Cost-Effectiveness Studies Applied to the Screening Of Colorectal Cancer

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Abstract

Screening for colorectal cancer (CRC) is an effective strategy to reduce its mortality and even its incidence. But due to the existence of multiple screening tests with their differences in costs, acceptability and effectiveness in terms of life years gained (LYG) well-designed studies are needed to assist the Health Authorities in the decision-making process. At this point a new technique of radiology, virtual colonoscopy, has emerged as part of CRC screening in the general population. When both types of colonoscopy were compared with the strategy of "no screening", the incremental cost-effectiveness ratio for colonoscopy and CV were respectively 20,000 and 30,000 euros per LYG, proving that both strategies are cost-effective according to most international acceptability thresholds. However, when both are compared to each other, traditional colonoscopy seems to be the most cost-effective. Since most of the studies are based on assumptions and estimates based on data from clinical trials and mathematical modeling, there is still much to be done to draw firm conclusions.

Keywords: virtual colonoscopy, screening, colorectal cancer, cost effectiveness.

Introduction

Colorectal cancer (CRC) is the second most common cancer in Western countries. It is expected an upcoming increasing incidence which runs parallel to population ageing (1). Moreover, its mortality rate is still so high and this fact places this disease as one of the most relevant problems to face in public health (1).

Recent advances in molecular biology and epidemiology have let us know in detail the causes and mechanisms involved in the development of this pathology and thus a progress towards more personalized treatments which eventually will increase the survival (2). However, this striking development has led to an enormous increase in costs which have been estimated by more than 200% since the nineties until 2003 (3,4). These expenses are unfortunately unaffordable by our modern societies which consequently should prioritize those policies aimed at reducing the incidence of the disease.

The largest proportion of CRC is sporadic type, while only 10% have a hereditary (5) component. In this way the largest impact in CRC figures would be achieved by decreasing the number of new cases in the average risk population. Thus the screening has emerged as an effective measure to reduce CRC morbidity and mortality (6), besides being cost-effective.

But despite having strong evidence favoring the screening (7), these programs generally cover less than 50-60% of the target population (8,9). Many uncertainties about the screening are still causing reluctance. Questions such as who should be the target population or the age at which these people should start the screening or the ideal interval between repeated studies and what test should be used and what are its potential risks or side effects or even how to deal with the fear of the results or the pain or discomfort due to the application of the test (10).

The pathogenic peculiarity presented by CRC, with an asymptomatic long phase (6), coupled with the fact that it is a highly curable disease in early stages, have made this cancer suitable to encourage people to participate in the population screening intended to reduce mortality. Furthermore, the fact that through the screening are detected and removed premalignant lesions (such as adenomatous polyps), thereby interrupting the path of adenoma-carcinoma transformation, could reduce the increased incidence figures. In fact it is well known that removal of adenomas through colonoscopy reduces the risk of cancer by 75% (11,12).

Two studies have directly evaluated the result of the ongoing increasing CRC treatment costs in the cost-effectiveness ratios of screening, and both have shown that the cost-effectiveness of screening is favorable compared to "no screening" and most screening strategies are even cost-saving compared to treatments (13,14). Consequently the introduction of screening programs has become a priority for health policy in many countries.
Colorectal Cancer
Epidemiology

Globally the CCR has a higher incidence in countries with Westernized lifestyle, more in men than in women and especially over 50 years (1). Globally this is the second most prevalent tumor only surpassed by Breast Cancer.

Between 1982 and 2002, the incidence in Europe for men and women was 38.5 and 24.6 (adjusted for age) per 100,000 population, while in the United States (USA) the figures were higher (38.6 and 28.3 in men and women respectively) (1). In contrast, mortality was higher in Europe with 18.5 and 10.7 in men and women compared to 13.5 and 9.2 respectively in US. The totals for 2002 reflected an estimated 529,000 deaths secondary to CCR in the world (1).

