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ORIGINAL PAPER

The influence of waiting times on cost-effectiveness: a case study of colorectal cancer mass screening

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Abstract When a cost-effectiveness analysis is implemented, the health-care system is usually assumed to adjust smoothly to the proposed new strategy. However, technological innovations in health care may often induce friction in the organization of care supply, implying the congestion of services and subsequent waiting times. Our objective here is to measure how these short run rigidities can challenge cost-effectiveness recommendations favorable to an innovative mass screening test for colorectal cancer. Using Markov modeling, we compare the standard Guaiac fecal occult blood test (gFOBT) with an innovative screening test for colorectal cancer, namely the immunological fecal occult blood test (iFOBT). Waiting time can occur between a positive screening test and the subsequent confirmation colonoscopy. Five scenarios are considered for iFOBT: no further waiting time compared with gFOBT, twice as much waiting time for a period of 5 or 10 years, and twice as much waiting time for a period of 5 or 10 years combined with a 25 % decrease in participation to confirmation colonoscopies. According to our modeling, compared with gFOBT, iFOBT would approximately double colonoscopy demand. Probabilistic sensitivity analysis enables concluding that the waiting time significantly increases the uncertainty surrounding recommendations favorable to iFOBT if it induces a decrease in the adherence rate for confirmation colonoscopy.

Keywords Health-care organization · Cost-effectiveness analysis · Waiting time · Colorectal cancer screening · Markov model

JEL Classification I19

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Introduction

The allocation of health-care resources is increasingly supported by cost-effectiveness analyses (CEA). When an existing health-care strategy is compared to an alternative, CEA usually implicitly assumes that the health-care system smoothly adjusts to the conditions of the alternative. However, the organizational impact resulting from the implementation of a new strategy may involve more or new procedures, additional skilled staff, new training methods, etc. Not taken into account in CEA, these changes in the production process can lead, in the short run, to overestimating the expected effectiveness and to underestimate the expected costs of the new strategy, which can eventually challenge the recommendations provided to the health decision makers [1].

Some production factors are indeed not flexible in the short run, meaning that the resources initially dedicated to the old strategy cannot be immediately freed and directed to the new one [2, 3]. Concurrently, the adoption of the new technology may create shocks in the demand for this new health care. When the health-care supply cannot immediately adjust to the new demand, organizational

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concerns appear that can raise considerable equity and efficiency problems. One of the main such concerns is probably waiting time. Admittedly, pricing could provide an answer to the adjustment problem [4]. Alternatively, a health insurance differential among patients reducing waiting time could also be envisaged [5]. These solutions may raise ethical concerns. We consider here the case when no pricing or insurance differential among patients is allowed. If these solutions are ruled out, then the congestion of health services implies waiting times. For other types of public services, congestion can be dealt with through a decrease in quality (a crowded swimming pool, for instance). Here, we do not consider this possibility. In our case, the waiting list is thus an indicator of imperfect adjustment between supply and demand of health care. The more imperfect the adjustment is, the longer the waiting list. What are the consequences of such imperfections in terms of efficiency? The methodological investigation by Koopmanschap et al. [6] demonstrates that waiting times could have a significant impact on cost-effectiveness, especially when they lead to irreversible health losses.

We concentrate here on waiting times associated with mass screening campaigns, with an empirical focus on colorectal cancer (CRC). Screening aims at shortening the time between the inception of a disease and its diagnosis in order to improve survival rates. Time management is therefore of major importance when evaluating a screening strategy of which clinical benefits are usually estimated in randomized clinical trials. These trials enable rigorously measuring the effects solely attributable to medical interventions. Nevertheless, they are performed in an artificial environment that necessarily differs from the actual practice and where no shortage in facilities or medical staff is usually observed [7]. To our knowledge, no study has ever investigated the consequences of waiting times on the robustness of CEA recommendations for a mass screening strategy. Our study proposes to use decision analytical modeling to measure how these short run rigidities can challenge CEA recommendations favorable to an innovative mass screening test for CRC.

Colorectal cancer is the second most prevalent cause of cancer-related mortality in most western countries [8]. Insofar as the removal of precancerous lesions (adenomas) and the detection of early asymptomatic CRC have been demonstrated to prevent the disease or to improve the survival rate, interest in mass screening has been growing. Currently in Europe the average risk population for CRC is mainly screened with a Guaiac fecal occult blood test (gFOBT) [9]. Patients with positive gFOBT results are referred to colonoscopy for a confirmation diagnosis. However, gFOBT is increasingly challenged by the immunological fecal occult blood test (iFOBT). This other fecal occult blood test is indeed more sensitive than gFOBT and may thus enhance the detection of adenomas and CRC [10]. Nevertheless, it is also less specific. In other words, a greater number of healthy patients may have positive screening tests, inducing invitations to unnecessary colonoscopies. Currently, iFOBT is not proposed for mass screening, but several pilots are being or have been carried out in France, Hungary, and The Netherlands [10–12].

Previous CEAs have demonstrated that iFOBT could increase the effectiveness of CRC screening at a reasonable cost in the French context [13–15]. However, none of them have considered the possible imperfect adjustment of the health-care system due to the significant increase in colonoscopy demand induced by iFOBT. Indeed, fecal occult blood tests merely enable selecting patients, while colonoscopy is the only way to diagnose cancer and to remove precancerous lesions. The waiting time between the positive screening test and the confirmation colonoscopy could thus impact both the effectiveness and the cost of the screening strategy: the longer a patient waits for the diagnosis, the more his or her cancer is likely to evolve toward an advanced stage, and consequently the lower the survival rate is and the more expensive treatment costs are. This problem is far from speculative. Kanavos and Schurer [9] have recently provided a strong rationale for empirical investigations in this field. Indeed, in their analysis of 17 countries, they highlight that a main concern with regard to CRC screening is the endoscopy capacity, pointing out that "[t]he proper management of this resource is vital" [9]. Many countries, like for instance the UK, indeed experience difficulties meeting the increasing colonoscopy demand [9, 16]. The case of Denmark is even more drastic since a national screening program has not yet been implemented partly due to shortages of skilled staff for colonoscopy [17].

