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The cost-effectiveness of immunochemical tests for colorectal cancer screening

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ABSTRACT

Background: The optimal immunochemical test to use for generalised mass screening is still under debate in France.
Aim: To compare the cost and effectiveness in biennial screening for colorectal cancer of fifteen strategies consisting of the three-stool sample un-rehydrated guaiac faecal occult blood test and three immunochemical tests: Magstream, FOB-Gold and OC-Sensor, at different positivity cut-off levels and stool-sample collection.
Methods: A Markov model was used to compare these strategies in a general population of 100,000 individuals aged 50–74 over a 20-year period.
Results: Immunochemical tests were efficient strategies compared with guaiac faecal occult blood test. When all 15 strategies were compared with each other, only five of them remained efficient: the one- and two-stool sample Magstream, the one- and two-stool sample FOB-Gold with the 176 ng/mL cut-off, and the two-stool sample OC-Sensor with the 150 ng/mL cut-off. Sensitivity analyses showed that, at an identical price, the one-stool sample OC-Sensor was the most efficient strategy, and outperformed FOB-Gold.
Conclusion: One-stool immunochemical testing can be considered a promising alternative to the guaiac faecal occult blood test for colorectal cancer mass screening in the general population. Competition between manufacturers should now be introduced to reduce purchase price differences.

1. Introduction

Since 2009, a colorectal cancer (CRC) mass screening programme based on a biennial guaiac faecal occult blood test (G-FOBT), followed by a colonoscopy in case of a positive test, has been implemented throughout France. The optimal FOBT to use for generalised mass screening is, however, still under debate. Although G-FOBT has been endorsed by the European Commission and recommended by the French Health Authorities, it has been criticised mainly for its poor sensitivity [1,2] and because it reacts to non-human heme in food. Faecal immunochemical tests (FITs), which are based on the use of a specific antibody of human haemoglobin, present major advantages over G-FOBT. Population-based studies showed that they are more sensitive than G-FOBT, but are also associated with lower specificity, leading to a higher number of colonoscopies [3–5]. They can be automatically analysed, allowing for reproducibility and quality control. Another advantage is the possibility of modifying the cut-off level for a positive test, although the optimal cut-off remains indeterminate, as well as the number of stool samples to collect. At the moment, three FITs allowing quantitative analysis are available: OC-Sensor (Eiken, Tokyo, Japan), FOB-Gold (Beckman Coulter, Brea, CA, USA) and Magstream (Fujirebio, Tokyo, Japan).

In a context of scarce resources, the decision to implement one of these three tests instead of G-FOBT in France will depend not only on test diagnostic performances at different cut-off levels compared with G-FOBT, but also on their efficiency. The economic burden associated with each of these three tests according to the different cut-off levels and the number of stool samples has yet to be established, as well as the final effectiveness over a long time period in the context of a generalised mass screening programme. Several cost-effectiveness analyses have already been published [6–14].

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Although they demonstrated the efficiency of different FITs compared with G-FOBT, none assessed simultaneously their efficiency compared with G-FOBT. Moreover, comparisons between studies remain tricky owing to differences in epidemiological (incidence rates, cut-off level, number of stool samples, participation rate, follow-up duration, screening interval) or economic considerations (analysis point of view, cost categories, effectiveness criteria).

In this context, the aim of this study was to use a Markov model to estimate, over a 20-year period in an average-risk population, the efficiency of G-FOBT and three FITs at different cut-off levels for positivity and stool-sample collection.

2. Methods

2.1. General description of the model

We used a validated Markov model to estimate the costs and effectiveness of different screening strategies for CRC. The general structure of the model is shown in Fig. S1. This model has already been described [15]. Briefly, it allowed disease progression to be simulated through several specified health states for a population of 100,000 individuals aged 50–74 invited to participate in a screening programme and monitored over a 20-year period, until either the age of 85 or death. Five health states were modelled: absence of CRC or advanced adenoma (i.e. adenoma over 1 cm in diameter, or with a villous component, or severe dysplasia), CRC, death from CRC and death from another cause. At each new cycle of one year, subjects could move from one state of health to another through defined probability transitions, and the model estimated the number of subjects in each state. Thus, at the end of the study period, the model was able to estimate the cumulative number of deaths related or not related to CRC, the cumulative number of life-years lost and the cumulative cost associated with each of the modelled screening strategies.

