening for mass CRC screening programs are described as well as adequate follow-up tests in order to guide the decision makers through the most appropriate policy. One example of the cases analyzed is the article published in 2007 by Pickhardt which compares the Computerized Tomography Colonography with a 6-mm threshold with the alternative of no screening. One of the results is that the program is cost-effective since the outcome is \$4,361 per LYG.

## 6. COST-EFFECTIVENESS ANALYSIS OF THE PROGRAM FOR EARLY DETECTION OF COLORECTAL CANCER IN NAVARRA

In order to analyze the costs of the colorectal cancer screening program, two perspectives will be implemented. The first one is the Health Service Provider which only takes into account the costs of equipment, time of the health professionals such as specialists and nurses, medicines, etc. This means only direct costs are estimated. The second point of view is the one of the patient who is been tested through a screening for colorectal cancer, his/her time and the time of his/her family members.

**Invitation.** When the program starts in a health area, the target people belonging to that area receive a personalized invitation letter which is sent to their homes. The invitation procedure is important since no time is required by the patient in order to get the invitation. However, a previous time is needed by the “Instituto de salud pública y laboral, sección de detección precoz” for the search of the people who are the target population for the program in the data base “padrón municipal” and a further search to select those who are eligible. In the letter is explained the campaign content. It includes the option to send the card to the issuer expressing the willingness to participate in the program. It also has to be taken into account the time consumed by the “Instituto de salud” for creating the cards with the information for the screening program.

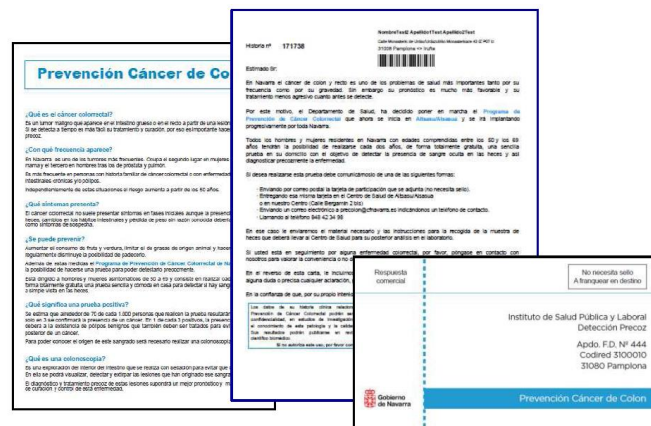


Figure 13. Letter and participation card sent to the target population.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

Confirm participation. To participate in the program, the patient can send the card by post to the address of the issuer. The card is pre-stamped which implies that the cost of delivery is paid by the health service. But the card can also be given to the health center in which the patient is enrolled, by calling to the following number: 848 42 34 98 or by sending an email to the address [precolon@navarra.es](mailto:precolon@navarra.es). Nevertheless, there is a physiological cost implied for those who are the target population (50-69 years old). People may become aware of their probabilities to have colorectal cancer or start thinking about this topic which were not on their minds until the card was sent to them or until they realize that colorectal cancer is in the top three for incidence and mortality through the sensitivity campaign.

Sensitivity campaign. In population-based screening programs, as it is the case, the objective is to decrease incidence and mortality and this is achieved if the patients who are asked to participate in the program do so. This means, that a sensitivity campaign is needed in order to make the population aware of the problems of colorectal cancer and the benefits of participating in the program.

A program is considered effective if it achieves at least a 60% of participation. Due to this reason, a sensitivity campaign needs to be implemented. The objective is not only the target population (50-69 years old population), but also to health professionals and the population as a whole.

Moreover, in addition to the personalized information the target population will receive, there are scheduled specific information and awareness actions for the health personnel involved (primary and specialized care professionals: digestive, anesthesia, pathology, surgery, radiology, oncology...). All these programs are taken as costs too: the time while the information meeting is taking place as well as the time of the personnel to organize those meetings.

The Institute of Public Health and Labor is also requesting the assistance of more than 10,000 companies and entities that can encourage the participation (pharmacies, municipalities, self-help groups, associations, clubs...). At this stage of implementation of the program sensitivity the costs taken into account are those of the administrative time consumed by the health system.

In addition, a communication campaign with the slogan "Choose 90. A simple test can save your life" is being conducted referring to the 90% of colorectal tumors which are curable if they are detected in time. The campaign includes print ads, radio, brochures, posters in

buses shelters and in buses as well as a web [www.cancercolon.navarra.es](http://www.cancercolon.navarra.es) with relevant information about the program where people can also learn about the accessions to the campaign. All the costs related to campaign (radio advertisement, print ads, making them) and the administrative paperwork behind it are also taken into consideration.



