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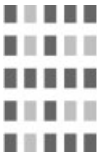

Cost-effectiveness analysis of two strategies for mass screening for colorectal cancer in France

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Summary

The implementation of colorectal cancer mass screening is a high public health priority in France, as in most other industrialised countries. Despite evidences that screening using guaiac fecal occult blood test may reduce colorectal cancer mortality, no European country has organised widespread mass screening with this test. The low sensitivity of this test constitutes its main limitation. Immunological tests, which provide higher sensitivity than the guaiac test, may constitute a satisfactory alternative. This study was carried out to compare the costs and the effectiveness of 20 years of biennial colorectal cancer (CRC) screening with an automated reading immunological test (Magstream) with those obtained with a guaiac stool test (Haemoccult).

The model used to estimate the costs and effectiveness of successive biennial CRC screening campaigns was a transitional probabilistic model. The parameters used in this model concerning costs and CRC epidemiological data were calculated from results obtained in the screening program run in Calvados or from published results of foreign studies because of the lack of French studies.

The use of Magstream for 20 years of biennial screening costs 59 euros more than Haemoccult per target individual, and should lead to a mean increase in individual life expectancy of 0.0198 years (i.e. about one week), which corresponds to an incremental cost-effectiveness ratio of 2980 euros per years of life saved.

Our results suggest that using an immunological test could increase the effectiveness of CRC screening at a reasonable cost for society. Copyright © 2003 John Wiley & Sons, Ltd.

Keywords colorectal cancer; cost-effectiveness; fecal occult blood test; mass screening; model simulation

Introduction

Colorectal cancer (CRC), which accounts for 15% of all cancers, is the second cause of cancer-related mortality in France [1]. More than 16 000 people die from colorectal cancer for 33 000 new cases diagnosed every year [2]. The implementation of efficient CRC mass screening is thus a high public health priority in France, as in most other industrialised countries.

Among the various techniques for screening CRC, search for occult blood in stools with the Haemoccult test is the most widely used. This test contains a vegetable substance (the guaïac) which has the property to change its colour in contact with haemoglobin. In case of positive test, a complementary examination is practised (colonoscopy) to confirm or not the presence of CRC or adenoma. The Haemoccult test can be used in two ways: with or without rehydration before lecture.

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In 1993, Mandel *et al.* were the first to demonstrate its effectiveness in a group of volunteers ; they found a 33% reduction in CRC-related mortality after 13 years of annual screening with the rehydrated test [3]. Nevertheless, the tests rehydratation entailed an increase of the positivity rate and led to practise a colonoscopy for a high proportion of persons screened. Considering such screening conditions could not be reproduced on large population, the two randomised trials performed in England and Denmark used a non-rehydrated Haemoccult test. They demonstrated a significant decrease in mortality of '15 and 18%' respectively after 8 and 10 years of biennial screening [4,5].

Despite these results, no European country has organised widespread mass screening with the rehydrated or non-rehydrated Haemoccult test. Decision makers and practitioners reluctance is mainly explained by the low sensitivity of this test. The test sensitivity defines the proportion of subjects with positive tests among people having the searched disease, while the test specificity defines the proportion of subjects with negative tests among healthy people. The low sensitivity of the non-rehydrated Haemoccult test contributes to the relatively minor decrease in specific mortality which it may be expected to obtain. In the English and Danish trials overall sensitivity of a biennial screening program with the test was about 50% [4,5]. It means that such a screening program detected only half of the asymptomatic cancers in the target population.

A number of countries such as Japan, the United States, Italy and Germany have become interested in a new type of test based on the use of a specific antibody of human haemoglobin. The most widely studied of these tests is the Immudia-HemSP test, more commonly known as HemeSelect test. In all of the comparative studies, the HemeSelect has been shown to have greater sensitivity than the Haemoccult test [6–9]. However, only two of these studies, the Italian and English ones, were performed on asymptomatic populations. The Italian study reported 100% sensitivity and 90.9% specificity for the HemeSelect and 85.7 and 96.2% for the rehydrated Haemoccult test [6]. The English study found 68.8% sensitivity and 94.4% specificity for the HemeSelect and 37.1 and 97.7% for the Haemoccult [7]. The HemeSelect test therefore seems to constitute a promising way of research for mass screening for colorectal cancer.