2.2. Screening strategies

Fifteen strategies were compared: screening with the unrehydrated G-FOBT (Hemoccult-II; Beckman Coulter, Brea, CA, USA) performed on three consecutive stool samples and repeated every two years, and screening with one of the three FITs repeated every two years, performed at different cut-off levels and based on one or two stool-sample collection. These strategies included the two-stool sample OC-Sensor at 150 ng/mL, 175 ng/mL, 200 ng/mL, 250 ng/mL and 300 ng/mL and one-stool sample OC-Sensor at 150 ng/mL; the corresponding threshold for two-stool sample FOB-Gold at 176 ng/mL, 205 ng/mL, 234 ng/mL, 293 ng/mL and 352 ng/mL, one-stool sample FOB-Gold at 176 ng/mL; and finally one-stool sample Magstream at 20 ng/mL.

2.3. Epidemiological parameters

Most epidemiological parameter values were directly provided by national population statistics and two controlled studies in Burgundy (France). The first study was aimed at comparing G-FOBT with no screening [16]. The goal of the second study, the IGOR study, was to compare G-FOBT with three biennial FITs in four French administrative areas (Côte d'Or, Haut-Rhin, Ile-et-Vilaine and Indre-et-Loire) [17,18].

Data provided by population statistics and introduced into the model concerned the age and gender of the population at beginning of screening, their age- and sex-specific mortality and life expectancy rates. Controlled studies provided the age- and sex-specific incidence rates for CRC, the distribution of CRC by stage among the subjects who participated, the non-responders, and among interval cancers, and the yearly survival rates by stage. These studies also provided data on FITs performance, including positivity rate, positive predictive value for advanced adenomas and false positive rate. CRC sensitivity for the two-stool sample OC-Sensor at 150 ng/mL, FOB-Gold at 176 ng/mL, and Magstream at 20 ng/mL was based on the data provided by the studies undertaken by Nakama et al. and Rozen et al., and was assumed to be 80% [19,20]. Using the sensitivity ratios obtained in the Burgundy population-based study, G-FOBT sensitivity was assumed to be 45% [17], an assumption confirmed by a meta-analysis [21]. Sensitivities for each FIT for the remaining cut-off levels and stool collection were estimated from the baseline assumption (80%), and the CRC relative miss rate estimated in Burgundy [17,18]. Sensitivity for colonoscopy was assumed to be 100% [22].

The Burgundy studies also provided data on compliance with screening test and colonoscopy: a 50% participation rate was considered the baseline value for G-FOBT [16]. We assumed a similar rate for FITs, according to van Roon et al. [23]. Participation in colonoscopy after a positive screen was estimated to be 90% [17,18].

All epidemiological parameters required by the model are shown in Table S1.

2.4. Cost data used in the model

The cost-effectiveness analysis was performed from the point of view of the funding sources, comprising the French Health Insurance System and the French Health Authorities. Only direct costs were considered in the analysis. They were expressed in 2011 prices (€). The following categories of costs were taken into account: screening campaign organisation cost, information cost, test distribution cost, processing cost, and cost of CRC or advanced adenoma treatment and follow-up. With the exception of the cost of diagnosis, care and follow-up management, which were issued from a previously published cost-effectiveness analysis [24], all other cost categories were assessed using the micro-costing method based on data provided by the coordination and centralised analysis centres of the IGOR Burgundy study [17,18].

The cost of organising the screening programme, informing and inviting the population were independent of participation. The distribution cost varied according to participation, but also to the purchase price of the test. The purchase price of the G-FOBT kit was 1.16 €. The purchase price of the OC-Sensor was estimated to be 5.90 € for a two-sample test and 3.48 € for one sample. The corresponding purchase prices were 3.04 € and 1.52 € for FOB-Gold, 2.59 € and 1.44 € for Magstream [25].

Further details concerning costs are provided in Appendix A. All costs are summarised in Table S2.