In this context, a stimulating study dealing with waiting times at a micro-level is provided by Berg et al. [18]. It uses a discrete event simulation model to identify, quantify, and cope with queues in a colonoscopy suite facing variations in demand for colonoscopy screening. Alternatively, at the macro-level of mass screening, Wilschut et al. [19] used CEA to define alternative iFOBT strategies that could be cost-effective compared with gFOBT taking into account colonoscopy capacities. Alternative scenarios with iFOBT are determined by varying the definition of the screened population, the frequency of the screening or surveillance of the treated population. They then select iFOBT strategies for which the generated demand for colonoscopy would not exceed supply. Conversely, our study investigates the consequences of the discrepancy between supply and demand for colonoscopy on recommendations initially favorable to iFOBT. In our study, the conditions under which iFOBT could be implemented in France are already set and therefore considered exogenous.

In order to determine whether waiting times could challenge previous recommendations favorable to immunological tests, our study is organized as follows. First, we present the screening model upon which the simulations are based. We then move on to the validation of this model with respect to existing screening campaigns at the regional level in France. After simulating colonoscopy demand according to various screening strategies, the impact of waiting times on cost-effectiveness recommendations is investigated. Final comments conclude our study.

Methods

In order to compare alternative screening strategies, we base our study on the modeling framework developed in Chauvin et al. [15]. The model enables describing the screening process, the treatment procedures and the follow-up of patients either screened or diagnosed by symptoms. The same epidemiological parameters as in [15] are used, and they are summarized in "Appendix 1". The decision tree illustrating the screening process is depicted in Fig. 1.

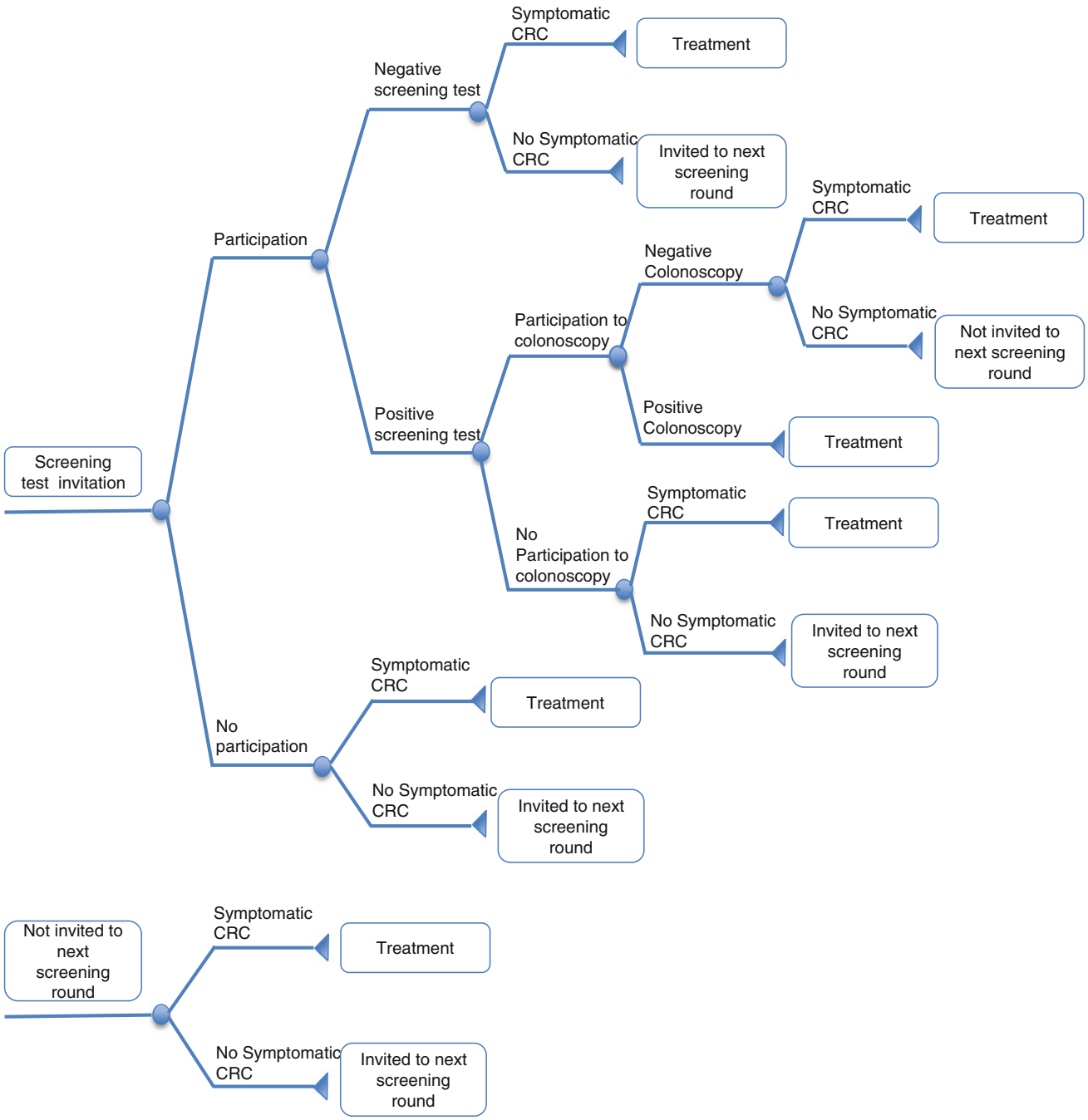

Fig. 1 Markov model

Table 1 Age distribution and adherence rate for screening tests of the population in Ille-et-Vilaine in 2003 according to age and gender