However, clinical effectiveness of a mass screening program is not a sufficient factor for justifying its introduction. Since the introduction of any new program requires the mobilisation of human and financial resources which could be earmarked for other public health expenditure, it is essential to demonstrate that the implementation of any new program is justified by the benefits that result from it. Until now, the HemeSelect test has been a more costly and time-consuming test than the Haemoccult test, so its wide scale use has not been possible. Yet now, there is a new automated reading technique available (Magstream) which considerably reduces laboratory costs and time. In France, in the Nord-Cotentin, a screening campaign in 43 000 people aged 50 to 74 years with this new generation of immunological test has been underway since January 2001.

The aim of the present study was to use a simulation model to analyse the costs and the effectiveness of 20 years of biennial CRC screening with an automated immunological test (Magstream) and to compare its results to those obtained with a guaiac stool test (Haemoccult).

Methods

The model

The model used to estimate the costs and effectiveness of the successive biennial CRC screening campaigns is a transitional probabilistic model (Markov model) [10]. Such a model makes it possible to simulate the trajectory of a hypothetical cohort through different states of health. It supposes that the timescale of the analysis is divided into several equal periods called "cycles". During each cycle, the members of the cohort move from one predetermined probability of a state of health to another. A cost and effectiveness (life expectancy) rating were assigned to each state of health. The model recalculated the population at each cycle after excluding deceased persons. Therefore, after successive iterations, the model estimated the cumulated costs and effectiveness for the whole cohort over the 20 years. The model was implemented using the TREEAGE DATA 3.5 software. The Markov decision tree is presented in Figure 1.

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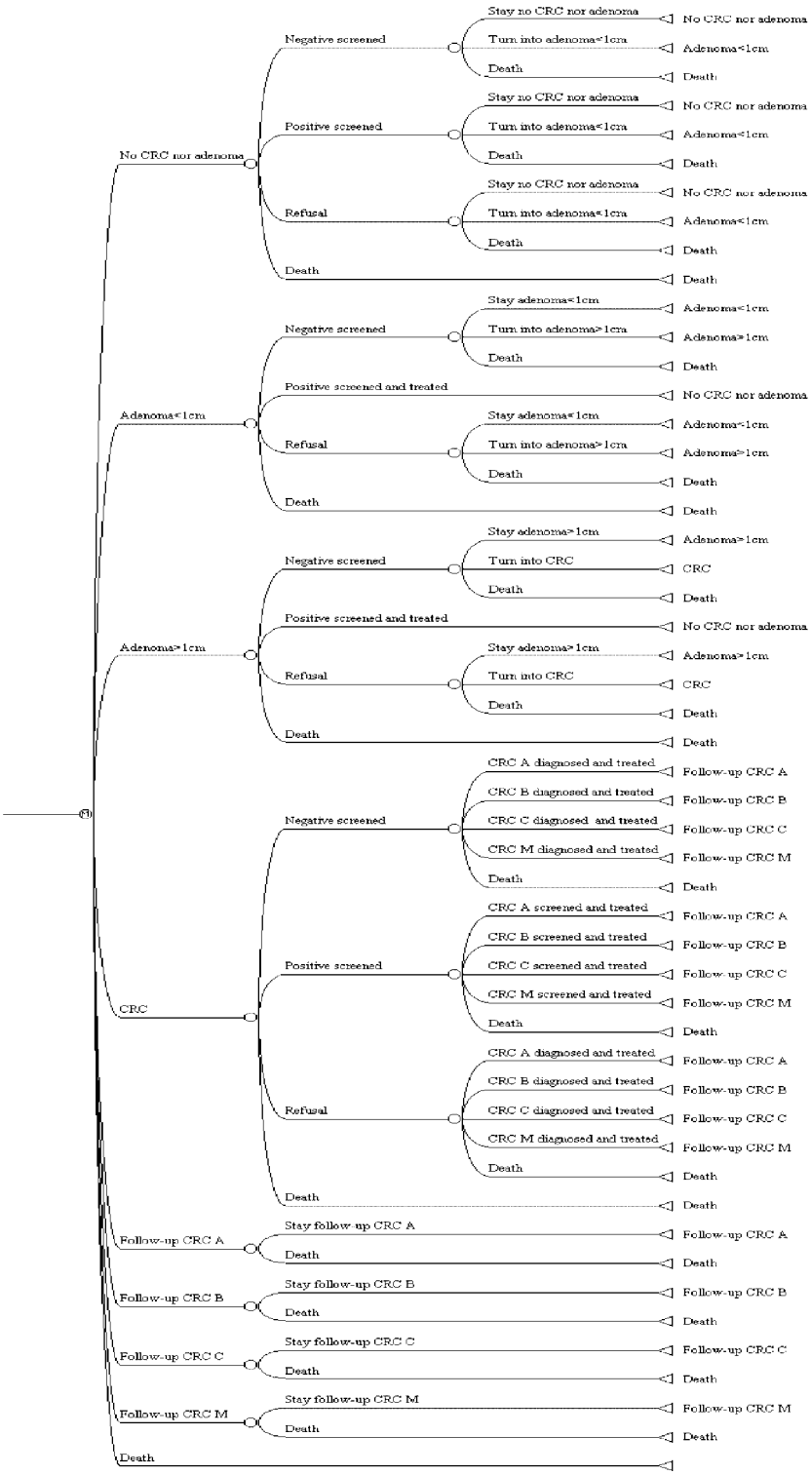