The relevance of this health problem is clearly reflected in the relationship between the incidence and mortality rate which is considered about half of the new cases (1). In Spain, according to data from 2000, the number of new cases per year is around 21,000 in both sexes, compared to 11,900 deaths, while the number of prevalent cases is 64,000 (28,000 in men and 36,000 in women ) (15). However, the incidence and mortality rates in Spain are substantially lower than those of northern European countries and even continental average rates (15).

Cost-Effectiveness Analysis

The cost-effectiveness analysis (CE) is a form of economic evaluation that compares health outcomes and economic consequences of different interventions or alternatives in health intervention programs. Costs are measured in monetary units and the benefits in natural units of effectiveness which vary according to the evaluation carried out (16, 17). Effectiveness refers to the impact or effect achieved with a healthcare intervention under real conditions (16).

The CE can be applied to programs or health interventions whose degree of effectiveness is different but share the same goals and therefore can be measured in the same unit of effectiveness. In fact the choice of effectiveness indicators may affect the relative efficiency of different options discussed and therefore this choice should take into account the final objectives of the analysis, the objectives of health policy and the availability of scientific information (16,17).

Finally, although these analysis cannot determine what the optimal intervention is, they can indicate which one provides the greatest health benefits at the lowest cost with the intention of thereby facilitate the decision making process in health policy. Aiming at this there are different mathematical models which put together the benefits estimation with each intervention and its potential complications and costs. Eventually this model will give a value to each of the potential effects in order to obtain a net effect, whether a benefit or harm (16,17).

The results are summarized in CE ratio and the cost-effectiveness comparison of two strategies is assessed by the ratio of incremental cost-effectiveness that shows the extra cost per extra year life with a strategy compared to the other. The latter is found by the fraction of the difference in life-years gained (LYG) with each intervention included in the numerator and the difference in costs associated with each strategy will be the denominator (16, 17).

The World Health Organization (WHO) states that a population screening program should only be started if it complies with the requirement to maintain a "good balance" between the benefits it provides in terms of health and the global costs involved. Unfortunately there is no universal definition of what "good balance" means (18). This implies that different countries may adopt different health policies regarding the screening without violating the WHO statement which in fact this is what happens. The CE applied to health generally consider a health intervention that provides extra LYG at a cost of $ 50,000. This is considered acceptable in most industrialized countries, but if the cost is $ 100,000 it would be very controversial whether acceptable or not (19).

Cancer Screening: General Principles and Colorectal Cancer

Screening as secondary prevention activity, is considered an effective method to control the figures of cancer at a population level. But this is only achieved if there exists a high individual participation, adequate and proper diagnosis and early treatment (15). To implement such a program is necessary to
assess adequately health outcomes and costs of all procedures by conducting randomized controlled trials. This requirement extends to all new screening tests, before entering the test into the routine clinical practice (1).

The screening program management is not easy and requires adequate resources, human, financial and material, to ensure the appropriate organization and quality. All these cancer screening programs should be offered to healthy people if they have proved efficacy in reducing the disease-specific mortality or the cancer incidence in general. Beforehand we need to know also their ratio benefits/risks, and if the cost-effectiveness is acceptable (not all the screening tests meet these criteria) (1).

Final decisions regarding the implementation of cancer screening programs are entitled to health authorities and should be taken as part of a general exercise of prioritization in the use of health resources.

For the CRC there are various tests that have been taken into consideration when deciding to launch a screening program (20). They can be classified into two types: tests that primarily detect cancer and tests to detect cancer and other advanced lesions (Table 1). The guidelines (21) for early detection of CRC in average-risk adults updated in 2008 (Table 2) through the consensus reached between the ACS (American Cancer Society) and U.S. Multi-Society Task Force (USMSTF) in CRC and American College of Radiology recommend starting screening at age 50 with one of the following options: fecal occult blood (FOB) (resin guaiac tests (G) or immunochemical (I)) annually, flexible sigmoidoscopy every 5 years, colonoscopy every 10 years, double contrast barium enema every 5 years or virtual colonoscopy (VC) every 5 years. Even though the rates of compliance with screening measures are highly variable but usually less than 50-60% of the population will adhere to these programs (8, 9). There are many reasons for this low participation. The study conducted by Vernon reflected that major discomfort to undergo these tests, overwork or family burden, lack of interest or even the absence of symptoms have been considered the most important causes (22). But there are other reasons for not performing these screening tests such as the concern about possible complications caused by them, such as pain, discomfort or too little overall acceptability because of its inconvenience (20). In order to break these barriers there are new screening test as the VC and colon capsule endoscopy (CCE) which are now emerging.

