Colorectal cancer screening program: cost effectiveness of systematic recall letters

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SUMMARY

Objectives — The French colorectal cancer screening program has planned a stepwise strategy for delivery of a fecal occult blood test kit (Hemocult II®) with an initial medical phase followed by systematic mailing of the test. Our aim was to ascertain the cost effectiveness of another recall method.

Methods — In the Bouches-du-Rhône administrative area, we conducted a cost effectiveness study comparing two second line delivery methods: mailing the test kit systematically to all non-responders to the initial medical phase (conventional strategy) and mailing the test kit to non-responders to the initial medical phase who requested a kit after receiving a recall letter (experimental strategy). After randomization, two groups were constituted among a sample of 10 930 persons.

Results — The participation rate was significantly higher in the conventional strategy group than with the experimental strategy group (14.7% vs 8.3%; P < 10^-5). The mean cost of the conventional strategy test was 33.59 euros compared to only 18.50 euros with the experimental strategy (kit mailed only to persons who requested it).

Conclusion — These findings suggest that mailing a recall letter with a test order coupon can lead to substantial economy with a lost of participation to the phase of systematic mailing of the test. Our aim was to ascertain the cost effectiveness of another recall method.

RÉSUMÉ

Dépistage organisé du cancer colorectal : coût/efficacité des relances systématiques

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Objectifs — Le programme français de dépistage des cancers colorectaux prévoit une stratégie séquentielle de délivrance du test Hémocult II® : phase médicale puis relance par envoi postal du test. L’objectif de l’étude était de tester l’efficacité et le coût d’une autre méthode de relance.


Après randomisation, deux groupes ont été constitués parmi un échantillon de 10 930 personnes.

Résultats — Le taux de participation au dépistage était significative ment plus élevé dans le groupe classique que dans le groupe expérimental (14.7 % vs 8.3 % ; P < 10^-5). Le coût unitaire du test lu est de 33,59 euros lorsque la stratégie classique est appliquée contre 18,50 euros quand la méthode d’envoi postal sélectif est utilisée.

Conclusion — L’envoi d’un bon de commande du test pourrait permettre une économie substantielle au détriment d’une baisse de participation à la phase d’envoi postal de 6,4 %. L’utilisation alternative (communication, information) des ressources dégagées pourrait peut-être permettre d’obtenir une participation plus élevée. Cette hypothèse mériterait d’être testée.

Introduction

Colorectal cancer affects 36,000 persons per year in France and is the second leading cause of death by cancer with 16,000 deaths annually [1]. The efficacy of population-based screening had been clearly demonstrated. Three controlled trials demonstrated that screening with a fecal occult blood test (FOBT) can decrease mortality by colorectal cancer by 15 to 18% [2-4], but this decrease in mortality is critically dependent on the level of participation in screening campaigns and of actual test execution. In light of these findings, and in consideration of national and European recommendations [5], in 2001 the French Ministry of Health initiated a pilot screening program for colorectal cancer among persons aged 50-74 years. This program, which used the Hémocult II® FOBT kit, was conducted in 22 administrative areas, including Bouches-du-Rhône in the south east of France. The program was financed by the social security health insurance fund and the Ministry of Health and was designed to determine a cost effective national strategy. The level of participation of the target population was considered to be essential [6].

According to the objectives outlined by the national committee for colorectal cancer screening [7] and in line with earlier experience in France [8], a mixed strategy for delivering the test kits was applied. An initial “medical” phase, during which the
A second “postal” phase was employed in the second phase of the screening campaign where the test kit was mailed to the entire population. Application of this two-phase recruitment scheme was expected to produce a participation rate above 50%, but at the expense of mailing the test kit to more than 50% of the population [8]. In another French experience [9], the first-phase participation rate of 41% was finally raised to 51.3% during the second phase, but at the cost of a recall letter to 59% of the population. This second phase, where the test kit was mailed systematically to all non-responders to the first phase, is costly if the rate of use of systematically delivered tests is low in the target population. Because of the high cost of this phase, we considered two recall strategies for non-responders to the first phase. The first strategy was a systematic recall where the test kit was mailed to all non-responders to the first phase. This is the classical strategy advocated by the national health authorities. The second strategy was based on a recall letter mailed with an order coupon for a free test kit. This was the experimental strategy.