Figure 1. Markov-cycle tree corresponding to the colorectal cancer screening problem

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Parameters of model

The model has been built as much as possible with French data, supplemented where necessary by values derived from other countries studies. Most of the parameters of the model such as epidemiological and costs data were given by the evaluation of a screening program run in Calvados from 1991 to 1994 [11].

All parameters of the model are presented in Table 1.

Table 1. Parameters of model

Parameters	Values (ranges)	References
Natural history of the disease		
Prevalence of adenomas in relation to age (in %)	21–53 (26.9–58.7)	[14]
Annual probability of transition of adenoma <1 cm into adenoma >1 cm	0.02 (0.01–0.04)	[16]
Annual probability of transition of adenoma >1 cm into cancer	0.0085 (0.00425–0.017)	[16]
Frequency of CCR in screened individuals in relation to age/100 000	42.1–288	[15]
Frequency of CCR in patients refusing test in relation to age/100 000	52–590	[15]
Occurrence and distribution of CRCs per diagnostic stage	—	Digestive Tumour Registry Calvados
Rate of specific mortality of CRC at 1 to 10 years per diagnostic stage	—	
Quality of guaiac test		
Sensitivity (for cancer) of biennial screening as %	52	[5]
Specificity as %	99.5	
Quality of immunologic test		[19]
Sensitivity (for cancer) of biennial screening in %	82 (70–90)	
Specificity as %	96 (90–100)	
Rate of participation in %	43.7 (20–60)	[11]
Annual cost per individual (in euros)		
Organisation of campaign	0.38	[20]
Immunologic test		—
Purchasing	2.6	
Distribution	1.06	
Revelation	5.18	
Total	8.84	
Guaiac test		–
Purchasing	4.6	
Distribution	1.06	
Revelation	5.32	
Total	10.98	
Colonoscopy	457.35 (150–1000)	—
Treatment of stage A cancer	17 579 (14 063–21 095)	[21]
Treatment of stage B cancer	21 858 (17 486–26 230)	
Treatment of stage C cancer	31 110 (24 888–37 332)	
Treatment of metastasised cancer	17 384 (13 907–20 861)	
Annual rate for discounting costs (as %)	5	—

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Population. Our model simulated the evolution of an imaginary cohort of 165 000 individuals aged 50–74 years undergoing biennial CRC screening for 20 years. The rate of participation to screening in the model was set at 43.7%, level observed in the Calvados experiment.

Natural history of disease. The natural history of colorectal cancer was defined using six states and the transitional probabilities were estimated according to the status of the individuals in relation to screening (refusal, positive or negative).

The first state of the natural history of the disease was no cancer nor adenoma. People were free of disease and were proposed CRC screening. The true negative or false positive rates were calculated using the participation rate and the specificity of the screening strategy.