Figure 14. Screenshot of the web page of the program of colorectal cancer.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)

Reception of the Kit. Days after showing the desire to participate, the person will receive at home a kit for sample collection and data tagged with the participant and a letter with instructions explaining how to perform the process of sampling and where to deliver it.

The cost implied in this stage of the process are those linked to the administrative personnel while sending the kit to those patients who have shown they desired to participate in the screening.

For convenience, the kit can also be taken in the health center or in the pharmacy.



Figure 10. Instructions for the sample collection.

(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)



The Fecal Occult Blood Test can be done at home, there is no need of stopping taking any medication and no special diet is needed. However, the sample must not be taken if the patients (women) are menstruating or if the patient has bleeding hemorrhoids.

Sample delivery. Once the test is done, the kit with the sample must be delivered to the health center in a maximum of three days. It should be deposited in specific containers identified with the program logo. Transportation costs are linked to the patient since there is time and money involved in the transportation of the sample from the patient's home to his/ her health center. However, there is no need to wait in a queue or to make an appointment because there is a specific container in each health center.



*Figure 15. Sample kit to collect the stools.*

*(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)*

Reporting of results. Once the samples are analyzed, results will be given in a maximum of 15 days. If the results are negative, the results will be communicated by letter. But if the results are positive, if blood is detected in the stools, the nurse assigned to the program will communicate personally to the patient the results and the patient will be referred to his/her health center to carry out a clinical evaluation and a diagnostic confirmation. The waiting time for the patient is critical not only for the effectiveness of the program but also for the restlessness of the patient the days before the test is done and while waiting for the results.

If the results are negative the patient is aware of how the government implements policies which increase the welfare of the society and feels relieve knowing that the result of the test implies he/she does not have colorectal cancer. Nevertheless, the patient is thinking through the whole process of the possibility of having colorectal cancer and the consequent problems which lead to a decrease in his/her well being.



It is estimated that the test will be positive in about 70 of every 1,000 people, but only 3 will be confirmed with colorectal cancer. In 1 out of 3 positive, the presence of blood will be due to the existence of benign polyps which should also be treated to avoid the future appearance of cancer.

Positive result test/colonoscopy. To find the source of bleeding a colonoscopy will be performed. This is a scan inside the whole intestine that is performed with sedation to prevent it from being painful. It will help visualize, detect and remove the lesions (suspicious looking areas such as polyps) that have caused the bleeding. Thus, there are more benefits than being able to apply an early treatment for cancerous tumor through the test. This technique removes precursor lesions and, consequently, avoids the appearance of the disease.

The patient should also sign a paper in which he/she consents being done a colonoscopy. Through the whole process, gastroenterologist, anesthetist and nurses' time are considered, and the cost of the colonoscope are taken into consideration too.

The colon and rectum should be clean by the time the colonoscopy is performed, so the doctor can see the inner linings during the test. The patient should take laxatives the day before the exam, an enema that morning and a special diet the previous days. As the American Cancer Society suggests, the diet should consists of drinking clear liquids (water, apple or cranberry juice, and any gelatin except red or purple) for at least a day before the test. Plain tea or coffee with sugar is usually okay, but no milk or creamer is allowed. Clear broth, ginger ale, and most soft drinks or sports drinks are usually allowed unless they have red or purple food colorings, which could be mistaken for blood in the colon.

The night of the test the patient will be told not to eat or drink anything after midnight the night before the test. If the patient takes prescription medicines, the doctor will suggests the steps which should be followed.

Once the patient is in the hospital, the anesthetist will provide the patient with sedation in order to prevent the colonoscopy to be painful. The colonoscopy will be performed lasting approximately 20 minutes and after that the patient will be moved to a recovery area in which the doctor will check if the person is recovering as he/she should be. The doctor will advice not to take an important decision that day and inform that the patient will have a small drowsiness, lack of reflections and probably really angry. A family member should be needed through the whole process.

If the bowel preparation has been inadequate and colon is not clean another colonoscopy should be made and the diet previous the test should be done again.

#### Colonoscopy's results.

An appointment with the gastroenterologist must take place so as to inform the patient about the results of the colonoscopy.

Significant benign pathology.

The patient will be cited in the Department of Gastroenterology for assessment. The nurses in charge of the screening program will send the patient a letter with the day of the appointment. The result of the test taken in that appointment will be provided by phone or letter in order to minimize the potential negative effects of the waiting queues. According to the final outcome of such assessment, the doctor would provide the appropriate monitoring.

Polyps and/or adenomas.