New Test Of Colorectal Cancer Screening

1. Colon capsule endoscopy (CCE)

The CCE can be a method to overcome poor adherence to screening CRC population (23). The device is a swallowable capsule with an attached video camera at either end that can take photos as it progresses through the gastrointestinal tract. PillCam Colon 1 (PCC1) was the first capsule for colon visualization, always after proper cleaning. PCC1 is a small device, measuring 11 mm x 31 mm and has got two cameras that allow the device to acquire video images with a wide coverage area, automatic control of light and a speed of four frames per second. The system includes a sensor array and a data register connected to the patient during the procedure. The recorded data are downloaded to the workstation for video review of colon (23).

The second generation of PillCam Colon 2 (PCC2) is similar to the above but this incorporates new developments as the viewing angle has increased to 172 degrees, adaptive frame rate depending on whether you are moving or stationary and a new simple software to estimate the size of the polyp. The cleaning procedure until swallowing the capsule is similar to that used for traditional colonoscopy. However, this must be more rigorous to achieve adequate sensitivity method (23). The standard of cleanliness was considered good to excellent in 72-88% of studies with PCC1. The sensitivity for detection of significant polyps (> 6 mm or more than 3 polyps> 3 mm) ranged from 63-88% and from 64% to 94% the specificities. However, PCC2 showed higher sensitivity (89%) and specificity (76%). Thus the CCE appears to be a safe and effective method to visualize the bowel mucosa without sedation or air insufflation (23). Although the sensitivity for polyps, advanced adenomas and cancer is lower compared to traditional colonoscopy, the progress continues and some improvements have been achieved. So far CCE is the least evaluated method for CRC screening.

2. Virtual Colonoscopy

There is a growing interest in the computed tomography (CT) colonography or virtual colonoscopy (VC). This interest is due to the favourable combination of the sensitivity and specificity of VC
combined with no invasive detection of biomarkers (SOH, fecal DNA).

Currently VC screening is integrated into the standard screening to replace barium enema in those cases in which colonoscopy incomplete 24. But much more important is its potential role in the first line screening, along the FOBT or flexible sigmoidoscopy or standard colonoscopy. Our objective should be to select individuals who will need to undergo other screening modalities.

In March 2008 the American College of Surgeons (ACS), US Multi-Society Task Force and American College of Radiologists reached a consensus resulting in the publication of guidelines for the screening in an average-risk population (Table 2). These guidelines distinguish between tests that can detect and reduce mortality from CRC and those which detect polyps and CRC, thereby decreasing incidence and mortality 20 (Table 1). The latter group of tests includes traditional colonoscopy, flexible sigmoidoscopy, double contrast barium enema and VC and the consensus suggests these tests to be repeated every 5 years from the age of 50.

Unfortunately the U.S. Preventive Services Task Force (USPSTF) (25) considered not sufficiently supported by scientific evidence the performance of VC because there was still uncertainty about the significance of the incidental findings of extracolonic lesions and the potential damage from radiation exposure. Besides there were not much data on cost-effectiveness of the test in the field and the problem of ideal bowel preparation ideal remained to be resolved.

Two other important groups such as Asia Pacific Working Group on CRC (26) and the American College of Gastroenterology (ACG) (27) consider the VC as a second-line test in screening, reserved for individuals who are unwilling or unable to undergo the colonoscopy or for which that was incomplete.

2.1 Diagnostic accuracy of VC

Much remains to be learned about its accuracy in detection of CRC and adenomas. The results of several projects (28-30) are contradictory but a meta-analysis has shown that the VC is highly specific for the detection of colonic polyps and neoplasias (31) (see images in Figures 1-3).