The second and the third states were adenoma <1 cm and adenoma >1 cm. Because prevalence of adenomas with regard to age in French population was not available, it was estimated from the results of three autopsy studies presented in Table 2 [12–14]. Since the study of Vatn *et al.* was the only one conducted on consecutive autopsy on cases from 50 years old, we used their results for the basic scenario of our model [14]. The ranges of the prevalence by age postulated in the sensitivity analysis resulted from the two other studies [12,13]. The proportion of adenoma <1 and adenoma >1 cm were respectively 80 and 20%. The detection rate of adenomas was based on the participation rate and the sensitivity of the screening strategy. We assumed that the test sensitivity for both types of adenomas was 3-fold inferior to the sensitivity for cancers. This hypothesis was based on the English trial results [7]. We also supposed that 100% of detected adenomas could be resected and patients with resected adenomas removed in the model in the state 'free of disease'. Among undetected adenomas, those <1 cm could turn into adenomas >1 cm, and adenomas >1 cm could turn into cancers. Probability of annual transition of adenomas <1 cm turning into adenomas >1 cm, and adenomas >1 cm turning into cancers were estimated from a Mayo Clinic study on non-resected adenomas [16].

The fourth health state was colorectal cancer stage A, B, C (according to Dukes classification) or metastasised. The occurrence and distribution of CRC according to age and diagnostic stage found in screening and according to the status of the individuals in relation to screening were calculated from results obtained in the screening program run in Calvados. The detection rate of cancers was based on the participation rate and the sensitivity of the screening strategy.

People with CRC diagnosed or screened were treated and then moved to the fifth state which was called 'follow-up'.

The last state was death. The probability of death among individuals who were free of disease was obtained from French life tables [17]. Specific CRC mortality rates at 1–10 years according to stage were obtained from the Digestive Tumour Registry in Calvados. Mortality resulting from accidents occurring during colonoscopic procedures was not taken into consideration owing to its low probability of occurrence (6/100 000) [18].

Characteristics of screening tests. Characteristics of screening tests estimates were issued from various population based studies presented in Table 3. The sensitivity and the specificity of biennial screening with the Haemoccult test were

Table 2. Autopsy studies of prevalence of adenomas by age (50–74 years).

Reference	Vatn *et al.* [14]	Arminski *et al.* [12]	Rickert *et al.* [13]
Subjects	445 autopsy examinations	1000 autopsy examinations	518 autopsy examinations
Prevalence by age (%)			
50–54	21	26.9	31.4
55–59			37.6
60–64	36	34.3	48.9
65–69			59.3
70–74	53	46.5	58.7

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Table 3. Characteristics of population-based studies of fecal occult blood (FOB) test for CRC screening

Reference	Subjects	Fecal occult blood test (FOBT)	Sensitivity (%)	Specificity (%)	Positivity rate
Mandel *et al.* [3]	46 551 volunteers offered annual screening	Haemoccult (rehydrated)	92	90.4	9.8%
Hardcastle *et al.* [4]	76 466 randomly participants allocated biennial screening	Haemoccult (unhydrated)	53	—	2.1% 1st screen, 1.2% 2nd screen
Kronborg *et al.* [5]	30 767 randomly participants allocated biennial screening	Haemoccult (unhydrated)	52	99.5	1% 1st screen, 1.8% 5th screen
Launoy *et al.* [11,25]	One screening round; 165 000 inhabitants of Calvados	Haemoccult (unhydrated)	66.3	—	2.8%
Faivre *et al.* [26,27]	Three screening rounds (45 500), Control (45 500)	Haemoccult (unhydrated)	48.7	—	2.3% 1st screen, 1.3% 2nd and 3rd screen.
Allison *et al.* [7]	8104 screenees	Haemoccult (unhydrated)	37.1	97.7	2.5%
		Immunological test	68.8	94.4	5.9%
Castiglione *et al.* [6]	1725 screenees	Haemoccult (rehydrated)	85.7	96.2	5.4%
		Immunological test	100	90.9	11.4%
Saito *et al.* [8]	5715 asymptomatic individuals who underwent flexible sigmoidoscopy as well as FOBTs	Immunological test	88.9	93.4	6.8%
Zappa *et al.* (19)	41 774 subjects offered biennial screening	Immunological test	82	—	4.5%1st screen, 3.7% at subsequent

estimated from results of the Danish trial to, respectively, 52 and 99.5% [5]. The Danish sensitivity estimate were judged more representative than the French's one because the French experience consisted in only one round screening. Sensitivity and specificity of screening with the immunologic test were estimated to be 82 and 96% on the basis of results of the Italian study since it presented the larger follow-up among studies on immunologic test [19], a large range of different values being used in the sensitivity analysis.