2.5. Cost-effectiveness results

The cost-effectiveness analysis was based on the calculation of an incremental cost-effectiveness ratio (ICER). ICER was expressed in terms of cost per additional life-year gained. ICER was calculated by dividing the incremental costs by the incremental life-years lost between each FIT and G-FOBT. Life-years lost were defined as the difference between the age at death and the age corresponding to life expectancy. Costs and effectiveness were discounted at an annual rate of 3%.

In a first analysis, all immunochemical strategies were compared with G-FOBT. In a second analysis, all screening strategies were compared with each other. First, strategies were ranked from the least to the most costly. Strategies that were most costly and less effective (i.e. presenting a higher number of life-years lost) than the next alternative were excluded by simple dominance. Strategies that presented a higher ICER than that of the next, more effective

Table 1
Estimated discounted costs, effectiveness and incremental cost-effectiveness ratios of biennial screening using immunochemical tests and the guaiac test (100,000 individuals aged 50–74 over a 20-year period).

	Cost[a] of the screening programme (€)	Number of life-years lost[a]	Incremental cost-effectiveness ratio (€ per life-year gained)	
			Compared to guaiac test	Compared to the previous less costly option
Magstream 1-stool sample – 20 ng/mL	74,723,716	13,711	Dominant	–
FOB-Gold 1-stool sample – 176 ng/mL	75,016,494	13,505	Dominant	1421
G-FOBT	75,109,845	14,566	–	−88
FOB-Gold 2-stool samples – 352 ng/mL	76,293,710	13,498	1108	1108
FOB-Gold 2-stool samples – 293 ng/mL	76,522,955	13,303	1119	1176
Magstream 2-stool samples – 20 ng/mL	76,818,273	13,082	1151	1336
FOB-Gold 2-stool samples – 234 ng/mL	76,886,147	13,161	1264	−859
OC-Sensor 1-stool sample – 150 ng/mL	77,118,529	13,307	1595	−1592
FOB-Gold 2-stool samples – 205 ng/mL	77,265,650	13,041	1414	553
FOB-Gold 2-stool samples – 176 ng/mL	77,865,893	12,932	1687	5507
OC-Sensor 2-stool samples – 300 ng/mL	79,018,571	13,311	3115	−3041
OC-Sensor 2-stool samples – 250 ng/mL	79,321,649	13,204	3092	2833
OC-Sensor 2-stool samples – 200 ng/mL	79,791,385	13,034	3056	2763
OC-Sensor 2-stool samples – 175 ng/mL	80,288,303	12,940	3185	5286
OC-Sensor 2-stool samples – 150 ng/mL	80,705,173	12,855	3270	4904

G-FOBT = guaiac faecal occult blood test.
[a] An annual discount rate of 3% was used.

alternative, were excluded by extended dominance. The remaining strategies were considered to be efficient and could be connected by a line, entitled 'efficient frontier', in the cost-effectiveness plan. All dominated strategies lie below this boundary.

2.6. Sensitivity analyses

Uncertainties related to epidemiological and economic data were processed using deterministic sensitivity analyses. The following parameters were tested: participation rate in screening tests, price for all two-stool- and one-stool-sample FIT kits, and price of an automated analyser in the costs of test processing. Further details concerning the choice of parameter values to be tested are provided in Appendix A.

3. Results

3.1. Baseline cost-effectiveness analysis

As shown in Table 1 the one-stool sample Magstream and FOB-Gold dominated G-FOBT, with screening programme costs decreasing by 0.5% and 0.1%, and a number of life-years lost decreasing by 5.9% and 7.3% respectively. All other immunochemical strategies were more effective and more costly. All presented a discounted incremental cost-effectiveness ratio under 3500 € per life-year gained. The two-stool sample OC-Sensor at 150 ng/mL was the most effective strategy with 12,855 life-years lost compared with 14,566 for G-FOBT, corresponding to an 11.7% effectiveness increase, but also the most costly alternative, with a 7.4% screening cost increase. It presented the highest ICER, with 3270 € per additional life-year gained.

When strategies were compared with each other, only five out of the 15 strategies remained efficient. The efficient frontier (Fig. 1) included the one- and two-stool sample Magstream, the one- and two-stool sample FOB-Gold with the 176 ng/mL cut-off level, and the two-stool sample OC-Sensor with the 150 ng/mL cut-off level. Among these, the one-stool sample FOB-Gold with a cut-off value of 176 ng/mL presented the lowest ICER (1421 € per life-year gained) and the two-stool sample OC-Sensor the highest ICER (36,874 €; Table 2).