We compared these two strategies to determine their efficacy (number of tests actually performed) and cost and thus calculate the incremental cost-effectiveness ratio.

Material and methods

Population

This study was based on the first screening campaign for colorectal cancer conducted in Bouches-du-Rhône beginning in November 2002. This campaign targeted people aged 50-74 years with a moderate risk of colorectal cancer.

In accordance with the national directives, all individuals in the targeted age group received a letter inviting them to attend a consultation with their general practitioner. After the physical examination, the physician delivered the FOBT kit to persons with no particular risk factor for colorectal cancer, in accordance with the national consensus guidelines for the management of colorectal cancer [10]. The invitation letter also included a response coupon so the recipient could decline the invitation for any reason. If there was no response to the first letter, a recall letter was sent three months later, again counselling the person to consult a physician who would deliver the test kit. Following this medical phase, and for persons who still had not responded, the kit was sent directly to them six months after the first invitation letter. This kit was accompanied by a stamped envelope for returning the executed test. At this phase, the test could again be declined without giving a reason. The entire procedure was free.

After presenting the study protocol to the National Technical Group, in 2004 we randomly assigned non-responders to the medical phase residing in the 10th arrondissement of Marseille (10,930 persons in the target age group) to one of two groups. The conventional strategy (systematic mailing of the test kit directly to non-responders) was applied for the first group. The test kit was not sent to persons in the second population who instead received a recall letter with an order coupon to request a free test kit. In this population, a test kit was thus mailed only to persons who explicitly requested one. After the end of this study, and in order to comply with the national directives for colorectal cancer screening strategy, the test kit was sent to all persons in the experimental population.

SPSS v12.0.1 software was used to randomly assign non-responders to one of the study arms.

Effectiveness

Effectiveness was determined from the number of tests actually performed in each group. The incremental cost-effectiveness was the extra cost of one strategy over the other to achieve one additional unit of efficacy (i.e. one additional test result obtained). It was defined as the ratio between the difference in mean cost for the two strategies and the mean number of tests results obtained for each of the two strategies.

Considering the data collected in our area in 2004 (percentage of positive tests, rate of colonoscopy and proportion of explorations detecting tumors and cancers), it was also possible to calculate the cost per additional tumor and the cost per additional cancer detected. These costs were determined at the end of a six-month period after the initial postal phase.

Cost

We adopted the perspective of a screening campaign managed locally. Costs considered are presented in table I. The structural costs were not taken into consideration because they were the same for the two strategies. The values assigned to each item were the real values measured in 2004.

Sensitivity analysis

A sensitivity analysis was performed to determine the impact of changing the unit cost of the FOBT test kit on the overall cost and the incremental cost-effectiveness ratio. Two scenarios were tested with the perspective of a lower unit cost for the FOBT test kit within a framework of tender submission for a generalized screening campaign (from 2.83 euros to 2 euros then to 1 euro).

Statistical analysis

SPSS v12.0.1 was used to apply the chi-square test to compare percentages and analysis of variance to compare means. The cost-effectiveness analysis was performed with Excel 2003.