Costs. The point of view adopted for this analysis was that of the screening organiser, i.e. the Social Security Service. Therefore, the modelling of costs included all direct costs related to management of cancers. This included the cost of organising the screening campaign (public information, running costs), costs of purchasing, distributing and interpreting the tests, costs of explorations performed in individuals with a positive test, costs of diagnosing cancers in individuals with a negative test, the cost of treating cancers and the cost of follow-up.

The costs of organising the campaign and the costs of explorations were considered to be those already incurred in the Calvados screening program. Total annual cost of organising the campaign had been assessed by the Social Security Department to 63 256 euros (which corresponded

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to 0.38 euros per target person), it comprised communication expenditures (meeting, poster, leaflet) and running expenditures (mission, office stationery, transport) [20].

The costs of purchasing and interpreting the guaiac and immunologic tests used in the model were taken to be those incurred by the Regional Health Institute in Tours, which had performed all tests of the Calvados screening campaign and which is performing all tests of the current study set up in the Manche department. Moreover, to the cost of the Magstream was added an additional 0.01 euros per individual corresponding to the cost of the machine used for performing the immunologic test.

The mean cost of colonoscopy was estimated to be 457.35 euros as observed in the Calvados screening experience. It ranged from 150 to 1000 euros depending on whether colonoscopy was practised in a surgery or in a private clinic.

Costs of treating cancers with regard to diagnostic stage were estimated using data from the Digestive Tumour Registry of Calvados and Social Security data on reimbursements for treating all CRCs incident in the Department of Calvados during the period 1st September 1997 to 31st August 1998 [21]. They were constituted of: hospital care (both public and private) and care given in the medical departments of retirement homes; outpatient care (specialised or non-specialised medical consultations, medical and paramedical acts); transportation for medical reasons; medical purchases such as pharmaceutical products and prosthesis (colostomy bags); and assistance provided to patients such as daily payments and other allowances (disability with or without recourse to a third person). Costs were estimated to be 17 579 euros for treating a Dukes A CRC, 21 858 euros for treating a Dukes B CRC, 31 110 euros for treating a Dukes C CRC and 17 384 euros for treating a metastasised CRC.

The cost of follow-up corresponded to the cost of one colonoscopy performed every three years as recommended by French gastroenterologists.

Results

Costs

Table 4 presents the costs of 10 and 20 years of biennial CRC screening with a guaiac test (Haemoccult) and an immunologic test (Magstream). It may be noted that the individual mean cost of managing CRCs (screening, diagnosis and treatment) was greater with the Magstream than with the Haemoccult test, whatever the duration of screening. Thus, five biennial screening campaigns cost 230 euros per target individual (including refusals) with the immunologic test compared to 177 euros per target person with the guaiac test. With the 10 biennial screening campaigns, the cost was 316 euros per target individual with the immunologic test and 234 euros per target individual for the guaiac test.

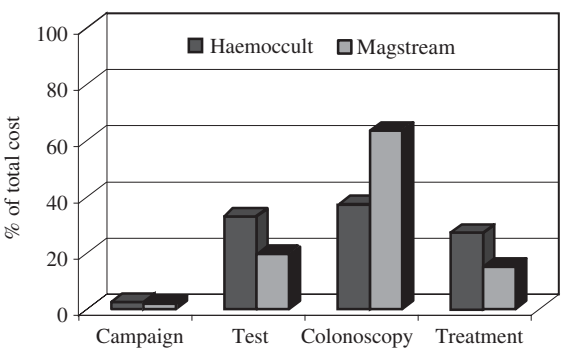

Figure 2. Costs distribution for 20 years of biennial screening for CRC with Haemoccult and Magsream tests

Table 4. Incremental cost-effectiveness ratio (in euros per YLS) of substituting Magstream test for Haemoccult test in relation to duration of screening.