Age range	Variables			
	Age distribution [21]		Adherence rate for screening test [22]	
	Male (%)	Female (%)	Male (%)	Female (%)
50–54	29	27	41	48
55–59	22	21	52	61
60–64	17	16	54	61
65–69	17	18	55	60
70–74	15	18	48	49

Individuals invited to screening are at average risk for CRC: they are between 50 and 74 years old without personal and family-related medical histories. When the screening test is positive, an optical colonoscopy (the confirmation test) is proposed. Adherence rates according to age and gender are presented in Table 1. Patients with a positive screening test are invited to a confirmation colonoscopy. The adherence rate to the confirmation proposal is assumed to be 90.7 % [20]. Patients with a negative confirmation test are not invited to the next screening round, while patients with a positive confirmation test are treated for their adenomas or CRC. If they survive, the follow-up of these patients consists of a colonoscopy every 5 years, for which we assume a 100 % participation rate. Markov modeling describing treatments and lifelong follow-up are not detailed in this article (see [15] for a full description of that embedded Markov model). Patients diagnosed by symptoms in the interval between two screening rounds are also treated for their CRC, and if they survive they benefit from the same follow-up as screened patients. Simulations are programmed with MATLAB®.

In order to properly predict variations in demand for colonoscopy, and conversely to most studies of mass screening that consider the evolution of a single cohort from the age of 50 (or any relevant starting age), our modeling framework considers here successive cohorts that are included year after year. The initial cohort has the same distribution for age and for gender (47 % males and 53 % females) as the population of Ille-et-Vilaine, a French administrative region (*département*) that is a pilot in screening campaigns [23]. The age distribution of the modeled population is detailed in Table 1. Every year, a new population of age 50 is added to the initial cohort. Eventually, we assume that there is no migration: once in the cohort, no individual leaves it (except of course when they die).

The time horizon is 20 years as in [13] and [14] for comparability purposes. Cycle length is 45 days (this cycle length will be justified later). In this framework, three strategies are compared. The first strategy is the absence of screening. The second and third ones are biennial gFOBT and biennial iFOBT respectively. Characteristics of the screening and confirmation tests are summarized in Table 2. The perspective is that of a third-party payer. Costs for colonoscopies and related complications are taken from the 2010 French classification for diagnosis-related groups (DRG) [24]. FOBT costs and treatment costs are based on published data [14, 25] and are inflated to 2010 values. "Appendix 1" describes how these inflated costs are computed.

The two screening strategies may face a variety of imperfect adjustments of the health-care system during their implementation, and the model could help identify and quantify them. We nevertheless restrict this imperfect adjustment to the waiting time elapsing between a positive screening test and the subsequent confirmation colonoscopy. Specifically, waiting time includes the intervals between: the (true or false) positive screening test result and the appointment with the general practitioner (GP); the appointment with the GP and the appointment with the endoscopist; the appointment with the endoscopist and the date of the confirmation colonoscopy. In practice, where gFOBT is implemented, waiting times do exist and they are taken as a benchmark for our study. This benchmark is put at 45 days. It corresponds to the actual waiting time between a positive screening test and the confirmation colonoscopy observed in the French pilot region Ille-et-Vilaine [22]. This benchmark also provides the rationale for the cycle length in our Markov model. The mean

Table 2 Characteristics of the screening and confirmation tests

Parameter (%)	gFOBT [26]	iFOBT [26]	Optical colonoscopy [20, 27, 28]
Sensitivity adenomas 1–5 mm	2	5	74
Sensitivity adenomas 6–9 mm	5	10.1	87
Sensitivity adenomas ≥10 mm	12	22	98
Sensitivity cancers	40	70	98
Specificity	98	95	100
Complication rate	*n.r*	*n.r*	0.22
Compliance after positive screening test	*n.r*	*n.r*	90.7

n.r not relevant

Table 3 Comparison of field and simulated results for the gFOBT strategy during the first screening round

	Field results [20]	Simulated results
Target population included	187,342	
Positive gFOBT results	2,477 (2.6 %)	2,880 (2.94 %)
Confirmation colonoscopies	2,246	2,603
Negative confirmation colonoscopies	1,266 (56 %)	1,074 (41 %)
Subjects with low-risk adenomas	484 (12 %)	803 (31 %)
Subjects with high-risk adenomas	259 (22 %)	484 (17 %)
Subjects with CRC	237 (11 %)	291 (11 %)

waiting time at the French national level is not known. Simulations of iFOBT consider five alternative scenarios. The first one involves no further waiting time than with gFOBT. This optimistic scenario is denoted iFOBT-45d. The second set of scenarios describes situations where the health-care system cannot immediately fully adjust to the new demand for colonoscopies, which doubles the waiting time to 90 days. When these rigidities are solved out (thanks to new trained endoscopists, new infrastructures, and so on), the waiting time falls again at 45 days. Two durations of the rigidity period are modeled for iFOBT: the 5 year (iFOBT-90d-5y) and 10 year (iFOBT-90d-10y). Finally, we investigate the possibility that the 90-day waiting time induces a decrease in participation with confirmation colonoscopies, since waiting time seems to have a negative impact on the adherence rate for colonoscopy after a positive screening test [29]. One can hypothesize that when facing delayed appointments for confirmation colonoscopy, a proportion of the patients may give up going on with the screening process. Although the underlying psychological or social causes of such behaviors fall beyond the scope of this study, the likelihood of dropouts in mass campaigns justifies investigating its consequences on cost-effectiveness. In this respect, screening campaigns are susceptible to such behaviors since subjects are not (yet) patients: diseased or not, they are wrongly or rightly asymptomatic, which can affect their degree of concern about the very interest of the battery of tests they are proposed to undertake. To our knowledge, no study has ever measured the magnitude of this decrease in patients' participation due to waiting time. We therefore decided on a pessimistic scenario where a 25 % decrease in participation is observed during the period when supply has not yet adjusted to demand. This decrease is successively included in the last two scenarios when rigidities last for 5 years (iFOBT-90d-5y-P) and for 10 years (iFOBT-90d-10y-P).

