Colonoscopy versus Fecal Immunochemical Testing in Colorectal-Cancer Screening

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ABSTRACT

BACKGROUND
Colonoscopy and fecal immunochemical testing (FIT) are accepted strategies for colorectal-cancer screening in the average-risk population.

METHODS
In this randomized, controlled trial involving asymptomatic adults 50 to 69 years of age, we compared one-time colonoscopy in 26,703 subjects with FIT every 2 years in 26,599 subjects. The primary outcome was the rate of death from colorectal cancer at 10 years. This interim report describes rates of participation, diagnostic findings, and occurrence of major complications at completion of the baseline screening. Study outcomes were analyzed in both intention-to-screen and as-screened populations.

RESULTS
The rate of participation was higher in the FIT group than in the colonoscopy group (34.2% vs. 24.6%, P<0.001). Colorectal cancer was found in 30 subjects (0.1%) in the colonoscopy group and 33 subjects (0.1%) in the FIT group (odds ratio, 0.99; 95% confidence interval [CI], 0.61 to 1.64; P = 0.99). Advanced adenomas were detected in 514 subjects (1.9%) in the colonoscopy group and 231 subjects (0.9%) in the FIT group (odds ratio, 2.30; 95% CI, 1.97 to 2.69; P<0.001), and nonadvanced adenomas were detected in 1109 subjects (4.2%) in the colonoscopy group and 119 subjects (0.4%) in the FIT group (odds ratio, 9.80; 95% CI, 8.10 to 11.85; P<0.001).

CONCLUSIONS
Subjects in the FIT group were more likely to participate in screening than were those in the colonoscopy group. On the baseline screening examination, the numbers of subjects in whom colorectal cancer was detected were similar in the two study groups, but more adenomas were identified in the colonoscopy group. (Funded by Instituto de Salud Carlos III and others; ClinicalTrials.gov number, NCT00906997.)
Colorectal cancer is the third most common cancer worldwide and the second leading cause of cancer-related deaths. Several studies have shown that colorectal-cancer screening is effective and cost-effective in the average-risk population.

Recommended strategies for colorectal-cancer screening fall into two broad categories: stool tests (occult blood and exfoliated DNA tests) and structural examinations (flexible sigmoidoscopy, colonoscopy, and computed tomographic colonography). Stool tests primarily detect cancer, and structural examinations detect both cancer and premalignant lesions. Stool tests for occult blood (guaiac testing and fecal immunochemical testing [FIT]) are predominantly used in Europe and Australia, whereas colonoscopy is the predominant screening method in the United States.

Colonoscopy is considered the most accurate test for early detection and prevention of colorectal cancer. Although data from randomized studies evaluating the effect of colonoscopy on the rate of death from colorectal cancer are lacking, the procedure is recommended as a first-line screening test on the basis of indirect data and observational studies. Population-based case-control studies have suggested that colonoscopy markedly reduces the risk of colorectal cancer and death. Recent evidence suggests that patients with no abnormalities on a previous colonoscopy have a markedly reduced risk of colorectal cancer. In a cohort of average-risk subjects, the use of screening colonoscopy was associated with a reduction in the incidence of colorectal cancer of 67% and a reduction in the rate of death of 65%. Cohort studies involving patients with adenomas have suggested that polypectomy can prevent approximately 80% of colorectal cancers.

Comparative studies have shown that the semi-quantitative FIT is more accurate than the guaiac test for the detection of colorectal cancer and advanced adenomas, and this new test is now recommended as the first-choice fecal occult blood test in colorectal-cancer screening. Although FIT is less effective for neoplastic detection than colonoscopy or sigmoidoscopy, evidence suggests that it may be better accepted, and higher acceptance may counteract its lower detection capacity. It has been suggested that FIT may be more effective and less costly than other screening strategies. We conducted a randomized, controlled trial to compare semiquantitative FIT with colonoscopy. We hypothesized that FIT screening every 2 years would be noninferior to one-time colonoscopy with respect to a reduction in mortality related to colorectal cancer among average-risk subjects. This interim report describes rates of participation, diagnostic findings, and the occurrence of major complications at the completion of the baseline screening.

**METHODS**

**STUDY DESIGN**

We conducted this randomized, controlled, noninferiority trial in eight Spanish regions (Aragón, Basque Country, Canarias, Catalonia, Galicia, Madrid, Murcia, and Valencia) with the participation of 15 tertiary care hospitals. The study was designed to assess the efficacy of one-time colonoscopy and biennial FIT for reducing the rate of death from colorectal cancer at 10 years (primary trial outcome). The study started in November 2008 with an informative nationwide campaign. The recruitment period was initiated in June 2009, and the first round finished in June 2011. Ten-year follow-up will be completed in 2021.