Duration of screening	Cost (in euros/ targeted person)		Discounted cost (in euros/targeted person)		Effectiveness (in life-years)		Incremental cost-effectiveness ratio (in euros/YLS)	Discounted incremental cost-effectiveness ratio (in euros/YLS)
	Mag-stream	Haem-occult	Mag-stream	Haem-occult	Mag-stream	Haem-occult		
10 years	230	177	195	151	9.7960	9.7901	8983	7458
20 years	316	234	238	179	16.7201	16.7003	4141	2980

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In order to explain the excess of expense relative to the use of Magstream rather than Haemoccult, we have detailed the costs structure over the 20 years as a function of the test (Figure 2). It shows that the relative costs of purchasing, distributing and interpreting the tests, the costs of colonoscopy and the costs of treatment were significantly different according to the test used. Relative costs related to colonoscopies were higher with the Magstream (63% of total cost) than with the Haemoccult test (37% of total cost). On the contrary, the proportional cost for purchasing, distributing and interpreting the Haemoccult tests was 68% greater (33% of total cost) than the proportional cost for purchasing, distributing and interpreting the immunologic test (20% of total cost). The treatment costs relative to screening with the Haemoccult test were also greater than those with the Magstream test (27% versus 15% of total cost).

Effectiveness

In view of the hypotheses contained in our model regarding the quality of the tests, immunologic testing proved to be more efficient than guaiac testing, whatever the duration of screening. Table 4 shows that 10 years of biennial screening with the Magstream test provided a mean survival per target individual of 9.796 years, while 10 years of screening with the Haemoccult test led to a mean survival per target individual of 9.7901 years. Similarly, 20 years of Magstream testing gave a mean survival of 16.7201 years as opposed to 16.7003 years for the Haemoccult test.

Cost-effectiveness ratios

The costs and effectiveness of the two screening strategies in relation to duration of screening were compared using incremental cost-effectiveness ratios in which the Haemoccult test was replaced by the Magstream test. These ratios (Table 4) were respectively 8983 euros per years of life saved (YLS) and 4141 euros/ YLS for 10 and 20 years of biennial screening. When the costs were discounted by 5%/year, these ratios were 7458 euros/YLS and 2980 euros YLS. In practice, this means that using the Magstream test for 20 years of biennial screening costs the equivalent of 59 euros more than the Haemoccult test per target individual, and should lead to a mean increase in targeted individual life expectancy of 0.0198 years (i.e. about one week).

Sensitivity analysis

Sensitivity analysis was performed to assess the ranges of the cost-effectiveness ratios using different assumptions about the participation, the cost of Haemoccult test, the cost of colonoscopy, the cost of CRC treatment, the quality of immunologic test, and the natural history of disease. Assumptions and results are presented in Table 5.

Incremental cost-effectiveness ratios were positively correlated to participation rates. For example, a decrease in participation from 43.7 to 20% led to a 50% decrease in incremental cost-effectiveness ratios, and an increase in participation from 43.7 to 60% led to a 1.3-fold greater incremental cost-effectiveness ratio for 10 years of biennial screening and a 1.5-fold greater for 20 years of screening.

While supposing that the total cost of the Haemoccult test was the same as the Magstream test, we obtained an incremental cost-effectiveness ratio of 4898 euros per YLS for 20 years of screening which corresponded to a 18% increase when comparing to the basic scenario.

Cost-effectiveness ratios were positively correlated to the costs of colonoscopy. When the latter increased from 457.33 euros to 1000 euros, cost-effectiveness ratios increased 1.5-fold. On the other hand, a decrease in the cost of colonoscopy from 457.35 euros to 150 euros led to a 93% decrease of the cost-effectiveness ratio when comparing to the basic scenario.

On the contrary, cost-effectiveness ratios were negatively correlated to the costs of treatment. A 20% increase of the costs of treatment led to a 2% decrease of the cost-effectiveness ratio for 20 years of biennial screening and a 20% decrease of the costs of treatment entailed a 4% increase of the cost-effectiveness ratio.

For a given specificity, cost-effectiveness ratios were negatively correlated to the sensitivity of the immunologic test. With a 90% specificity and screening lasting 20 years, the cost-effectiveness ratio was 26 107 euros/YLS if sensitivity was taken to be 70%, while it was only 13 102 euros/YLS with sensitivity at 90%. For a given sensitivity, cost-effectiveness ratios were negatively correlated to the specificity. Therefore, with 70% sensitivity,

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Table 5. Sensitivity analysis of incremental cost-effectiveness ratio (in euros YLS) of substituting Magstream test for Haemoccult test in relation to duration of screening.