3.2. Sensitivity analyses

The participation rate was tested first of all. The National Institute of Cancer reported rates varying between 25% and 55% according to French areas participating in the generalised mass screening programme, and thus 30%, 40% and 60% rates were tested [26]. The influence of participation on the ICERs is illustrated by Table 2. The one-stool sample FOB-Gold remained the most efficient strategy, and presented ICERs varying between 1592 € per life-year gained when a 30% participation rate was assumed and 1322 € per life-year gained when participation increased to 60%.

A second analysis consisted of using a 2.50 € price for all two-stool sample FIT kits and 1.50 € for all one-stool sample kits. Therefore, distribution costs per test performed were estimated to be 15.84 € for all two-stool samples OC-Sensor, FOB-Gold, and Magstream kits (instead of 26.09 €, 17.20 € and 16.06 € respectively), and 13.32 € for all one-stool sample kits for all three FITs with a 1.50 € price (instead of 19.55 €, 13.37 € and 13.16 € respectively). The hierarchy between strategies was greatly modified when a 2.50 € purchase price was used for all two-stool sample FITs, and 1.50 € for all one-stool sample FITs. The one-stool sample OC-Sensor became the most efficient strategy, presenting an estimated ICER of only 762 € per life-year gained compared with the Magstream (not shown).

Table 3 also shows that among all screening alternatives, all one-stool FITs were associated with one of the lowest increases in the number of colonoscopies to be performed compared with G-FOBT. Moreover, colonoscopies due to false-positive results represented 3.2% of the total cost of the screening programme at the most when one-sample FITs were used, whereas they could reach 4.8% of the total cost when a two-sample FIT was modelled.

The last sensitivity analysis included the price of an automated analyser in the test processing costs. At baseline, test processing cost was estimated at 4.84 € per analysed test for the OC-Sensor and FOB-Gold, and 4.35 € for the Magstream. Given a purchase price of 100,000 € and after depreciation, test processing costs were estimated to be 4.89 and 4.39 € respectively. Results were not modified by the increase in the cost of test processing related to the purchase of an automated analyser by the central analysis centres.