A probabilistic sensitivity analysis (PSA) for every screening strategy with 1,000 simulations is finally carried out to test the robustness of our recommendations because of uncertainty in model parameters. Cost and frequency parameters are respectively assumed to be log-normally distributed and beta-distributed [30]. Cost-effectiveness acceptability curves are then used to express the probability to be optimal over a given range of the willingness to pay (WTP) of the third-party payer [31].

Results

Validation

In order to check the consistency of our modeling, we first compare our simulation results for the gFOBT strategy after the first screening round with what has been observed in the French administrative region Ille-et-Vilaine during its first colorectal screening campaign in the average-risk population. This first round was carried out in 2003 and 2004, and its results are detailed in Manfredi et al. [20]. Our base case results being computed with the adherence rates for screening and colonoscopy observed in Ille-et-Vilaine during this first round, we can directly compare our results with those of Manfredi et al. [20]. Results of simulation for the whole screened population are shown in Table 3. Simulation results distinguishing male and female results are presented in Table 9 in "Appendix 2".

Estimated positivity rates between simulated and field results are rather close. The most noticeable difference stems from a greater number of detected adenomas in the simulation. This difference may be due to a higher adenoma prevalence rate in the simulated population than in the Ille-et-Vilaine target population, subsequently inducing a higher positivity rate for the screening test. As a consequence, our model may somewhat overestimate the number of colonoscopies required by the screening campaign.

The second step of validation involves a middle-term assessment of a screening campaign by Faivre et al. [32]. Their randomized controlled trial included nearly 100,000 individuals aged 45–74 years who were allocated to either gFOBT screenings (six rounds were performed) or to no screening. After 11 years of implementation of biennial gFOBT, Faivre et al. [32] estimated a 17 % mortality reduction for CRC. To compare our modeling results with this randomized controlled trial, we use the mean

Table 4 Simulated colonoscopy demand over a 20-year horizon

	No screening	gFOBT	iFOBT
Interval CRC colonoscopy (I-COL)	5,371	3,342	2,303
Confirmation colonoscopy (C-COL)	0	27,195	59,732
Surveillance colonoscopy (S-COL)	2,002	15,349	28,588
Total	7,373	45,886	90,623

adherence rates for screening (55.3 %) and for colonoscopy (87 %) observed in [32] while keeping other parameters unchanged. Our simulation reaches a 13 % mortality reduction after 11 years of biennial gFOBT screening. Our model may thus underestimate the mortality reduction, so the increase in effectiveness consecutive to the implementation of gFOBT may be underestimated. Still, we find the results consistent with this reference study.

Simulation of colonoscopy demand

When a screening program is implemented, colonoscopy demand takes three forms. The first category is denoted I-COL (I for interval between two screening rounds); it encompasses colonoscopies triggered by symptomatic CRC. They can involve individuals who were non-compliant to screening as well as compliant subjects whose lesions were missed at screening. The second category, C-COL, represents confirmation colonoscopies after a (true or false) positive screening test. The third category consists of surveillance colonoscopies, denoted S-COL, for treated patients. Table 4 sums up the demand for those three categories of colonoscopy for each considered strategy.

Screening strategies logically involve a decrease in the number of I-COLs, that is to say colonoscopies associated with symptomatic CRC in the average risk population. Thanks to its greater sensitivity, the iFOBT strategy induces the lowest number of I-COLs. Conversely, screening strategies lead to a significant increase in the total number of procedures due to an increased number of C-COLs and S-COLs. First, screening enables early detections of CRC and pre-cancerous lesions, which improve survival rates and consequently increase the number of patients with previously diagnosed adenomas or CRC followed up with S-COL. Second, screening strategies generate numerous C-COLs, colonoscopies after positive screening. The striking fact here is that iFOBT screening approximately doubles C-COL and S-COL demands compared with gFOBT screening. Such an increase plausibly has an impact on the adjustment between demand and supply for colonoscopies.

Estimation of the impact of waiting time for C-COL on cost-effectiveness

In order to study the effect of extra waiting time if iFOBT were to be implemented, we consider here the following scenarios. Initially, we assume that there is no extra waiting time compared with gFOBT between the result of the screening test and the confirmation colonoscopy C-COL (i.e., 45 days). Then, we add successive tensions in the matching between supply and demand, allowing first for extra waiting time during two periods of time (respectively 5 and 10 years) and second for a decrease in the adherence rate for C-COL during the non-matching period. The incremental cost-effectiveness ratios (ICER) are shown in Table 5.

As expected, compared with gFOBT-45, the greater the waiting time is and rigidities last, the less effective the iFOBT strategies are. Greater waiting time indeed generates CRCs diagnosed at more advanced stages and lower survival rates. A decrease in adherence rate due to waiting time also enlarges the negative effect on the effectiveness of iFOBT.