If those benign polyps or adenomas found require special controls, the follow-up will be according to the protocol adopted following the recommendations of the European Guidelines. The high-risk adenomas requires colonoscopy every year and intermediate-risk every 3 years. The low-risk adenomas return to the PDPCCR (if not excluded by age).

#### Cancer treatment.

If malignant adenomas are found, the patient will be performed a blood test and an electrocardiogram for more information for future events. The patient is required to assist to an appointment with the oncologist and solutions such as chemotherapy, radiation therapy, surgery and a combination of those options will be mentioned. Through this process nursing assistant, specialists, operating room, surgical instruments costs ... are taken into consideration.

The early detection of this type of cancer is really important because if it is detected in a high stage (stage D, using Duke's stage at diagnosis), there is a possibility of using a bag as the last step of the digestive system and this solution to the illness can lead to allergies.

## 6.1. Cost of the program for the Health Service Provider

The analysis of the costs of the screening for colorectal cancer which follows, has only taken into account the cost for the Health Service Provider. This means that only direct costs for the Servicio Navarro de Salud have been accounted. Those costs are the ones mentioned before: costs of equipment, time of the health professionals such as specialists and nurses, medicines, etc. Costs generated by screened men and women (transportation, loss of working hours, colonoscopy-associated intangible costs) have not been taken into account.

Other direct costs for the health provider have not been accounted for. These are: sending the FOBT kit by mail, leaflets, letter with the identification sticker for the sample test, the software for the program, the free phone line and other expenses such as trips of the coordination team.

If initial participation of 60% is assumed, the volume of samples which should be processed would be 23,258 annually.

<b>1ª vuelta</b>	<b>Total</b>	<b>Pamplona</b>	<b>Tudela</b>	<b>Estella</b>
Población invitada	77.528	59.092	10.805	7.631
Muestras recibidas	46.517	35.455	6.483	4.579
<b>Muestras por año</b>	<b>23.258</b>	<b>17.728</b>	<b>3.241</b>	<b>2.289</b>

*Table 4. Estimation of the samples collected in one year.*

*(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)*

According to the data of the prevention program, it is estimated that 7% of the sample will be positive. This leads to 1,628 positive Fecal Occult Blood Test.

<b>1ª vuelta</b>	<b>Total</b>	<b>Pamplona</b>	<b>Tudela</b>	<b>Estella</b>
TSOH realizados	46.517	35.455	6.483	4.579
TSOH positivos	3.256	2.482	454	321
<b>TSOH positivos por año</b>	<b>1.628</b>	<b>1.241</b>	<b>227</b>	<b>160</b>

*Table 5. Estimation of the positive results from the Fecal Occult Blood Test in one year.*

*(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)*

According to the population figures and participation rate, 1,758 colonoscopies will be performed annually so as to confirm the diagnosis of cancer. This amount of colonoscopies also includes the ones which have been made again for poor preparation of the patient or for an incomplete result. This explains why the number of colonoscopies is higher than the number of positive test for fecal occult blood.

<b>1ª vuelta</b>	<b>Total</b>	<b>Pamplona</b>	<b>Tudela</b>	<b>Estella</b>
TSOH positivos	3.256	2.481	454	321
Primeras Colonoscopias	2.930	2.233	401	289
Colonoscopias por repetición	586	447	82	58
Total colonoscopias	3.516	2.680	483	347
Colonoscopias-año	1.758	1.340	242	174
Colonoscopias-semana	40	30	6	4

*Table 6. Estimation of the colonoscopies performed due to the screening program.  
(Source: Programa de Detección Precoz de Cáncer Colorectal de Navarra, 2012)*

To sum up, it is estimated that about 70 in every 1,000 people taking the test will be positive, but only 3 will be confirmed to have cancer. In 1 out of 3 positive cases, the presence of blood will be due to the existence of benign polyps that should also be treated to avoid the future appearance of cancer.

The following table (table 7) shows the cost of the program described above. These costs also show the recruitment of a doctor and two nurses. The costs described are unitary costs of the health system provided by the web page of the community of Navarra ([www.navarra.es](http://www.navarra.es)).

	Price (2014 €)	Patients	With program	Without program
Doctor salary (A)	25,281.76	1	25,281.76	
Nursing salary (B)	21,268.80	2	42,537.60	
<b>LABORATORY</b>				
- Microbiological analysis with identification (known germ)	31.29	23,258	727,742.82	
<b>PRIMARY CARE SERVICES</b>				
- Medical check (7% FOBT)	84	1,628	136,752	5,860.80
<b>GASTROENTEROLOGIST</b>				
- Colonoscopy with or without biopsy	535	1,758	940,53	37,327.71
- First visit	220	70	15,4	
<b>ONCOLOGY</b>				
- First visit	220	70	15,4	15,4
<b>TOTAL COST OF THE PROGRAM</b>			<b>1,903,644.18</b>	<b>58,730.00</b>

Table 7. Estimation of the total cost per year of the screening program and the alternative of not implementing it.