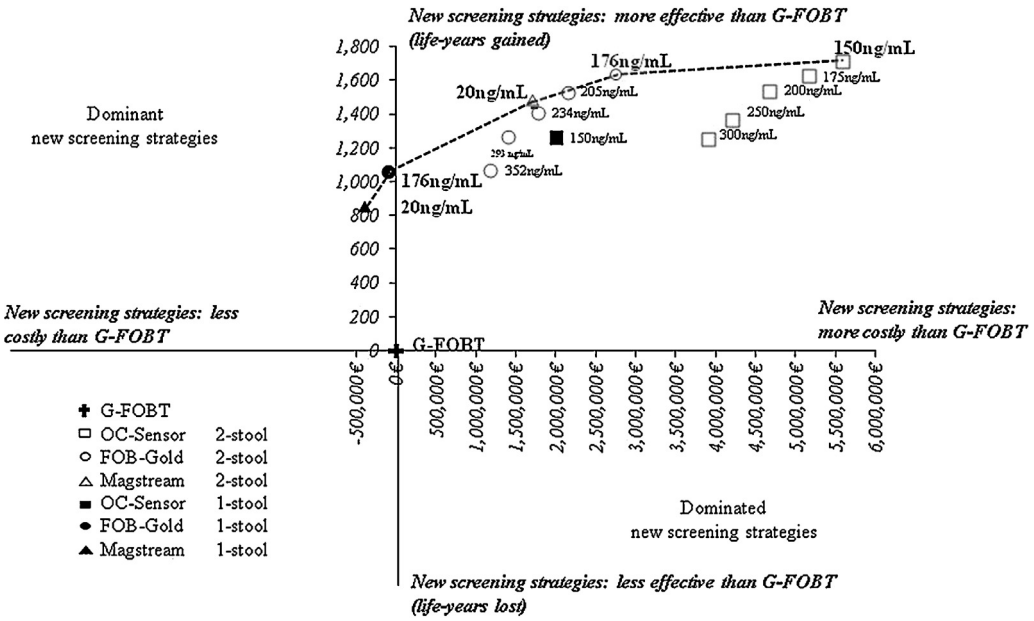

Fig. 1. Guaiac faecal occult blood test (G-FOBT)is represented by the intercept. The x-axis represents the incremental cost of faecal immunochemical tests (FITs) compared with G-FOBT. The y-axis represents the incremental effectiveness of FITs compared with G-FOBT. Screening strategies in the northwest quadrant are less costly and more effective than G-FOBT. They are highly efficient and are considered dominant compared with G-FOBT. Screening strategies in the northeast quadrant are more costly and more effective than G-FOBT. The closer they are to the y-axis, the more efficient they are (i.e. the lower the incremental cost-effectiveness ratio). Screening strategies in the south-west quadrant are less costly but also less effective than G-FOBT. Screening strategies in the southeast quadrant are inefficient (less effective and more costly than G-FOBT): they are dominated by G-FOBT. The dotted line represents the efficient frontier, which was determined by excluding simple and extended dominated strategies. G-FOBT = guaiac faecal occult blood test, FIT = immunochemical test.

4. Discussion

The results of this study confirmed the efficiency of the three FITs in the general population in France, especially when only one-sample is used for screening. Confidence can be placed in this model. It was validated using data from the Danish randomised study performed in Funen. Estimates of our model did indeed show an extremely close concordance between the simulated mortality reduction and the results observed in the Danish study [15].

A major advantage of our study is that most parameters were based on population-based data collected from two French studies performed within organised screening programmes [16–18]. The IGOR Burgundy study, aimed at comparing G-FOBT performance with three biennial FITs in four French administrative areas enables us to have access to the programme's CRC sensitivity and positive predictive value for advanced adenomas for one round only [17]. However, the experience of CRC screening in Burgundy for over 20 years has given us the opportunity to obtain a G-FOBT positivity rate according to gender and age (five-year groups) for successive screening rounds [16]. Therefore, in the present model, assumptions concerning the evolution of the positivity rate of G-FOBT and FIT over time were made: we assumed a progressive decrease in this parameter over the first five rounds, followed by its stabilisation for the remaining time frame. Access to these data allows to clearly present the clinical and epidemiological reality of a screening programme.

Our study is also interesting since it simultaneously compares each of the three main FITs available on the market with G-FOBT, and evaluates the efficiency of one-day and two-day samplings for different cut-off values. However, a limitation was that with one-day sampling, we had no data with which to analyse cut-off levels under 150 ng/mL using the OC-Sensor, or the corresponding values under 176 ng/mL using the FOB-Gold. Another limitation lies in the characteristics of the Magstream. Only the 20-ng/mL cut-off level was modelled. This was the only cut-off recommended by the manufacturer for this semi-quantitative test, which does not allow evaluation of test performances at different cut-off values. Therefore, it does not allow to take into account the economic and clinical impact over time according to cut-off level.

Our findings are consistent with those of recent studies which analysed the efficiency of immunochemical tests compared either with G-FOBT or with the absence of screening [7–14]. In particular, our conclusion was close to the results obtained by Wilschut

Table 2
Impact of changes in values of epidemiological and economic parameters on the efficient screening strategies.

	Baseline incremental cost-effectiveness ratios[a]	Participation in screening test			Purchase of an automated analyser
		30%	40%	60%	
Magstream 1-stool sample – 20 ng/mL	–	–	–	–	–
FOB-Gold 1-stool sample – 176 ng/mL	1421	1592	1516	1322	1437
Magstream 2-stool samples – 20 ng/mL	4260	4705	4509	3987	4252
FOB-Gold 2-stool samples – 176 ng/mL	6984	7764	7398	6594	7006
OC-Sensor 2-stool samples – 150 ng/mL	36,874	47,457	42,231	30,893	36,873

These five strategies are the result of the overall comparison of the original fifteen, after exclusion of simple and extended dominated strategies.

[a] Incremental cost-effectiveness ratios were calculated by comparing immunochemical tests with each other.

Table 3
Colonoscopy feasibility indicator, and cost of diagnostic colonoscopies performed after false positive results within the total cost of the screening programme (100,000 individuals aged 50–74 over a 20-year period).