More surprisingly, the greater the waiting time is and rigidities last, the less expensive iFOBT is. Insofar as more advanced stage CRC is associated with more expensive treatment, waiting time could be expected to increase the overall costs of the screening strategy. However, as explained above, waiting time induces a decrease in the

Table 5 ICER of gFOBT and iFOBT according to waiting time scenarios

	No screening	gFOBT-45d	iFOBT-45d	iFOBT-90d-5y	iFOBT-90d-5y-P	iFOBT-90d-10y	iFOBT-90d-10y-P
Discounted costs (€)	118,791,842	175,581,734	223,960,831	223,481,238	219,574,337	223,101,741	215,573,798
Discounted life years lived (*n*)	5,641,966	5,647,420	5,650,285	5,650,183	5,649,637	5,650,119	5,649,151
ICER (ref. no screening)		10,411	12,641	12,740	13,138	12,794	13,469
ICER (ref. gFOBT-45)			16,887	17,340	19,849	17,610	23,106

survival rate of the screened population, which subsequently decreases the number of patients to be followed up after treatment. A decrease in the adherence rate strengthens this result.

Overall, long-lasting rigidities increase the cost per life-year gained from implementing iFOBT. The decrease in participation in colonoscopy due to augmented waiting times has the greatest impact on cost-effectiveness results.

Cost-effectiveness acceptability curves

Probabilistic sensitivity analysis enables to compute the expected ICER of iFOBT from the respective expected costs and expected effectiveness of iFOBT and gFOBT. Whatever the considered scenario, the iFOBT strategy is optimal from 19,000€/LYG. However, besides the expected ICER of iFOBT, information relative to the robustness of this result is paramount to provide a relevant recommendation. Acceptability curves provide this information and are plotted in Fig. 2. The acceptability curve of a given strategy depicts the proportion of the 1,000 simulations generated by the PSA where this strategy is preferred. Figure 2 depicts how the probability of being optimal for iFOBT evolves if short-term rigidities are observed for either 5 or 10 years for a willingness to pay ranging from 0 to 100,000/LYG. We observe that short-term rigidities are responsible for an increase in the uncertainty surrounding recommendations favorable to iFOBT. Moreover, thanks to our alternative scenarios, we can disentangle how short-term rigidities and their consequences on the demand for colonoscopies can impact the robustness of CE recommendations. The robustness of these results is significantly lower when the additional waiting time for colonoscopy involves a decrease in the adherence rate, whatever the length of the non-matching period. For instance, an additional waiting time for 10 years along with a 25 % decrease in the colonoscopy adherence rate implies that the probability for iFOBT to be optimal never exceeds 86 %. If this level of confidence is too low for the decision maker, we cannot conclude that iFOBT is preferred over gFOBT, whatever the WTP for this new strategy.

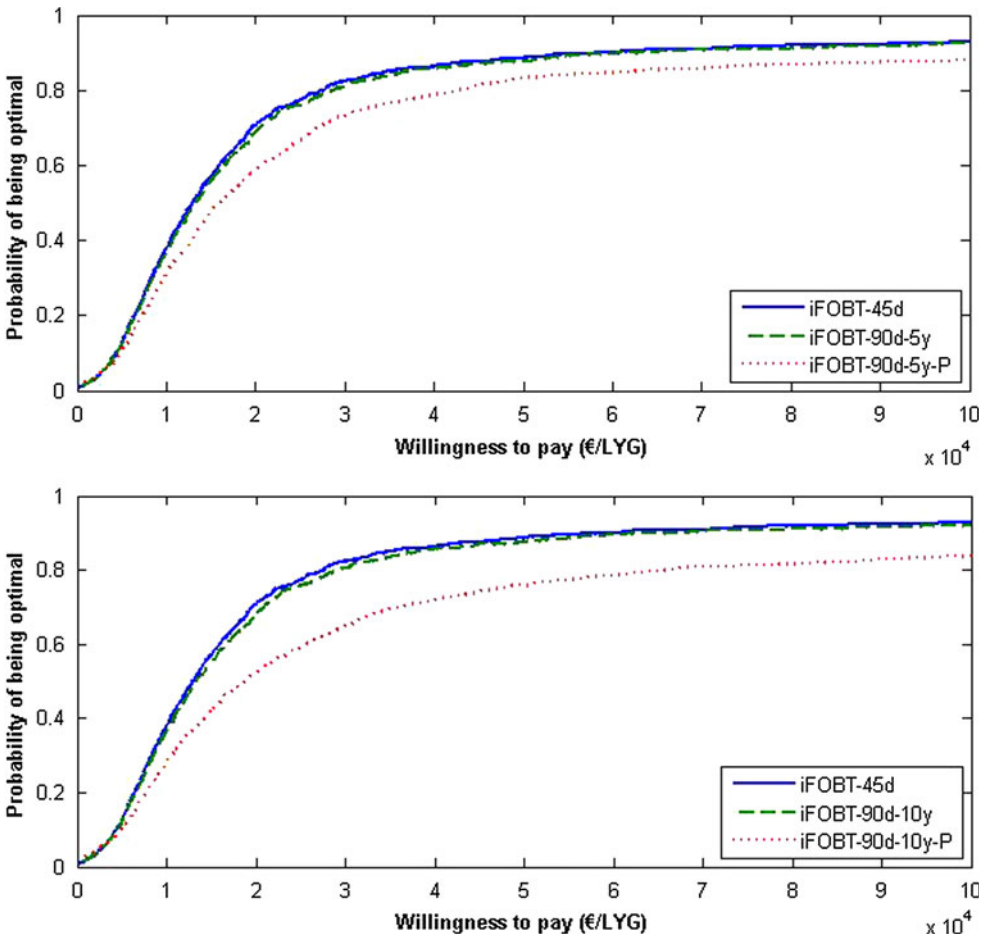

Fig. 2 Acceptability curves of gFOBT and iFOBT according to waiting time scenarios

Conclusion

Cost-effectiveness analysis is a powerful tool to investigate the relevance of dedicating scarce resources to competing strategies aiming at a given medical objective. Surprisingly, the problem of the congestion of medical services stays to a large extent aside from the evaluation process. If the existing supply were unable to cope with the induced demand for specific procedures, the very efficiency of the strategy could be questioned. In this study, we examined how waiting time resulting from imperfect adjustment between demand and supply of a given medical care can impact CEA recommendations for a mass screening strategy, using a decision analytical model.