Results

Among the 10930 persons residing in the 10th arrondissement in Marseille who were invited to participate in the screening campaign, 2283 (20.9%) performed the FOBT during the medical phase of the campaign, 393 (3.6%) mailed kits did not reach their destination and 1,238 (11.38%) medical exclusions were recorded. The rate of participation among the population eligible for screening was thus 24.5% (2,283/(10930-1238-393)). At the end of the medical phase, 7,016 persons out of 10,930 (64.2%) had not responded (these persons had not attended a medical consultation or had not returned the response coupon). These 7,016 persons were randomly assigned to the two strategy groups (3508 to the conventional strategy where the kit was systematic mailed to all non-responders and 3,507 to the experimental selective mailing strategy, figure 1). Mean age and gender distribution were comparable for the two groups. Mean age was 61.3 years in the conventional strategy group and 61.2 years in the experimental strategy group; 54.5% were females in the conventional strategy group and 54.6% in the experimental strategy group.

Table 1 – Unit costs (2004 French local market costs).

<table>
<thead>
<tr>
<th>Product description</th>
<th>Unit cost in euros</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hémoccult IP® test kit</td>
<td>2.83</td>
</tr>
<tr>
<td>Information sheet</td>
<td>0.001</td>
</tr>
<tr>
<td>Plastic bag</td>
<td>0.01653</td>
</tr>
<tr>
<td>Packaging</td>
<td>0.33</td>
</tr>
<tr>
<td>Laboratory determination of test result</td>
<td>4.5</td>
</tr>
<tr>
<td>Envelope for kit</td>
<td>0.02451</td>
</tr>
<tr>
<td>Cover envelop</td>
<td>0.03214</td>
</tr>
<tr>
<td>Printing+packing+routing</td>
<td>0.153</td>
</tr>
<tr>
<td>Paper (+address tags)</td>
<td>0.0615</td>
</tr>
<tr>
<td>Other postal costs</td>
<td>0.31</td>
</tr>
<tr>
<td>Stamps</td>
<td>0.57</td>
</tr>
<tr>
<td>Processing exclusions</td>
<td>0.45</td>
</tr>
</tbody>
</table>
After the mailings were completed, 12 persons had died (four in the conventional group and eight in the experimental group) and 97 did not reside at the address indicated (54 and 43 respectively). Thus the second mailing was effectively sent to 3,450 persons (98.3%) in the conventional strategy group versus 3,457 persons (98.5%) in the experimental strategy group. Age and gender were comparable in these two groups.

Refusals and medical exclusions

Among the populations studied, 498 persons returned the response coupon indicating they had not performed the test: 221 (6.4%) in the conventional group versus 277 (8%) in the experimental group (P < 0.01).

In the conventional group 86 persons (2.5%) declared they declined participation. In the experimental group, 73 persons (2.1%) declared they declined participation. The difference was not significant.

Two types of responses were distinguished among the other coupons received: temporary exclusion from the screening campaign and definitive exclusion, corresponding to persons with a high risk of colorectal cancer. These results are presented in table II.

Table II – Persons excluded for medical reasons.

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>Duration of exclusion</th>
<th>Conventional group (N=3,450)</th>
<th>Experimental group (N=3,457)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of polyps</td>
<td>Definitive</td>
<td>25 (0.72%)</td>
<td>48 (1.39%)</td>
</tr>
<tr>
<td>History of colorectal cancer</td>
<td></td>
<td>4 (0.12%)</td>
<td>9 (0.26%)</td>
</tr>
<tr>
<td>History of inflammatory bowel disease</td>
<td></td>
<td>1 (0.03%)</td>
<td>2 (0.06%)</td>
</tr>
<tr>
<td>History of colorectal cancer in 1st degree relative</td>
<td></td>
<td>3 (0.09%)</td>
<td>12 (0.35%)</td>
</tr>
<tr>
<td>Fecal occult blood test de sang within last year</td>
<td>2 years (advised to participate in next campaign)</td>
<td>16 (0.46%)</td>
<td>29 (0.84%)</td>
</tr>
<tr>
<td>Normal coloscopy within last five years</td>
<td></td>
<td>71 (2.06%)</td>
<td>84 (2.43%)</td>
</tr>
<tr>
<td>Scheduled colonoscopy</td>
<td></td>
<td>11 (0.32%)</td>
<td>9 (0.26%)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>4 (0.12%)</td>
<td>11 (0.32%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>135 (3.91%)</td>
<td>204 (5.90%)</td>
</tr>
</tbody>
</table>

Medical exclusion was more frequent in the experimental group (5.9% versus 3.9%, \( P < 10^{-5} \)). This trend was also observed for definitive exclusion: 71 (2%) persons in the experimental group and 33 (1%) in the conventional group (\( P < 10^{-5} \)). The persons who indicated a definitive exclusion were younger in the experimental group (62.1 years versus 65 years, \( P < 0.05 \)) with no difference by gender.