	Colonoscopy feasibility[a]		Proportion of diagnostic colonoscopies[b] cost within the total cost of the screening programme
	n	%	
G-FOBT	5998	–	2.6%
Magstream			
2-stool samples 20 ng/mL	+9222	+54%	4.1%
1-stool sample 20 ng/mL	+6744	+12%	2.7%
OC-Sensor			
2-stool samples 150 ng/mL	+11,523	+92%	3.8%
2-stool samples 175 ng/mL	+10,991	+83%	3.5%
2-stool samples 200 ng/mL	+10,127	+69%	3.1%
2-stool samples 250 ng/mL	+9402	+57%	2.7%
2-stool samples 300 ng/mL	+9109	+52%	2.4%
1-stool sample 150 ng/mL	+9111	+52%	2.7%
FOB-Gold			
2-stool samples 176 ng/mL	+10,739	+79%	4.8%
2-stool samples 205 ng/mL	+9984	+66%	4.3%
2-stool samples 234 ng/mL	+9485	+58%	4.0%
2-stool samples 293 ng/mL	+8808	+47%	3.5%
2-stool samples 352 ng/mL	+8113	+35%	3.2%
1-stool sample 176 ng/mL	+7857	+31%	3.2%

G-FOBT = guaiac faecal occult blood test.
[a] Colonoscopy feasibility was defined as the number of colonoscopies performed after each positive test in a population of 100,000 individuals aged 50–74 and followed over a 20-year period (50% participation rate)
[b] Diagnostic colonoscopies correspond to colonoscopies performed after a false positive result delivered by screening test.

et al. [14] who showed that FITs were more efficient at lower cut-off levels for positivity than at higher levels. Goede et al. also corroborate our findings, by demonstrating that, for the same screening test, one-sample FIT was associated with an equal or greater number of life-years gained at lower costs compared with two-sample FITs [10]. Finally, results issued from the sensitivity analysis on the price of FITs were similar to those obtained by van Rossum et al. who concluded that the one-sample OC-Sensor with a cut-off level of 100 ng/mL dominated G-FOBT [13]. Our work was also in accordance with studies concerning the impact of participation on the cost-effectiveness results [12,14]. Our results suggested that a lower participation rate resulted in a higher ICER. This outcome is mainly explained by the decreased effectiveness due to the lower detection rate of advanced adenomas, and the detection of more advanced CRC in the population. Despite these similarities, caution must be taken in comparing these analyses, because of differences in the assumptions concerning the natural history of CRC, but also concerning the reference screening strategy, screening interval, cut-off levels for positivity results, participation rate, effectiveness criterion, perspective of the economic analysis, cost categories included in the analysis, and follow-up duration [6–14]. Concerning this latter parameter, our model was calibrated for only a 20-year period. This choice was explained by the fact that the population of the model was not a dynamic cohort. Therefore, most of the simulated population will be more than 75 years of age at the end of the study, with a high probability of comorbidity. Another justification is the small difference in clinical benefit obtained between a 10- and a 20-year period of follow-up. A previous publication showed that the CRC mortality reduction was 15.1% at 10 years and 17.7% at 20 years (when G-FOBT was compared with the absence of CRC screening) [24].

Our work could also have been limited by some of the assumptions we made. At first, we did not take into account the possible multiple adenomas that could result in a higher probability of having a positive test than individuals presenting a single lesion. Omitting this differentiation may have resulted in an underestimation of the effectiveness of the screening programme. However, we considered that advanced adenoma was the most important screening target. Another limitation is the exclusion in the false positive rate of the presence of small and medium adenomas, which are systematically removed during colonoscopy. This may have underestimated the cost of the screening programme. Finally, we assumed a 100% colonoscopy sensitivity for colorectal lesions, and we did not take into account the possible false negative cases.