Regarding mass screening for CRC, a number of CEAs conducted in France have demonstrated that the innovative iFOBT is cost-effective compared with the standard gFOBT [13–15]. However, the capacity of the French health-care system to handle the organizational consequences of the implementation of such large-scale programs has not been examined yet. The problem is far from anecdotical: the average risk population for CRC is indeed about 16 million subjects [33]. In particular, the move from gFOBT to iFOBT may involve significant variations in the number of colonoscopy procedures, as we have shown here. Whether the health-care system is able to cope with such changes is a question that is probably still underestimated.

Our study aimed at considering how short-run organizational obstacles can challenge recommendations in favor of iFOBT. In this specific case, the major organizational consequence of the technological shift is not the change of screening test but the shock in the demand for the diagnostic test, namely confirmation colonoscopy, for which a shortage of the extra required resources is already being observed in Europe (qualified staff, etc.) [9]. If shortages are not anticipated during the strategy shift, these rigidities can yield efficiency losses [3], taking into account that short-run rigidities in CEA enable providing more realistic estimations and therefore more robust recommendations in terms of both efficiency and organization. Moreover, if they are anticipated and their importance is quantified, proposals for increasing the colonoscopy supply can help minimize the consequences of extra demand. In the UK, for instance, nurse endoscopists were trained to perform colonoscopy to handle this shortage issue [16].

Our method used here consisted of using Markov modeling to assess the consequences of waiting times on the cost-effectiveness of screening strategies. Our model was validated with respect to the field results of actual campaigns at short and middle term. The PSA we conducted confirmed that, whatever the considered scenario, the iFOBT strategy is optimal for a reasonable WTP (from 19,000€/LYG). However, the consequences of imperfect demand-supply adjustments on the robustness of cost-effectiveness results depend on whether waiting times trigger a drop in participation rates. Indeed, while the iFOBT strategy would be optimal at a rather high level of confidence when waiting times do not impact participation rates, a decrease in the adherence rate during the non-matching period significantly reduces the robustness of the results. In the most pessimistic scenario, when an additional waiting time for colonoscopy induces a 25 % decrease in the adherence rate to this colonoscopy for 10 years, the iFOBT strategy would be preferred with a probability of being optimal that never reaches more than 86 %. In that configuration, waiting times do matter significantly if this level of confidence is considered as being too low for the decision maker. In such a case, we can no longer conclude that iFOBT is preferred over gFOBT.

In France and also probably in many other countries, we lack information about the mean waiting time for colonoscopies at the national level or about the potential capacity of the health-care system to handle the expected increase in colonoscopy demand if the iFOBT screening strategy is to be adopted. Our model has shown that a sharp increase in colonoscopy demand is to be expected. Waiting times are thus likely to occur in the short run and may become an important dimension of screening management and organization. In this context, additional research should be carried out in order to determine the extent to which waiting time may discourage asymptomatic patients from undergoing the medical tests proposed during screening campaigns.

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European conference of the Society for Medical Decision Making, 2010, Hall in Tirol.

Appendix 1: Model parameters

Epidemiological parameters

This appendix gathers epidemiological parameters used to describe the modeled population. They were obtained from published international data and are described in Table 6. Parameters such as prevalence, incidence, and mortality rate were differentiated according to gender.

Costs

Costs for colonoscopies are taken from the 2010 French Classification for Diagnosed Related Groups (DRG) [24]. When several DRGs are used to describe one procedure, we compute an average cost for this procedure weighted with its case mix (Table 7).

Costs for CRC treatment are drawn from published data [25], as are costs for FOBT tests [14]. These costs are then inflated to 2010 values using the medical care component of the Consumer Price Index (CPI) as shown in (Table 8).

Table 6 Epidemiological parameters

Variable	Values		References
	Males	Females	
Prevalence (at 50 years old), %			
Non-adenomatous polyps	38.48	40.33	
Low-risk adenomas	11.36	7.05	[34]
High-risk adenomas	6.94	3.81	
Carcinomas	1.07	0.49	
Annual incidence rates (50–59, ≥60 years old), %			
All neoplasias			
History			
None	10.1/11.4	6.7/7.3	[35]
Low-risk adenoma	22.2/25.1	14.1/20.4	
High-risk adenomas	26.7/24.4	16.3/10.7	
High-risk adenoma			
History			
None	0.25/0.48	0.31/1.00	
Low-risk adenoma	0.67/1.36	0.51/1.30	
High-risk adenomas	2.56/0.96	2.05/2.26	
Pathology of polyps according to size (≤6 mm/≥6 mm), %			
Non-adenomatous polyps	86/14		
Low-risk adenomas	85/15		[36]
High-risk adenomas	9/91		
Annual transition rates, %			
From <6 mm to ≥6–9 mm	2		[37]
From low-risk adenoma to high-risk adenoma	1.5		[38]
From high-risk adenoma to stage I CRC (male/female)	3.95/4.38		[39]
From stage I CRC to stage II CRC	30		[37]
From stage II CRC to stage III CRC	45		[38]
From stage III CRC to stage IV CRC	50		[38]
Annual CRC symptom detection rates (stage II/III/IV), %	22/60/90		[38]
Five-year survival (stage I/II/III/IV), %	94/80/47/5		[40]