Three major trials have been designed to clarify these uncertainties (32,33).

The ACRIN (American College of Radiology Imaging Network) (32) was designed with the aim to compare the feasibility of VC with standard colonoscopy in asymptomatic individuals at average risk.

By contrast the IMPACT (Italian Multicenter Computed Tomography Colonography Polyps Accuracy) (33) was performed in mixed population of high risk asymptomatic subjects and in patients referred due to a positive FOBT test. The third of the studies is the SIGGAR (Special Interest Group in Gastrointestinal and Abdominal Radiology) carried out in the UK, in symptomatic patients in order to detect CRC (34) but it is still pending conclusive results.

The results of the IMPACT and ACRIN showed a sensitivity for the detection of polyps> 10 mm of 90% and 78-85% for polyps> 6 mm, while the specificity was extremely good regardless of the size of the lesion. The major limitation of ACRIN was its poor positive predictive value (PPV) which was 23% for polyps ≥ 10 mm. This would affect negatively the screening program as it would be necessary the performance of many colonoscopies with consequent unnecessary discomfort, risks, potential complications and very costly. PPV in IMPACT trial showed better result as shown in Table 3. The data published from highly experienced hospitals (Korea group) confirmed this PPV (69% if> 6 mm and 92% for> 10 mm). In contrast, the negative predictive value (NPV) was high in both trials, approaching 100%, which is very important to ensure the patient with negative results the validity of such test (32, 33). Other studies confirm the importance of the CV when compared with the traditional colonoscopy. The screening project conducted at the University of Wisconsin (35) illustrated detection rates for advanced adenomas of 3.2% and 3.4% for VC and colonoscopy respectively without statistically significant differences. Although HP had no complications while in 7 cases of group colonoscopy perforations were observed. The group of Colorectal Cancer Prevention Trial Munich (36) recruited 300 healthy subjects and obtained excellent results compared with other screening tests such as colonoscopy, flexible sigmoidoscopy and FOBT.

Anyway, several issues are still open such as what is the significance of diminutive polyps (<6 mm), the management of intermediate (6-9 mm) or what the rate of detection of polyloid or flat lesions (37) and the relevance of extracolonic findings. A systematic review published by Hassan et al (38) concluded that tiny polyps have no or minimal clinical impact (Table 4). That way if it decides to set the threshold for
polypectomy in 6 mm, would identify 95% of subjects with advanced adenomas, whereas if less of 10 mm would identify 88%. Management of intermediate polyps (6-9 mm) is still under debate. Currently any polyps ≥ 6 mm should be referred for colonoscopy and polypectomy (ACS guidelines) 24 although there are some studies that consider alternative monitoring of the polyp (39). On the other hand the VC presents some difficulty detecting polyoid or flat lesions or though because these represent a subset of sessile polyps is considered that most are slightly elevated (37). This favors detection by VC which has shown a sensitivity of 80-90% for flat adenomas (40).

2.2 Rate of participation

The colonoscopy is considered the best screening technique but has very low participation rate of the population. Very recent data from an Italian study underscore the difficulties in implementing this technique which presents participation rates of 2.8 to 12.4% (41).

The involvement of the population in screening programs is critical because it directly affects the effectiveness of the program. In fact if traditional colonoscopy reduces CRC incidence by 76% assuming 100% participation, when it drops to only 20% of the population, the benefit in reducing incidence falls to 15% (42).

Theoretically VC could increase population adherence. The three major problems that reduce participation in traditional colonoscopies are screening the need for bowel preparation, shame on the type of test and the fear of pain (43) that would be solved with the use of sedation.

The advantage of the VC is the use of a softer preparation laxative or even without, a minimization of pain due to distension which make the patient feel more comfortable during the examination (44).

However, it remains unclear whether the VC could increase participation rates. A study in Australia (45) has shown that 28.4% of the target population agreed to undergo screening and that 67% of them preferred the colonoscopy but more data are needed before a definitive conclusion.