The manner in which economic analysis was conducted could also be discussed. First, we excluded from the analysis some indirect costs corresponding to short-term and long-term disabilities, and costs due to premature deaths from CRC. However, the estimation of these costs required individual data that were not available at the time of the study. Complications due to colonoscopy were not taken into account in the model. They are estimated to be less than 3 per 1000 colonoscopies [27]. However, the robustness of our models' results leads us to conclude that the analysis might not be greatly modified by this parameter. Finally, data concerning treatment cost only covered the first year after diagnosis. It would have been relevant to take into account treatment data on a longer period of follow-up. However, because of differences in health care systems, using such cost data may not have been representative of the French context. Finally, we made the choice to perform a cost-effectiveness analysis and not a cost utility based on the use of Quality-adjusted Life-Years (QALYs). This choice was justified by the fact that the main clinical result in a screening programme is CRC mortality reduction. Moreover, utility scores have not been estimated during the French trial comparing G-FOBT with FITs and once more, and we found it tricky to use data issued from other countries.

Our work showed that purchase price of FIT kits strongly influenced the cost-effectiveness results. The hierarchy between tests was greatly modified when a 2.50 € price was applied to all FITs. The OC-Sensor performed better than the FOB-Gold. However, it must be underlined that the data used in this model were based on the first generation of buffers. The stability of all the tests has now been increased. This result should make decision-makers cautious when interpreting cost-effectiveness results, because efficiency is highly dependent on economic assumptions and market changes. Moreover, performance and screening test effectiveness,

but also data on reproducibility and temperature stability should not be forgotten in decision-making. In France, decisions are still based on a multi-attribute decision-making approach. Assessment of efficiency is one of the criteria contributing to the decision to change the present screening test for an FIT [28]. However, no cost-effectiveness threshold is used as a decision tool in France, as in the United Kingdom with £20,000–30,000 per additional quality-adjusted life-year threshold. In our work, all ICERs were below this limit whatever the hypothesis and the results of the sensitivity analyses. Another important issue for decision-making is the system's ability to perform colonoscopy in the case of a positive test. Considering the annual number of additional colonoscopies to be performed, we showed that all three one-stool FITs were associated with one of the lowest numbers of additional colonoscopies compared with G-FOBT. Cut-off value is also of importance. It is known to influence the trade-off relationship between sensitivity and specificity. Our work showed that the costs related to diagnostic colonoscopies due to falsepositive screening results as part of the total cost of the screening programme were at their lowest when one-stool FITs were performed, compared with two-stool FITs.

In conclusion, this work suggested that the one-stool sample FIT test could be of real interest from a cost-effectiveness point of view. These results should be considered as an additional tool for decision-making and should provide relevant information to pharmaceutical firms and the national authorities concerning the best strategy to adopt for organisational, economic and public health issues related to colorectal cancer screening.

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Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dld.2013.07.018.