Table 7 Costs for colonoscopies

Colonoscopy costs	2010			Mean cost weighted with the case mix (€)
Variable	References	Values (€)	Case mix (*n*)	
Optical colonoscopy	24K28Z	733.81		733.81
Optical colonoscopy with polypectomy of non-adenomatous polyps	24K26Z	888.29		888.29
Optical colonoscopy with polypectomy of adenomas (50–69/≥70 years old)	06M091	1,561.87	12,662	2,827
	06M092	3,621.54	5,686	
	06M093	5,707.58	2,632	
	06M094	8,663.76	673	
Optical colonoscopy with diagnosis of cancer (50–69/≥70 years old)	06M051	1,860.66	7,493	3,696
	06M052	4,654.03	5,001	
	06M053	6,015.85	2,682	
	06M054	9,697.78	456	
Complication (bleeding or perforation)	06C041	6,449.22	11,381	10,027
	06C042	8,752.69	9,813	
	06C043	11,644.72	13,898	
	06C044	17,843.77	4,958	

Official French coding: http://www.atih.sante.fr/ (2010). Accessed 2 April 2012

Table 8 Inflated costs

Costs parameters	Cost (€)	Year of estimation	CPI* (medical care component)	Inflated costs (year 2010)
Guaiac test	16.30	2006	103.42	16.21
Immunological test	23.00	2006	103.42	22.87
Optical colonoscopy	733.81	2010	102.85	733.81
Optical colonoscopy with polypectomy of non-adenomatous polyps	888.29	2010	102.85	888.29
Optical colonoscopy with polypectomy of adenomas (50–69/≥70 years old)	2,827.39	2010	102.85	2,827.39
	2,827.39	2010	102.85	2,827.39
Optical colonoscopy with diagnosis of cancer (50–69/≥70 years old)	3,695.84	2010	102.85	3,695.84
	3,695.84	2010	102.85	3,695.84
Complication (bleeding or perforation)	10,227.13	2010	102.85	10,227.13
Treatment costs of colorectal cancer stage I	17,596.00	2004	103.4	17,502.40
Treatment costs of colorectal cancer stage II	20,472.00	2004	103.4	20,363.11
Treatment costs of colorectal cancer stage III	29,013.00	2004	103.4	28,858.68
Treatment costs of colorectal cancer stage IV	35,059.00	2004	103.4	34,872.52

* Available at: http://www.indices.insee.fr/bsweb/servlet/bsweb?action=BS_SERIE&BS_IDBANK=000637733&BS_IDARBO=06000000000000

Appendix 2: Validation

See Table 9.

Table 9 Detailed results of the Markov simulation for the first screening round

	Male	Female	Total
Population	88,835	98,507	187,342
Adherence rate (%)	49	55	52
Number of positive gFOBT results	1,378	1,501	2,880
Positivity rate (%)	3.17	2.76	2.94
Confirmation colonoscopies (C-COL)	1,245	1,358	2,603
Negative confirmation colonoscopies	441	633	1,074
Subjects with low-risk adenomas	402	401	803
Subjects with high-risk adenomas	242	194	436
Subjects with CRC	160	130	291

At the national level [23], the positivity rate for the gFOBT test is 3.2 % for males (against 3.17 % from the simulation) and 2.2 % for females (against 2.76 % from the simulation)