At this point all efforts should aim at achieving more accepted techniques and greater compliance rate or adopt strategies to maintain good cost-effectiveness ratio despite the compliance rate. The Vijan et al (46) study indicates that traditional colonoscopy meet the last requirement and maintains its cost-effectiveness ratio even lower rate of compliance, which would make this the preferred technique for population screening.

Cost-Effectiveness Analysis Applied to the Screening Of CRC

The CRC screening tests vary considerably in terms of acceptability by the general public, cost, rate of complications or side effects and effectiveness. FOBT test and traditional colonoscopy represent the two extremes of a range of potential screening strategies. The first method is characterized by its low cost and simplicity of implementation, while the second is characterized by its effectiveness and thoroughness.

Multiple studies evaluating the relative cost-effectiveness of different screening strategies have shown that traditional colonoscopy, flexible sigmoidoscopy and FOBT are cost-effective alternatives.

a) Compared to "no screening"

A systematic review published in 2002 (47) showed that the cost-effectiveness ratios for Guaiac-FOBT ranged from $ 5,691 to 17,805 per LYG. For flexible sigmoidoscopy $ 12,477-39,359; for the combination of G-FOBT and flexible sigmoidoscopy the figures were 13,792 to 22,518 $ and finally to the traditional colonoscopy 9,038-22,012 $ per LYG. The authors concluded that compared with "no screening" the cost-effectiveness ratio was less than $ 50,000 per each LYG, which means that most of the industrialized countries would consider acceptable.

Other studies published since 2001 have confirmed that CRC screening is cost-effective and do not establish which strategy is more cost-effective or has got a better incremental cost-effectiveness ratio (46, 48). Screening programs of European and Asian countries have better cost-effectiveness ratios than those in U.S. studies (≤$ 10,000 per LYG) when compared with "no screening" but also the costs of the test are cheaper (49, 50). O'Leary et al showed that the ratio of incremental cost-effectiveness for flexible sigmoidoscopy was acceptable versus "no screening" ($ 16,801 per LYG). Also traditional colonoscopy ($ 19,285 per LYG). But annual or biennial FOBT strategies were less cost-effective ($ 46,900 and $
41,183 per LYG respectively) (51). And although FOBT effectiveness has been demonstrated in three randomized clinical trials and one nonrandomized controlled using Guaiac-FOBT, the sensitivity is very low and its impact on the detection of precancerous lesions is very limited. The Immune-FOBT tests are more accurate but also more expensive and with higher rate of false positives. This fact could overload the screening program unnecessarily and even increase more the costs due to the need of completing the study with endoscopy without any impact on effectiveness. The problem of acceptance and participation rate remain significant and the fact that the test has been recently simplified this test could improve the compliance. Furthermore it has been suggested that an automated reading process could improve the sensitivity of the test while maintaining acceptable specificity. Recently it has been introduced the fecal DNA test but a study conducted in the US found that the cost-effectiveness ratio for this test compared to "no screening" is 13,000 to $30,000 per LYG. However, FOBT test is more effective (i.e. greater number of LYG achieved) at a lower cost and hence the DNA test proves to be the strongly dominated strategy. Therefore this should not be implemented (53).

b) Comparison between different strategies

A systematic review published in 2002 (47) which compared the cost-effectiveness ratios of different strategies against other showed no definite conclusion. Half of the included studies concluded that the combination of flexible sigmoidoscopy and G-FOBT were the most cost-effective strategies, but the other half concluded that it was the traditional colonoscopy.

On the other hand if the threshold per LYG is fixed in $20,000 to be acceptable, it has been found that at least one warranted to study each screening tests as preferred.

In Europe most of the CE strategy adopted as standard screening test G-FOBT (54), followed in number by sigmoidoscopy flexible (55), while only three studies evaluated colonoscopy as screening (56) technique.