The program will cost annually 1,903,644.18€ in contrast with the alternative of not implementing the program: 58,730.00€; being the difference 1,844,914.18€.

## 6.2. Effectiveness

The effectiveness of the program for early detection of colorectal cancer has been taken from the literature (Telford MD, et al., 2010).

The data taken is the Quality Adjusted Life Years gained for the screening test of low-sensitivity guaiac Fecal Occult Blood Test (performed annually) as show in the following table:

**Table 3:** Cost and effectiveness of three strategies for screening for colorectal cancer over the lifetime of 100 000 individuals who commence screening at age 50 years, relative to not screening

Strategy	Cost, 2007 Can\$	Quality-adjusted life- years gained	Deaths prevented	Decrease in mortality rate, %	Cases of cancer prevented	Decrease in incidence, %
Low-sensitivity guaiac fecal occult blood test, performed annually	63 139 823	6 914	2113	55	2748	44
Fecal immunochemical test, performed annually	65 429 821	10 491	2834	74	4081	65
Colonoscopy, performed every 10 years	76 094 757	12 013	3157	83	5082	81

Table 1. Cost and effectiveness of three strategies for screening for colorectal cancer.

(Source: Telford MD, et al., 2010)

There are other factors which reflect the effectiveness of the screening test using low-sensitivity guaiac fecal occult blood test. These measures are decrease in mortality rate (55%) and decrease in incidence (44%).

These quantities are the ones which have been chosen because the low- sensitivity guaiac fecal occult blood test is the closest to the one being implemented in Navarra (quantitative immunological fecal occult blood test). However the range of exploration is different since the test from the literature has been performed annually and the interval between tests for the screening test in Navarra is performed every two years. This limitation should be taken into account.

This data applied to the program for the early detection of colorectal cancer in Navarra is the one shown below. It shows the effectiveness of the quantitative immunological Fecal Occult Blood Test for colorectal cancer over the lifetime of 23,258 individuals who are expected to participate in the program annually, relative to not screening.

<b>Quantitative Immunological Fecal Occult Blood Test, relative to no screening</b>	
<b>Quality Adjusted Life Years Gained</b>	1,608*
<b>Decrease in mortality</b>	55%
<b>Decrease in incidence</b>	44%

Table 8. Effectiveness estimators of the screening program using Fecal Occult Blood Test.

\*(23,258/100,000\*6914)

However, this result is an approximation of the cost and effectiveness of the program which has not still finish the first round. This outcome is subjected to modifications and a more accurate analysis of the costs.

### 6.3. Incremental Cost Effectiveness Ratio (ICER)

The early detection program of colorectal cancer will cost annually 1,903,644.18€ in contrast with the alternative of not implementing the program: 58,730.00€. This means that the variation of implementing the program versus the alternative of not implementing it, is 1,844,914.18€.

The effectiveness analysis has been taken from the literature and if the information found in the article mentioned before is approximated to the number of patients who participate annually in the program in Navarra, the Quality Adjusted Life Years gained (comparing with no screening) is 1,608.

$$ICER = \frac{C1 - C0}{E1 - E0} = \frac{1,844,914.18\text{€}}{1,608 \text{ QALY}} = 1,147.29 \frac{\text{€}}{\text{QALY}}$$

This implies that the cost-effectiveness ratio is 1,147.29€ per Quality-Adjusted of Life-Years gained, which is cost-effective because this quantity is under the threshold of 30,000 €/QALY (Sacristan, et al., 2002).

## 7. LIMITATIONS

This study was made given the following restrictions. Model-based economic evaluation is subject to the existing data in the medical literature, which is under constant change. When a new article comes out, the previous ones become outdated. It should also be considered, as Lansdorp-Vogelaar et al. (2010) say, that: “The natural history of colorectal cancer is based on assumptions regarding the progression from adenoma to carcinoma and the transition time from a low-risk polyp to a malignant neoplasm.”

Another limitation is the untested assumptions considered to analyse the screening program for colorectal cancer: participation and acceptance rates, characteristics of the Fecal Occult Blood Test, incidence of adenomas, number of colonoscopies made by bad performance .... The model has not taken into account the infrastructure of the costs of the Health Provider (Servicio Navarro de Salud) such as buildings and its maintenance, transportation costs for the FOBT screening test and so on.