References

[1] Gyrd-Hansen D, Sogaard J, Kronborg O. Analysis of screening data: colorectal cancer. International Journal of Epidemiology 1997;26:1172–81.
[2] Launoy G, Smith TC, Duffy SW, et al. Colorectal cancer mass-screening: estimation of faecal occult blood test sensitivity, taking into account cancer mean sojourn time. International Journal of Cancer 1997;73:220–4.
[3] Guittet L, Bouvier V, Mariotte N, et al. Comparison of a guaiac based and an immunochemical faecal occult blood test in screening for colorectal cancer in a general average risk population. Gut 2007;56:210–4.
[4] Hol L, Wilschut JA, van Ballegooijen M, et al. Screening for colorectal cancer: random comparison of guaiac and immunochemical faecal occult blood testing at different cut-off levels. British Journal of Cancer 2009;100:1103–10.
[5] van Rossum LG, van Rijn AF, Laheij RJ, et al. Cut-off value determines the performance of a semi-quantitative immunochemical faecal occult blood test in a colorectal cancer screening programme. British Journal of Cancer 2009;101:1274–81.
[6] Barouni M, Larizadeh MH, Sabermahani A, et al. Markov's modeling for screening strategies for colorectal cancer. Asian Pacific Journal of Cancer Prevention 2012;13:5125–9.
[7] Berchi C, Bouvier V, Réaud JM, et al. Cost-effectiveness analysis of two strategies for mass screening for colorectal cancer in France. Health Economics 2003;49:3–9, 6.
[8] Berchi C, Guittet L, Bouvier V, et al. Cost-effectiveness analysis of the optimal threshold of an automated immunochemical test for colorectal cancer screening: performances of immunochemical colorectal cancer screening. International Journal of Technology Assessment in Health Care 2010;26: 48–53.
[9] Chen LS, Liao CS, Chang SH, et al. Cost-effectiveness analysis for determining optimal cut-off of immunochemical faecal occult blood test for population-based colorectal cancer screening (KCIS 16). Journal of Medical Screening 2007;14:191–9.
[10] Goede SL, van Roon AH, Reijerink JC, et al. Cost-effectiveness of one versus two sample faecal immunochemical testing for colorectal cancer screening. Gut 2012;62:727–34.
[11] Sobhani I, Alzahouri K, Ghout I, et al. Cost-effectiveness of mass screening for colorectal cancer: choice of fecal occult blood test and screening strategy. Diseases of the Colon and Rectum 2011;54:876–86.
[12] Telford JJ, Levy AR, Sambrook JC, et al. The cost-effectiveness of screening for colorectal cancer. CMAJ 2010;182:1307–13.
[13] van Rossum LG, van Rijn AF, Verbeek AL, et al. Colorectal cancer screening comparing no screening, immunochemical and guaiac fecal occult blood tests: a cost-effectiveness analysis. International Journal of Cancer 2010;128: 1908–17.
[14] Wilschut JA, Hol L, Dekker E, et al. Cost-effectiveness analysis of a quantitative immunochemical test for colorectal cancer screening. Gastroenterology 2011;141:1648–55.
[15] Lejeune C, Arveux P, Dancourt V, et al. A simulation model for evaluating the medical and economic outcomes of screening strategies for colorectal cancer. European Journal of Cancer Prevention 2003;12:77–84.
[16] Faivre J, Dancourt V, Lejeune C, et al. Reduction in colorectal cancer mortality by fecal occult blood screening in a French controlled study. Gastroenterology 2004;126:1674–80.
[17] Faivre J, Dancourt V, Denis B, et al. Comparison between a guaiac and three immunochemical faecal occult blood tests in screening for colorectal cancer. European Journal of Cancer 2012;48:2969–76.
[18] Faivre J, Dancourt V, Manfredi S, et al. Positivity rates and performances of immunochemical faecal occult blood tests at different cut-off levels within a colorectal cancer screening programme. Digestive and Liver Disease 2012, 700-04.
[19] Nakama H, Yamamoto M, Kamijo N, et al. Colonoscopic evaluation of immunochemical fecal occult blood test for detection of colorectal neoplasia. Hepato-Gastroenterology 1999;46:228–31.
[20] Rozen P, Comaneshter D, Levi Z, et al. Cumulative evaluation of a quantitative immunochemical fecal occult blood test to determine its optimal clinical use. Cancer 2010;116:2115–25.
[21] Rosman AS, Korsten MA. Effect of verification bias on the sensitivity of fecal occult blood testing: a meta-analysis. Journal of General Internal Medicine 2010;25:1211–21.
[22] Pickhardt PJ, Hassan C, Halligan S, et al. Colorectal cancer: CT colonography and colonoscopy for detection – systematic review and meta-analysis. Radiology 2011;259:393–405.
[23] van Roon AH, Wilschut JA, Hol L, et al. Diagnostic yield improves with collection of 2 samples in fecal immunochemical test screening without affecting attendance. Clinical Gastroenterology and Hepatology 2011;9: 333–9.
[24] Lejeune C, Arveux P, Dancourt V, et al. Cost-effectiveness analysis of fecal occult blood screening for colorectal cancer. International Journal of Technology Assessment in Health Care 2004;20:434–9.
[25] INCa Institut National du Cancer. Synthèse relative aux modalités de migration vers l'utilisation des tests immunologiques de dépistage; 2012. http://www.e-cancer.fr/toutes-les-actualites/235/6706-linca-publie-une-synthese-relative-aux-modalites-de-migration-vers-lutilisation-des-tests-immunologiques-de-depistage
[26] INCa Institut National du Cancer. Dossier de Presse: campagne de mobilisation pour le dépistage organisé du cancer colorectal; 2012. http://www.e-cancer.fr/la-presse/dossiers-de-presse
[27] Pox CP, Altenhofen L, Brenner H, et al. Efficacy of a nationwide screening colonoscopy program for colorectal cancer. Gastroenterology 2012;142:1460–7, e2.
[28] Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. Health Economics 2004;13:437–52.