This is because in many European countries colonoscopy is not considered an option for population screening due to the absence of randomized trials that endrse and partly to the reduced availability of endoscopic resources and preference for other tests (not invasive) by the general population. There is another difference between US and Europe regarding the mode of establishing screening recommendations. In US these recommendations are made by consensus between different organizations or societies not pressed for economic reasons, while in Europe (at least in many European countries) the decision is based primarily on the availability of resources, costs and the effectiveness of the alternative screening options. This strategy should be adapted to each country without screening generalizability. The study by Vijan et al (10) showed that colonoscopy may be the most cost-effective technique to compliance and participation levels seen in actual clinical practice. In fact colonoscopy performed twice from 50 years old would probably be the preferred test for CRC screening.

The sensitivity analysis shows that the rate of compliance, the cost of the test and the proportion of cancers arising from polyps are the key factors that determine the relative cost-effectiveness of this screening strategy. Thus flexible sigmoidoscopy and FOBT combined would be the choice if 50% of CRC arose from polyps, compliance was ≥75%, and test costs were moderate. Or if compliance was 50%, 50% of polyps arose from CRC, and the cost of colonoscopy was $1,000 or more (57).

Anyway, as the effectiveness of colonoscopy screening has not been evaluated in randomized clinical trials, neither was the combination of flexible sigmoidoscopy and FOBT. Olynyk et al (58) published a study in 2001 showed that flexible sigmoidoscopy compared with SOH turned out more efficient in terms of reduced need for colonoscopies and detected more cases of CRC. On the contrary O'Leary et al (59) showed that flexible sigmoidoscopy was less effective than FOBT and colonoscopy. In fact the incremental cost-effectiveness ratio of colonoscopy and FOBT compared to sigmoidoscopy were $25,769 and $141,496 respectively, so the authors concluded that colonoscopy had an acceptable cost-effectiveness ratio but not the FOBT. However, when evaluating the impact of compliance, the cost-effectiveness ratio varied little for flexible sigmoidoscopy with a 100% compliance ($13,958 per LYG compared to the option of "no screening") while it did for annual and biennial FOBT, dramatically improving the cost-effectiveness. The evaluation of the double contrast barium enema as a screening test has proven to be less effective than traditional colonoscopy and VC. In this regard its use as a screening technique is highly debated, considered only in countries with limited availability of resources for other examinations (1).
Cost-Effectiveness Analysis With New Screening Test

So far only one cost-effectiveness study has been conducted (60) with CCE. The study of Hassan et al showed that the cost-effectiveness ratio of this technique when compared with "no screening" ranges between $25,000 to 29,000 per LYG. Thus, colonoscopy has been shown to produce a better cost-effectiveness ratio than CCE. The authors concluded that the cost-effectiveness ratio of the CCE depend primarily on its ability to improve the adherence of the population to this technique and thus increase their participation.

Moreover CE draw conclusions for the CV is a difficult task due to the absence of real data. The data are based solely on mathematical models. There are seven major studies that have evaluated the cost-effectiveness ratio of CV as a primary tool for CRC screening. Of these, five (46,48,61-63) were performed in the U.S., one in Italy (56) and another one in Canada (64). Except one of ellos63, other economic models used analytical decision had similar structure. Assessed the total costs and benefits associated with CRC screening strategies. They evaluated hypothetical cohorts of individuals at least 50 years of age undergoing CRC screening at regular intervals. If polyps were identified undergoing colonoscopy for polypectomy. In three studies (48,63,64) diminutive polyps (<6 mm) were not considered as positive findings were ignored. In addition to individuals with detectable neoplasia were treated according to stage and who underwent polypectomy became considered high risk and therefore entered a phase of periodic review. But the study by Lin et al (63) used data from a randomized clinical trial with the aim of developing a risk rating to identify low-risk individuals who might benefit from screening CV rather than traditional colonoscopy. These authors considered only the costs of screening and short-term benefits as the number of advanced neoplasms detected. All studies considered only direct medical costs including the costs of the trial, the polypectomy and complications and treatment of CRC. Health outcomes were measured in AVG and compared with the traditional CV, although most included an option of "no screening", three included and one flexible sigmoidoscopy also considered combining SOH and SOH-sigmoidoscopy. All jobs that included a strategy of "no screening" suggested that any form of screening is cost-effective with incremental cost-effectiveness ratios <$30,000 per LYG. The CV was the strategy favored over flexible sigmoidoscopy and the incremental ratio of cost-effectiveness against SOH was <$25,000 per LYG. Also benefited (both 2D and 3D CV) with recurrence intervals of five years, compared to the combination of flexible sigmoidoscopy and FOBT. Now, five studies (46,61-64) concluded that when CV was compared with traditional colonoscopy that one was not cost-effective. Some of them considered CV more expensive and less effective and the rest of the studies showed that while CV was more expensive, the incremental cost-effectiveness ratio was $10,500 (61) and 7,700 per LYG (46).