References

1. Adang, E.M.: Economic evaluation of innovative technologies in health care should include a short-run perspective. Eur. J. Health Econ. **9**, 381–384 (2008)
2. Van de Wetering, G., Woertman, W.H., Adang, E.M.: Time to incorporate time in cost-effectiveness analysis. Eur. J. Health Econ. **13**(3), 223–226 (2012)
3. Van de Wetering, G., Woertman, W.H., Adang, E.M.: A model to correct for short-run inefficiencies in economic evaluation in healthcare. Health Econ. **21**, 270–281 (2012)
4. Farnworth, M.G.: A game theoretic model of the relationship between prices and waiting times. J. Health Econ. **22**(1), 47–60 (2003)
5. Johannesson, M., Johansson, P.O., Soderqvist, T.: Time spent on waiting lists for medical care: an insurance approach. J. Health Econ. **17**(5), 627–644 (1998)
6. Koopmanschap, M.A., Brouwer, W.B.F., Hakkaart-van Roijen, L., van Exel, N.J.A.: Influence of waiting time on cost-effectiveness. Soc. Sci. Med. **60**(11), 2501–2504 (2005)
7. Sculpher, M., Fenwick, E., Claxton, K.: Assessing quality in decision analytic cost-effectiveness models: a suggested framework and example of application. PharmacoEconomics **17**(5), 461–477 (2000)
8. Ferlay, J., Autier, P., Boniol, M., Heanue, M., Colombet, M., Boyle, P.: Estimates of the cancer incidence and mortality in Europe in 2006. Ann. Oncol. **18**(3), 581–592 (2007)
9. Kanavos, P., Schurer, W.: The dynamics of colorectal cancer management in 17 countries. Eur. J. Health Econ. **10**(Suppl 1), 115–129 (2010)
10. Guittet, L., Bouvier, V., Mariotte, N., et al.: Comparison of a guaiac based and an immunochemical fecal occult blood test in screening for colorectal cancer in a general average risk population. Gut **56**, 210–214 (2007)
11. Boncz, I., Brodszky, V., Péntek, M., et al.: The disease burden of colorectal cancer in Hungary. Eur. J. Health Econ. **10**(Suppl 1), 35–40 (2010)
12. Schurer, W.: The status of colorectal cancer care in the Netherlands: past, present and future. Eur. J. Health Econ. **10**(suppl 1), S51–S56 (2010)
13. Berchi, C., Bouvier, V., Réaud, J.M., et al.: Cost-effectiveness analysis of two strategies for mass screening for colorectal cancer in France. Health Econ. **13**, 227–238 (2004)
14. Lejeune, C., Dancourt, V., Arveux, P., Bonithon-Kopp, C., Faivre, J.: Cost effectiveness analysis of screening for colorectal cancer in France using a guaiac test versus an immunochemical test. Int. J. Technol. Assess. Health Care **26**, 40–47 (2010)
15. Chauvin, P., Josselin, J.M., Heresbach, D.: Incremental net benefit and acceptability of alternative health policies: a case study of mass screening for colorectal cancer. Eur. J. Health Econ. **13**(3), 237–250 (2012)
16. Schurer, W., Kanavos, P.: Colorectal cancer management in the United Kingdom: current practice and challenges. Eur. J. Health Econ. **10**(Suppl 1), 85–90 (2010)
17. Vrangbaek, K., Nielsen, M.: Colorectal cancer in Denmark: status and dilemmas. Eur. J. Health Econ. **10**(suppl 1), S5–S13 (2010)
18. Berg, B., Denton, B., Nelson, H., Balasubramanian, H., Rahman, A., Bailey, A., Lindor, K.: A discrete event simulation model to evaluate operational performance of a colonoscopy suite. Med. Decis. Making **30**(3), 380–387 (2010)
19. Wilschut, J.A., Habbema, J.D., van Leerdam, M.E., Hol, L., Lansdorp-Vogelaar, I., Kuipers, E.J., van Ballegooijen, M.: Fecal occult blood testing when colonoscopy capacity is limited. J. Natl. Cancer Inst. **103**(23), 1741–1751 (2011)
20. Manfredi, S., Piette, C., Durand, G., et al.: Colonoscopy results of a French regional FOBT-based colorectal cancer screening program with high compliance. Endoscopy **40**(5), 422–427 (2008)
21. INSEE. http://www.insee.fr/fr/themes/detail.asp?reg_id=99&ref_id=estim-pop. Accessed 2 April 2012
22. ADECI35. Information available on request. http://www.adeci35.fr/
23. Goulard, H., Boussac-Zarebska, M., Bloch, J.: Epidemiological assessment of the pilot programme for organized colorectal cancer screening, France, 2007. Bulletin épidémiologique hebdomadaire. INVS **2–3**, 22–25 (2009)
24. Official French coding: http://www.atih.sante.fr/ (2010). Accessed 2 April 2012
25. Clerc, L., Jooste, J., Lejeune, C., et al.: Cost of care of colorectal cancers according to health care patterns and stage at diagnosis in France. Eur. J. Health Econ. **9**, 361–367 (2008)
26. Zauber, A.G., Lansdop-Vogelaar, I., Knudsen, A.B., et al.: Evaluating test strategies for colorectal cancer screening. Ann. Intern. Med. **149**, 659–669 (2008)
27. Van Rijn, J., Reitsma, J.B., Stoker, J., et al.: Polyp miss rate determined by tandem colonoscopy: a systematic review. Am. J. Gastroenterol. **101**, 343–350 (2006)
28. Denis, B., Ruetsch, M., Strentz, P., et al.: Short term outcomes of the first round of a pilot colorectal cancer screening programme with guaiac based faecal occult blood test. Gut **56**, 1579–1584 (2007)
29. Denberg, T.D., Melhado, T.V., Coombes, J.M., et al.: Predictors of non-adherence to Screening Colonoscopy. J. Gen. Intern. Med. **20**, 989–995 (2005)
30. Briggs, A.H.: Handling uncertainty in cost-effectiveness models. Pharmacoeconomics **5**, 479–500 (2000)
31. Barton, G.R., Briggs, A.H., Fenwick, E.A.L.: Optimal cost-effectiveness decisions: the Role of the cost-effectiveness acceptability curve (CEAC), the cost-effectiveness acceptability frontier (CEAF), and the expected value of perfection information (EVPI). Value Health **11**, 886–897 (2008)
32. Faivre, J., Dancourt, V., Lejeune, C., et al.: Reduction in colorectal cancer mortality by fecal occult blood screening in a French controlled study. Gastroenterology **126**, 1674–1680 (2004)

33. Chevreul, K.: Colorectal cancer in France. Eur. J. Health. Econ. **10**(suppl 1), S15–S20 (2010)
34. Regula, J., Rupinski, M., Kraszewska, M., et al.: Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. N. Engl. J. Med. **355**, 1863–1872 (2006)
35. Yamaji, Y., Mitsushima, T., Ikuma, H., et al.: Incidence and recurrence rates of colorectal adenomas estimated by annually repeated colonoscopies on asymptomatic Japanese. Gut **53**, 568–572 (2004)
36. Church, J.: Clinical significance of the small colorectal polyps. Dis. Colon Rectum **47**, 481–485 (2004)
37. Pickhardt, P.J., Hassan, C., Laghi, A., et al.: Cost-effectiveness of colorectal cancer screening with computed tomography colonography: the impact of not reporting diminutive lesions. Cancer **109**, 2213–2221 (2007)
38. Hur, C., Chung, D.C., Schoen, R.E., Gazelle, G.S.: The management of small polyps found by virtual colonoscopy: results of a decision analysis. Clin. Gastroenterol. Hepatol. **5**, 237–244 (2007)
39. Brenner, H., Hoffmeister, M., Stegmaier, C., et al.: Risk of progression of advanced adenomas to colorectal cancer by age and sex: estimates based on 840 149 screening colonoscopies. Gut **56**, 1585–1589 (2007)
40. French ministry of health. http://www.santejeunesse-sports.gouv.fr/IMG/pdf/annexes-3.pdf. Accessed 02 Feb 2011