**Tests performed**

In the conventional group, 3,508 test kits were mailed. In the experimental group, test kits were sent to the 389 persons (11.1%) who requested them. The number of tests actually executed was different. In the conventional group, 489 persons (14.2%) performed the test versus 271 (7.8%) in the experimental group (\( P < 10^{-5} \)). Expressed as the proportion of tests actually performed among the total number of test kits mailed, the rate of tests performed was 13.9% in the conventional group and 69.7% in the experimental group (\( P < 10^{-5} \)). Considering the persons who performed the screening test, there was no difference between the groups for age or gender (61 years and 56.6% females in the conventional group and 60.1 years and 57.7% females in the experimental group).

The rate of participation among the population eligible for screening was \( 71/3457 \times 100 \) = 2% in the conventional group and \( 271/(3457 - 204) \times 100 \) = 8.3% in the experimental group (\( P < 10^{-5} \)).

Taking into consideration the rate of participation achieved during the medical phase, the overall rate of participation in the population eligible for screening was 36.6% with the conventional strategy of systematic mailing to 7,016 persons and 32.1% with the experimental selective mailing strategy.

**Cost-effectiveness analysis**

The total cost of the operation was 16424 euros in the conventional group and 5013 euros in the experimental group (11141 euros less expensive). The unit cost per test result was 33.59 euros with the conventional strategy and 18.50 euros (11411 euros less expensive). The incremental cost-effectiveness ratio was 52.34 euros for the systematic mailing strategy versus the selective mailing strategy. Systematic mailing of the test kit was more effective but also more costly than targeted mailing. Thus to achieve one additional test result with systematic mailing, the cost was 52.34 euros greater than with selective mailing.

Taking into consideration persons excluded from the cost-effectiveness analysis for medical reasons, which is the same as using the rate of participation of the eligible population to determine the incremental cost-effectiveness ratio, this cost decreases slightly from 52.34 euros to 51.24 euros per additional test result.

Considering the results obtained during the first screening campaign in our area (table IV), the cost per additional tumor discovered was 7124 euros and the cost per additional cancer detected (irrespective of stage) was 18927 euros.

**Sensitivity analysis**

The cost of the screening test kit considered for this analysis was the price paid to suppliers by the structures in charge of organizing the screening campaign in France in 2004. If the cost of the kit (Hémoccult®) were reduced from 2.83 euros to 2 euros then 1 euro, the incremental cost-effectiveness ratio for the systematic mailing strategy compared with the selective mailing strategy would decrease from 52.34 per additional test result to 40.47 euros then 26.16 euros.