The study protocol (available with the full text of this article at NEJM.org) was approved by the ethics committee at each hospital, and all subjects provided written informed consent.

**STUDY POPULATION**

Asymptomatic men and women between the ages of 50 and 69 years were eligible for enrollment. Exclusion criteria, which were ascertained after randomization by means of a questionnaire at the local screening office, included a personal history of colorectal cancer, adenoma, or inflammatory bowel disease; a family history of hereditary or familial colorectal cancer (i.e., ≥2 first-degree relatives with colorectal cancer or 1 in whom the disease was diagnosed before the age of 60 years) and death; a severe coexisting illness; and previous colectomy. Subjects were also temporarily excluded if they had undergone fecal occult blood testing in the previous 2 years or sigmoidoscopy or colonoscopy within the previous 5 years or if they had symptoms requiring additional workup. The subjects with previous screening tests became eligible when sufficient time had elapsed since the tests, and those with symptoms became eligible if the results of the clinical workup were negative.
Randomization
Subjects were identified through each Community Health Registry, sorted according to household, and stratified according to age (in 5-year age groups) and sex. Households were randomly assigned in a 1:1 ratio to undergo either one-time colonoscopy or biennial FIT. Randomization was performed before invitation with the use of a computer-generated allocation algorithm on the basis of a randomized-blocks method. Subjects were sent a preinvitation letter containing information on colorectal-cancer screening and the rationale for the study. Two weeks later, an invitation letter was sent indicating the subject’s study-group assignment. Two additional, reminder letters were mailed 3 and 6 months after the invitation to subjects who did not respond to the first mailed invitation. Subjects who agreed to participate in the study received an appointment at the local screening office, where they completed the questionnaire. The study design allowed for crossover between the two study groups.

Study Interventions
Among patients undergoing colonoscopy, bowel cleansing and sedation were performed as described previously. All colonoscopies were performed by experienced endoscopists (those who had performed >200 colonoscopies per year). Polyps were categorized as non-neoplastic or neoplastic. Adenomas measuring 10 mm or more in diameter, with villous architecture, high-grade dysplasia, or intramucosal carcinoma, were classified as advanced adenomas. Invasive cancer was considered to be present when malignant cells were observed beyond the muscularis mucosae. Advanced neoplasm was defined as advanced adenoma or invasive cancer. Tumor staging, performed according to the classification system of the American Joint Committee on Cancer, was based on the most advanced lesion.

The FIT strategy consisted of analysis of a single stool sample with the use of the automated semi-quantitative OC-Sensor (Eiken Chemical) without specific restrictions on diet or medication use. Samples were processed as described previously at each regional hospital. Subjects who were found to have a hemoglobin level of 75 ng per milliliter or more were invited to undergo colonoscopy.

Details regarding quality indicators for colonoscopy are provided in the study protocol and in Table 1 in the Supplementary Appendix, available at NEJM.org.

Study Oversight
Palex Medical and Biogen Diagnóstica donated supplies and automated fecal occult-blood analyzers used for FIT but provided no other support for the study. The companies were not involved in the design of the study, in the analysis or interpretation of the data, or in the preparation of the manuscript.

Statistical Analysis
This study was based on the assumption that screening average-risk subjects by means of biennial FIT would not be inferior to one-time colonoscopy with respect to the rate of death from colorectal cancer at 10 years. The calculations were based on an overall compliance rate of 30% and a crude 10-year rate of death from colorectal cancer of 6.96%. Therefore, assuming a crude 10-year rate of death from colorectal cancer of 1.74% among subjects undergoing colonoscopy (a 75% reduction) and of 3.41% among those screened by means of FIT (a 51% reduction) and accepting a noninferiority condition if the absolute difference was below 1.6 percentage points, we determined that a sample of 55,498 subjects (27,749 in each study group) would provide a power of 80%. A P value of less than 0.025 was considered to indicate statistical significance with the use of a one-sided test of proportions.

We assessed study outcomes in both intention-to-screen and as-screened analyses. In the latter analysis, the detection rate was calculated as the number of subjects with true positive results divided by the number of subjects who actually underwent testing. The diagnostic yield was the number of subjects with true positive results divided by the number of eligible subjects in the intention-to-screen analysis. Subjects were excluded from the intention-to-screen analysis if they attended the screening office visit and met one or more exclusion criteria. Subjects who did not attend the screening office visit and thus did not provide information about exclusion criteria were classified as eligible and were included in the intention-to-screen analysis. Between-group differences in rates of participation, diagnostic yield, detection, and complications were established by logistic-regression analysis, with adjustment for age, sex, and participating center, and are reported as odds ratios with 95% confidence intervals. All analyses were performed with the use of SPSS statistical software, version 15.0.
RESULTS

STUDY POPULATION
Overall, 57,404 subjects were randomly assigned to undergo either colonoscopy or FIT. Of these subjects, 1970 could not be contacted and 2132 were excluded either permanently (1.7% in the colonoscopy group and 1.3% in the FIT group, \( P = 0.20 \)) or temporarily (2.2% in the colonoscopy group and 2.2% in the FIT group, \( P = 0.11 \)) (Fig. 1). The eligible population consisted of 26,703 subjects in the colonoscopy group and 26,599 in the FIT group. The two groups were almost identical regarding both mean (±SD) age (59.2±5.5 years in the colonoscopy group and 59.3±5.6 years in the FIT group, \( P = 0.35 \)) and the proportion of subjects who were women (53.5% in the colonoscopy group and 54.3% in the FIT group, \( P = 0.25 \)).