Variable	Base-case values	Sensitivity analysis Values	Source or hypothesis	Incremental cost–effectiveness ratios in relation to duration of screening (in euros/YLS)	
				10 years	20 years
Reference				8983	4141
Participation	43.7%				
		20%		4400	2260
		50%		15250	9700
		60%		21166	11000
Total cost of guaiac test (in euros)	10.98	8.84	Equal to total cost of immunologic test	10 678	4898
Cost of colonoscopy (in euros)	457.35				
		150		508	303
		—			
		600		12 881	5960
		1000		23 518	10909
Cost of CRC treatment according to stage (in euros)	(Table 1)				
		—	Base case value decreased of 20%	9322	4293
		—	Base case value increased of 20%	8644	4040
Sensitivity (Se) and specificity (Sp) of immunologic test	Se = 82%, Sp = 96%				
		Se = 70%, Sp = 90%		52 013	26 107
		Se = 70%, Sp = 100%		−6923	−3607
		Se = 90%, Sp = 90%	6, 7, 8, 19	33 830	13 102
		Se = 90%, Sp = 100%		−3617	1953
Prevalence of adenomas in relation to age	21–53%				
		31.4–58.7%	13	11 202	5750
		26.9–46.5%	12	9608	4704
Annual transition rate					
Adenoma < 1 cm to adenoma > 1 cm	0.02				
		0.01	Base case value *0.5	13 500	7107
		0.04	Base case value/0.5	7091	2872
Adenoma > 1 cm to cancer	0.0085				
		0.00425	Base case value *0.5	10 501	5764
		0.017	Base case value/0.5	7843	3227

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the cost-effectiveness ratio was 26 107 euros/YLS if specificity was taken to be 90%, while it was −3607 euros/YLS with a 100% specificity. Such a change in sign of the incremental cost-effectiveness ratios indicated that screening with the Magstream was then more efficient and less costly than with the Haemoccult test.

Cost-effectiveness ratios were also very sensitive to variations in the natural history of CRC. When we replaced the adenoma prevalence state in our model with those obtained in the study by Rickert *et al.* [13], cost-effectiveness ratios were until 38% greater than those obtained in our model. On the other hand, when we used the adenoma prevalence data obtained by Arminsky *et al.* [12], this had a lesser impact on our results since it led to an increase in cost-effectiveness ratios of only 7 and 14% according to the duration of screening. With regard to the evolution of CRC, cost-effectiveness ratios decreased as the speed increased at which adenomas <1 cm became adenomas >1 cm and the speed at which latter became cancers.

Discussion

Our model makes it possible to estimate the incremental cost–effectiveness ratio resulting from substituting the Magstream automated interpretation immunologic test for the Haemoccult test. With a 20-year period involving biennial screening and a 43% participation rate, the discounted ratio is 2980 euros/YLS. The Magstream test costs 59 euros more per target person than the Haemoccult test, and led to a mean increase in individual life expectancy of 0.0198 years (about one week). The added cost incurred through using the Magstream test is mainly due to the larger number of colonoscopies performed because of an higher positivity rate. Our data show that using an immunological test like the Magstream could increase the effectiveness of CRC screening by the search for occult blood in the stools at a reasonable cost for society.

The reliability of the results obtained with this model is mainly due to the pertinence of the initial hypotheses.

The analysis of sensitivity performed on the variable parameters of our model (participation rate, cost of Haemoccult test, cost of colonoscopy, cost of CRC treatment, quality of immunologic test, prevalence of adenomas, rate of evolution of adenomas) made it possible to evaluate the robustness of the results obtained.

