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# Diagnostic yield of a one sample immunochemical test at different cut-off values in an organised screening programme for colorectal cancer

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**Abstract** ***Background:*** Quantitative immunochemical faecal occult blood tests have become the recommended tests for colorectal cancer screening. The aim of this study was to complete our knowledge on the performance of one of the quantitative immunochemical tests available, FOB-Gold, and to propose a possible strategy for an organised screening programme.
***Patients and methods:*** Within the French organised screening programme, 23,231 average-risk individuals, aged 50–74 performed both a 3-day Hemoccult test and a 1-day FOB-Gold test. Performances of the immunochemical test were evaluated at different cut-off levels.
***Results:*** The positivity rate for the Hemoccult was 2.1% and for the FOB-Gold varied between 4.6% (cut-off value of 100 ng/mL, the lowest studied cut-off) and 2.1% (cut-off value of 352 ng/mL). The number of colonoscopies decreased with increasing cut-off values by 21.5% (150 ng/mL), 35.4% (200 ng/mL) and 53.3% (352 ng/mL). The corresponding miss rate for CRC was respectively 6.4%, 11.1% and 22.2%, and for advanced adenoma respectively 16.3%, 29.2% and 43.6%. Compared with the reference cut-off for the FOB-Gold (100 ng/mL) the miss rate for Hemoccult was 53% for CRC and 77% for advanced adenoma.
***Conclusion:*** The study suggests that in countries with colonoscopy facilities compatible with a screening test positivity rate of up to 5%, use of a 1-day test with a cut-off value between 100 and 150 ng/mL could be the recommended strategy. Further increasing the cut-off value up to the same positivity rate as Hemoccult could be used in areas with limited access to colonoscopy.


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## 1. Introduction

Colorectal cancer is a major public health problem in most West and East European countries. It is the second most common cancer and the second most common cause of death by cancer.[1] Population-based studies have shown that guaiac faecal occult blood testing can reduce colorectal cancer (CRC) mortality.[2–4] However, these tests have been criticised for their low sensitivity and because they react to non-human haem in food. A second generation of faecal occult blood tests, immunochemical tests, which are specific to human haemoglobin, is now available. Particular attention has been paid to quantitative faecal immunochemical tests (FIT) with an automated system for the interpretation of the test. They are easier to interpret, and minimise human error in test processing thus making them a more objective laboratory test with excellent quality control. They can determine the concentration of human haemoglobin in faecal samples. It is thus possible to determine a cut-off value to define a positive test. It is now clear from available data that FITs outperform guaiac tests for the detection rate of both CRC and advanced adenoma, and for participation.[5–8] They should therefore be preferred for CRC screening.[9] The one-sample strategy has now been adopted in most screening programmes as it has been shown that by decreasing the cut-off value similar performances can be achieved with one-compared with 2-day sampling[10,11] and at a lower cost.[12]

In France, an organised screening programme using the Hemoccult test has been available throughout the country since 2009. The Ministry of Health has announced the shift to FIT. A tendering procedure to choose the FIT is still to be organised. The Health Authorities need to determine the optimal cut-off value on the basis of the balance between resources and an acceptable proportion of missed cancers. Most previous studies to evaluate the performance of FIT were conducted during the first screening round using the OC-Sensor test. There is a lack of data on the diagnostic yield of FIT within an on-going screening programme, in particular compared with other FITs and relatively low cut-off values. The aim of this study was therefore to provide further information on the performance of one-sample FIT (FOB-Gold) over a range of different cut-off values within the organised CRC screening programme using the Hemoccult test.

## 2. Patients and methods

### 2.1. Study population

Within the organised screening programme for CRC currently underway in France, subjects living in well-defined areas of Burgundy, aged 50–74, were invited in 2011 to perform both a guaiac test: the Hemoccult test (Beckman Coulter, Brea, USA), and a FIT test: FOB-Gold (Sentinel, Milan, Italy for Beckman Coulter, Brea, USA).

In accordance with French guidelines concerning CRC screening, published in the Official Journal of the Republic,[13] the following subjects were excluded from FOBT screening: those with digestive symptoms, a previous history of CRC or adenoma, a first-degree relative of an index case who had CRC before 65 and those with at least two first-degree relatives whatever the age, affected by extended Crohn's disease or ulcerative colitis for at least 15 years. A screening colonoscopy is recommended in these situations. Subjects with a normal colonoscopy performed during the past 5 years or a severe illness contra-indicating screening were also excluded from the study.

The screening round began by sending an information letter to each participant along with an information brochure. During the first 6 months of the screening campaign, general practitioners were asked to offer the screening test free of charge to the eligible subjects seen at their practice. For patients who did not complete the test during this medical phase, the coordination centre in charge of organising the screening campaign subsequently mailed the test. Prior to the start of the screening round, general practitioners were thoroughly informed about the research project. Individuals were asked to perform both the Hemoccult test and the FIT. As the two tests were not provided during the entire screening campaign, it was not possible to calculate the participation rate.

### 2.2. Faecal occult blood tests

The completed tests were sent by mail to the central analysis centre in the prepaid envelope provided. The tests were stored at room temperature before mailing. Patients were instructed to send the tests as soon as they were completed. The median time between faeces deposit and processing of the test was 5 days. Twenty-five per cent of the tests were interpreted within 3 days and 75% within 6 days. The maximum time between the data of first faeces deposit and processing of the test had to be less than 10 days. Samples were assayed by trained staff on the day they were received. The Hemoccult test and the FOB-Gold test were processed independently.

The Hemoccult was performed by taking two samples from separate points of three consecutive stools. No diet or drug restrictions were imposed. Studies in the UK and France[3,4] indicated that in the absence of restrictions, the positivity rate of the Hemoccult remained low at under 2.5%. This strategy was thus adopted in these two countries within the organised screening programme. The tests were processed without rehydratation by trained staff according to a standardised procedure.