**Table IV**. – Cost per additional tumors and cancers observed at the recall phase per strategy.

<table>
<thead>
<tr>
<th>Event</th>
<th>Systematic mailing strategy</th>
<th>Selective mailing strategy</th>
<th>Difference</th>
<th>Cost per additional event in euros</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-responders to first medical phase</td>
<td>311 324 (rate applied)</td>
<td>311 324 (rate applied)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Letters actually received</td>
<td>306 177 (98.3%)</td>
<td>306 798 (98.5%)</td>
<td>-621</td>
<td></td>
</tr>
<tr>
<td>Screening tests</td>
<td>42 559 (13.9%)</td>
<td>23 930 (7.8%)</td>
<td>18628</td>
<td>52.3</td>
</tr>
<tr>
<td>Positive tests(^a)</td>
<td>851 (2%)</td>
<td>479 (2%)</td>
<td>373</td>
<td>2615</td>
</tr>
<tr>
<td>Colonoscopy after positive test(^b)</td>
<td>709 (83.3%)</td>
<td>399 (83.3%)</td>
<td>310</td>
<td>3139</td>
</tr>
<tr>
<td>Tumors detected(^a)</td>
<td>313 (44.1%)</td>
<td>176 (44.1%)</td>
<td>137</td>
<td>7124</td>
</tr>
<tr>
<td>Cancers detected(^a)</td>
<td>118 (16.6%)</td>
<td>66 (16.6%)</td>
<td>52</td>
<td>18927</td>
</tr>
</tbody>
</table>

\(^a\) rate observed in this study; \(^b\) rate determined from data from the first campaign (2002-2004) in Bouches-du-Rhône.
Implementation of a nationwide screening program for colorectal cancer should not lead to a decrease in the total expenditure devoted to this disease. The results of one French study [11] on the cost of care for colorectal cancer suggest that the implementation of an organized screening plan does not reduce the cost of management during the first year. According to Labadaum et al. [12], although cost related to cancer management should decline, the cost of operating the screening campaign leads to an increase in total expenditure to the order of 9 to 85% depending on the strategy adopted (from 9% for annual search for fecal occult blood using a guaiac test to 83% for a test based on fecal DNA). In this perspective, and in the current context in France where the screening program is gaining intensity, it appeared important to study the initial systematic mailing phase of the campaign as planned in the national strategy and to compare it with a method of selective mailing.

Application of one or other of these strategies leads to differences in responses. The selective mailing strategy requires an additional response from the targeted person who has to request the test kit explicitly. To be compliant with the national directives, this additional action should not be required. This additional effort led to a smaller number of persons actually performing the testing: 271 (7.8%) versus 489 (14.2%) for the systematic mailing strategy. On the contrary, from a pragmatic point of view and taking into consideration the letters which were not distributed (deceased persons or persons not residing at the address indicated), the experimental mailing system was more selective since 69.7% of the tests mailed were performed versus 13.9% for the systematic mailing strategy.

An unexpected observation was the significantly greater number of persons in the experimental group compared with the conventional group responding that they did not participate for medical reasons: 204 (5.9%) versus 135 (3.9%). There might be two explanations. The first would be a sampling bias, which can be excluded since the assignment to the two groups was randomized and the objective criteria (age, gender) were not different. The second would be a need for justification related to the way the selective recall letter was drafted. Nevertheless, the reality of the facts voluntarily reported by the responders who did not perform the test cannot be questioned on the basis of the study methodology which used a self-administered questionnaire. The application of the experimental strategy did not however increase the number of persons declining participation.

During the postal phase, the participation rate fell 6.4% with the selective mailing strategy compared with the systematic strategy, but also produced a cost saving to the order of 26.16 to 52.34 euros per test result, depending on the kit cost figure estimated in France [14]. A new analysis would be necessary to compare application of selective mailing of the immunological test and systematic mailing of the same test in order to take into consideration its specific cost and its diagnostic characteristics.

Randomization was insufficient to ensure comparability between the two groups, but a double-blinded methodology is not possible for this type of study.

The results of this study require an intention-to-treat analysis which leads to a pragmatic, rather than explanatory, interpretation of the results.

In the current phase of implementation of organized screening for colorectal cancer in France, several pilot administrative areas have experienced difficulty in achieving the goal of a participation rate above 50%. In this context, lowering the participation rate during the postal phase by 6.4%, or for the entire program by 4.5%, might appear unacceptable. Nevertheless, our study raises the question of the use of the resources saved by the selective mailing strategy, and of the impact of such use on screening performance. If these resources were invested in improving the population’s awareness of the problem and in health education, there might be a significant increase in the participation rate after application of a selective mailing strategy.

REFERENCES