The rate of participation is one of the most uncertain variables in CRC screening. In France, the health care system is characterised by a strong liberal tradition, and, due to lack of public health awareness, high participation rates are more difficult to achieve than in North-European countries such as Great Britain, Sweden and Denmark. To assess the consequences of variations in participation rate on the incremental cost-effectiveness ratios, we applied three hypotheses. The 'pessimistic' hypothesis postulated a 20% participation rate, the 'median' hypothesis a 50% participation rate and the 'optimistic' hypothesis considered participation to be 60%. Results show that the incremental cost-effectiveness ratios increased as the participation rate increased as it has been observed in a previous study [22]. The extra costs increase due to participation rate increase seem not be compensated by gains in effectiveness (higher mortality reduction).

The costs of Haemoccult and Magstream tests used in our analysis were those practised by the suppliers at the moment of the study. However, the evolution of these prices is unknown. If the marketing of the Magstream test would come into general use, the Haemoccult supplier is likely to drop the price to face to competition. While supposing that the cost of the Haemoccult test was the same as the Magstream test, we established an 18% increase of the incremental cost-effectiveness ratio. Such a strategy would reinforce the cost advantage of the Haemoccult screening strategy.

In France, there is a wide variety of practice concerning the conditions in which colonoscopies are performed, in particular the sedation modalities used. Therefore, the cost of colonoscopies varies considerably according to the place in which they are practised (in the surgery, in public or private hospitals forming part of the public network, or in private clinics). In our analysis of sensitivity, we postulated that the cost of a colonoscopy varied from 150 to 1000 euros. Incremental cost-effectiveness ratios were very sensitive to these variations, decreasing considerably as colonoscopy costs decreased. This effect was probably compounded by the fact that the difference in cost between the two screening strategies is mainly due to the number of colonoscopies performed.

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In view of the paucity of results regarding the effectiveness of screening with immunologic tests, we also tested various hypotheses concerning the qualities of this test. We found that the higher the specificity and the lower the sensitivity, the lower the cost-effectiveness ratio, which was not surprising. In the extreme scenario, where specificity was maximal (100%), the strategy with Magstream test was at once more effective and cheaper.

Moreover, cost-effectiveness ratios proved to be very sensitive to variations concerning the natural history of adenoma and cancer. The influence of these factors has already been demonstrated in various cost-effectiveness studies [22,23] and underlines the importance of a better understanding of the course of CRC in order to improve estimation of the effectiveness of screening strategies.

Except two scenarios (in which specificity was supposed to be 100%), the sensitivity analysis results are very consistent to suggest that the strategy with immunologic test was more effective and more expensive than the strategy with guaiac test. Since most of parameters included in our model are derived from French studies, our results fit well with screening organisation in France. The way they can be generalizible for other countries mainly depend on differences in costs: colorectal cancer treatment cost in a minor extent and colonoscopy cost in a greater extent.

Since the point of view adopted for the cost analysis was that of the social insurance, costs were proxied by charges data, although we recognize that charges do not always represent true costs. At our knowledge, better estimates of costs in relation to CRC were not available in France. This approach may lead to an underestimation of costs. However, the cost of a biennial screening program estimated with our model is higher than that obtained in the only other French study (in Burgundy) having analysed costs and effectiveness of CRC screening [24]. That study used a simulation model to evaluate the effectiveness of various CRC screening strategies using the Haemoccult test. It estimated the non-discounted cost of offering screening every two years to all members of the French population between 45 and 74 years to be the equivalent of 1 311 823.793 euros for a 45% participation rate. This corresponds to a cost of about 76.22 euros per target individual. In our study, this cost was 234 euros per target individual for screening with the Haemoccult test and 316 euros per target individual for screening with the Magstream test. The costs of treatment in relation to stage of extension of cancers in our model were greater than those in the Burgundy study. Moreover, all people with a positive screening test were supposed to undergo a colonoscopy in our study while acceptability of colonoscopy were of 85% in the Burgundy study. However, these differences cannot explain the whole extent in difference in cost per target individual and one must invoke differences in model parameters especially those concerning natural history of the disease.

In conclusion, our results suggest that immunologic fecal occult blood test could provide a substantial increase in sensitivity and thus in screening effectiveness. Moreover, the use of automated interpretation allows to get such a benefit with a reasonable increase in costs. Forthcoming results of French population based experiment with immunologic test will confirm or not our hypothesis concerning quality of immunologic test. In a positive case, immunologic fecal occult blood tests with automated interpretation will provide the health authorities with a satisfactory alternative to guaiac tests, both in terms of effectiveness and cost.

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