Contrary studies Pickhardt et al and Hassan et al found a traditional colonoscopy more effective and also more expensive and therefore less cost-effective. Pickhardt et al (48) concluded that if ignored tiny lesions (<6 mm) the CV was the most cost-effective test. Although the method used for this statement was not considered the ideal for which we applied the ratio of cost-effectiveness. This showed that the ratio when compared with traditional colonoscopy CV was $64,000 per LYG (surpassing the $50,000 threshold) and when considering all polyps regardless of size, the figure is $42,000 per LYG that is also much higher than those previously described. The problem is that most of the cost-effectiveness ratio of the front to the traditional CV is due to the very small differences in cost-effectiveness between the two tests estimated. Thus Pickhardt et al (48) estimated the incremental benefit of colonoscopy against the VC was LYG 0.266 per 100 individuals undergoing screening or 0.375 if you ignore the tiny polyps. While those studies that considered more cost-effective than traditional colonoscopy was considered more effective, 0.622-1.623 additional LYG per 100 individuals undergoing screening. To this must be added that two other studies that also ignored the presence of tiny polyps, favored traditional colonoscopy.

On the other hand the work published by Hassan et al (56) found that the CV was more cost-effective based on the estimation of the incremental cost-effectiveness of colonoscopy versus the CV of 15,000 euros per LYG they considered very high. Now, although the decision to consider acceptable threshold is arbitrary strategy, it is true that this result would have been considered acceptable in the U.S. and most industrialized countries which would mean that it would eventually cost CV-effective when compared with traditional.
Overall, these results were very sensitive to the rate of compliance, so that the sensitivity analysis showed that if the rate is higher than the CV, this would be the most cost-effective. There is some evidence that this may be the preferred technique but not a universal finding.

Moreover extracolonic lesions finding was not taken into account in these economic studies and evidence suggests that costs could increase with CV. But if this rise is not followed by improved health outcomes in the cost-effectiveness ratio would be worse than estimated. And conversely if you can take steps to increase life expectancy (as in cases of kidney cancer or abdominal aortic aneurysm) would improve its cost-effectividad (65) relationship.

Furthermore cost ratio efectividad (56) also varied according to the estimated prevalence in advanced malignancy tiny polyps. That way when I was a 0.8% ratio fell incremental cost-effectiveness to <$ 100,000 while if the estimate was 0.09% in tiny polyps ≤ 5 mm the ratio was $ 464,407 per LYG and if estimated 0.5% for intermediate polyps (6-9 mm), the ratio is $ 59,015 per LYG.

All these data must be added the importance of the quality of colonoscopy as a key point also when considering the cost-effectiveness ratio of the CV. Pickhardt et al (56) and Sonnemberg et al (61) studies found differences of up to 10 times in the detection of adenomas between different endoscopists and the detection of adenomas ≥ 10 mm varied between 3-4 times.

The study of Heitman et al (64) showed that CV would be cost-effective if the perforation rate was 2 per thousand. Figures drilling recently described screening colonoscopy vary more than 20 times from 2.3 1000 to 0.1 per 1,000. Finally cecal correct intubation is highly variable and this is an important variable because it would increase the costs with the need to repeat the test. Studies in the U.S. have shown a cecal intubation rate of 97% (66) and the guides from this country are considered adequate if it reaches the 95% (67). The problem is that the CE studies do not include this variable in their estimates to compare the cost-effectiveness ratios between traditional colonoscopy and CV.