The model studied has the perspective of a third-party payer; this means that only direct costs are estimated without taking into consideration the cost for the patient and his/her family. Only cost from the health care system has been accounted and not the one from the societal perspective.

The economic analysis of the program for early detection for colorectal cancer has been done with the prices of Navarra's Health System. Therefore, the direct comparison between countries is limited. However, it can be useful if the health care system is similar to the one in Navarra. As Lansdorp-Vogelaar et al. (2010) say: “Generalization of cost-effectiveness analyses from one country to another cannot be done, because screening costs, resource capacity and population preferences for different screening tests vary from country to country.” Moreover, the costs analyzed for the Health System in Navarra are the ones up to the first visit to the oncologist. This is an important constraint because the cost of colorectal cancer treatments vary on the stage the cancer is found. The higher the stage the cancer is found, the higher the cost of the treatment.



## 8. CONCLUSION

In this article, the importance of colorectal cancer has been explained through indicators such as incidence, survival and mortality rate. This type of cancer is a problem for all the developed countries. In Europe, the European Union Council advises to implement a program of early detection for colorectal cancer using a Fecal Occult Blood Test as a tool to do the screening program. It has also been explained what are the risk factors that cause this disease as well as the types of screening test according to the invasion level.

The reasons why an economic evaluation is crucial for a decision-maker have been exposed as well as the main principles used for an economic evaluation of a health technology. The most common economic evaluation techniques are: cost-benefit analysis, cost-effectiveness analysis and cost-utility analysis. Given these evaluating methods, the outcomes of the money spent in a specific program or technology can be analyzed, showing the relation between the resources and the results of those resources consumed. However, an economic analysis is only one of the factors that a politician should take into account; because there are factors such as equity and social sensitivity that should also be considered.

An analysis of the situation of the colorectal cancer in Navarra has also been made by using the *Sistema Nacional de Salud, Padrón de Navarra* and the resources the *Instituto de Salud Pública y Laboral, sección de Detección Precoz*, has, for example the *Registro de Cáncer de Navarra*. International databases have also been used such as the Eurocare. In addition, an explanation about the objectives of the program has been made; these goals are the reduction of the incidence and mortality from colorectal cancer. The target population are women and men between 50-69 years old (population at average risk of developing the disease). Since the program is population-based, the participation rate is crucial, that is why along this months an awareness campaign is been implemented.

Implementing this screening program increases the welfare of the people tested because if the disease is detected early, it can dramatically change the course of the illness. And the cure rate can also be increased. Moreover, an appealing fact to do this screening test is that a colonoscopy (a further test of the screening) can detect polyps. These precursor lesions can be removed and can prevent the cancer cycle from beginning in the first place.

The costs of the program which have been analyzed have been the direct costs to the health provider. However, the costs for the patients and their families have only been described.

The sum of these costs and the costs of the alternative of not implementing the program, provide the information to calculate the Incremental Cost-Effectiveness Ratio (ICER). This measure is one tool of the cost-utility analysis. The numerator is the difference of costs and the denominator of this ratio is the effectiveness of the program versus the alternative of not implementing it. The program will cost annually 1,903,644.18€ in contrast with the alternative of not implementing the program: 58,730.00€. This implies a difference of 1,844,914.18€ per year. The effectiveness of the program has been calculated by adapting the Quality Adjusted of Life Years (QALYs) obtained from the literature to the specific case of Navarra. The result proves the screening program in Navarra to be cost-effective since the result is below the threshold of 30,000 €/QALY for efficiency (Sacristan, et al., 2002). The ICER is 1,147.29 €/QALY which means that in order to gain a Quality-Adjusted of Life-Years the government would need to spend 1,147.29 €.

There has also been a review through the literature about economic evaluations for the different types of screening test for colorectal cancer. These analyses have been made by using Quality Adjusted Life Years (QALYs) or Life Years Saved (LYS). There have also been found other indicator of effectiveness such as decrease in mortality and decrease in incidence. All the articles conclude that the screening tests are cost-effective. However, not all agree which tests are dominated by the rest of screening tests. The tools to achieve these conclusions have been incremental cost, incremental cost-effectiveness ratio, cost-effectiveness acceptability curve or probabilistic sensitivity analysis.

In conclusion, this report helps the decision makers to allocate the budget they have for the expenditures of the health department. It has been proved by the literature and by the results from the base-case analysis, that the screening test for Fecal Occult Blood Test is cost-effective. However, an effort must be made to sensitize the population, because an important factor for the effectiveness of a population-based screening program (FOBT) is the participation rate.

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