Conclusion

Most economic studies for the evaluation of the CV as the initial method of screening for CRC’s considered at least as cost-effective as traditional colonoscopy when tiny polyps are ignored. But these results are very sensitive to increased costs, rates of compliance and effectiveness of colonoscopy. Tiny lesion prevalence and natural history also impacts the results.

Moreover since the relative costs of the CV and traditional colonoscopy and acceptance and compliance rates are highly variable depending on the health system considered, the CV can be cost-effective in some places and not in others. Thus studies are needed with real data that could prospectively compare strategies to obtain definitive conclusions.

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References

9. Brown ML, Potosky AL, Thompson GB, Kessler LG. The knowledge and use of screening tests for


Illustrations

Illustration 1

Table 1: Screening tests in average-risk adults (20).

<table>
<thead>
<tr>
<th>Tests to detect primarily cancer</th>
<th>Tests to detect cancer and advanced lesions</th>
</tr>
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<tbody>
<tr>
<td>Guaiac-FOBT</td>
<td>Colonoscopy</td>
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<td>Inmune-FOBT</td>
<td></td>
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<tr>
<td>DNA-FOBT</td>
<td>Virtual colonoscopy</td>
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<td></td>
<td>Flexible Sigmoidoscopy</td>
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<td></td>
<td>Double-contrast enema</td>
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### Illustration 2

Table 2: Screening recommendations in average-risk population.

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendations</th>
</tr>
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<tbody>
<tr>
<td>American Cancer Society, US Multi-Society Task Force en Colorectal Cancer, and the American College of Radiology</td>
<td>Tests to detect primarily cancer and adenomas (acceptable options)</td>
</tr>
<tr>
<td></td>
<td>Older than 50 years Flexible sigmoidoscopy every 5 years. Colonoscopy every 10 years.</td>
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<tr>
<td></td>
<td>Double-contrast enema every 5 years.</td>
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<tr>
<td></td>
<td>Virtual colonoscopy every 5 years.</td>
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<tr>
<td>American College of Gastroenterology</td>
<td>Tests to detect primarily cancer (acceptable options)</td>
</tr>
<tr>
<td></td>
<td>Older than 50 years G-FOBT yearly</td>
</tr>
<tr>
<td></td>
<td>Inmune-FOBT yearly Fecal DNA (interval not clear)</td>
</tr>
<tr>
<td></td>
<td>Other options: FOBT yearly (level A), flexible sigmoidoscopy every 5 years, or combination of both.</td>
</tr>
</tbody>
</table>
Illustration 3

Table 3: ACRIN and IMPACT in diagnostic accuracy.

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Polyps &gt; 10 mm</th>
<th>Polyps &gt; 6 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSITIVITY ACRIN IMPACT</td>
<td>90%</td>
<td>78%</td>
</tr>
<tr>
<td>IMPACT</td>
<td>91%</td>
<td>85%</td>
</tr>
<tr>
<td>SPECIFICITY ACRIN IMPACT</td>
<td>86%</td>
<td>88%</td>
</tr>
<tr>
<td>IMPACT</td>
<td>85%</td>
<td>88%</td>
</tr>
<tr>
<td>POSITIVE PREDICTIVE VALUE ACRIN</td>
<td>23%</td>
<td>40%</td>
</tr>
<tr>
<td>IMPACT</td>
<td>Not evaluated</td>
<td>62%</td>
</tr>
<tr>
<td>NEGATIVE PREDICTIVE VALUE ACRIN</td>
<td>99%</td>
<td>98%</td>
</tr>
<tr>
<td>IMPACT</td>
<td>Not evaluated</td>
<td>96%</td>
</tr>
</tbody>
</table>
Illustration 4

Figure 1: Polyp in CV
Illustration 5

Figure 2: Polyp and rest of the colon in CV.
Illustration 6

Figure 3: Polyp and rest of the colon in CV.
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