PARTICIPATION
Among subjects who were assigned to undergo colonoscopy, 5649 subjects accepted the proposed strategy, whereas 1706 requested to be screened by means of FIT (Fig. 1). Of the 5649 subjects who agreed to undergo colonoscopy, 4953 actually did so, and 1628 underwent FIT, for a participation rate of 24.6%, according to the intention-to-screen analysis (average age, 59.1±5.5 years; proportion of subjects who were women, 53.4%). Among subjects who were assigned to undergo FIT, 9353 subjects accepted the proposed strategy, whereas 117 asked to be screened by colonoscopy. A total of 8983 subjects underwent FIT, and 106 underwent colonoscopy, for an overall participation rate of 34.2% (average age, 59.3±5.6 years; proportion of subjects who were women, 54.4%). Therefore, there were differences between study groups regarding both the rate of participation (odds ratio in the colonoscopy group, 0.63; 95% confidence interval [CI], 0.60 to 0.65; \( P < 0.001 \)) and the crossover rate (odds ratio, 16.8; 95% CI, 13.9 to 20.2; \( P < 0.001 \)).

DIAGNOSTIC YIELD
In the intention-to-screen analysis, colorectal cancer was detected in 30 subjects (0.1%) in the colonoscopy group and in 33 subjects (0.1%) in the FIT group (odds ratio in the colonoscopy group, 0.99; 95% CI, 0.61 to 1.64; \( P = 0.99 \)) (Table 1). Advanced adenomas were found in 514 subjects (1.9%) in the colonoscopy group and in 231 subjects (0.9%) in the FIT group (odds ratio, 2.30; 95% CI, 1.97 to 2.69; \( P < 0.001 \)). Nonadvanced adenomas were found in 1109 subjects (4.2%) in the colonoscopy group and in 119 subjects (0.4%) in the FIT group (odds ratio, 9.80; 95% CI, 8.10 to 11.85; \( P < 0.001 \)).

When the diagnostic yield was analyzed according to the location of lesions, no significant between-group difference was found for either proximal or distal colorectal cancer (Table 2). However, colonoscopy performed significantly better than FIT in the diagnosis of advanced and nonadvanced adenomas that were either proximal or distal to the splenic flexure. The superior diagnostic yield of colonoscopy for advanced adenomas was most evident for lesions in the proximal colon (Table 2).

DETECTION RATE
On the basis of the screening that was actually performed, 5059 subjects underwent colonoscopy and 10,611 underwent FIT (Fig. 1). Among subjects who were screened by means of FIT, 767 (7.2%) tested positive, and 663 of these subjects (86.4%) underwent colonoscopy. Among subjects who were screened by means of colonoscopy, 27 (0.5%) were found to have colorectal cancer, as compared with 36 subjects (0.3%) who were screened by means of FIT (odds ratio, 1.56; 95% CI, 0.93 to 2.56; \( P = 0.09 \)) (Table 3).

Tumor staging was similar in the two groups. In the FIT group, 24 tumors were stage I, 6 were stage II, and 6 were stage III. In the colonoscopy group, 19 tumors were stage I, 6 were stage II, and 2 were stage III (\( P = 0.52 \)). Colonoscopy was superior to FIT in the rates of detection of advanced adenomas (odds ratio, 4.32; 95% CI, 3.69 to 5.07; \( P < 0.001 \)) and nonadvanced adenomas (odds ratio, 25.98; 95% CI, 21.27 to 31.74; \( P < 0.001 \)) (Table 3).

No significant difference was observed in the rate of detection of colorectal cancer when subjects were stratified according to tumor location (Table 2 in the Supplementary Appendix). However, colonoscopy performed better than FIT with respect to detection rates for advanced and nonadvanced adenomas in both the proximal and distal colon.

ANALYSIS OF RESOURCES
The numbers of subjects who needed to be screened to find one colorectal cancer were 191 in the colonoscopy group and 281 in the FIT group, and the numbers who needed to be screened to find any advanced neoplasm were 10 and 36, respectively (Table 3 in the Supplementary Appendix). However,
57,404 Patients underwent randomization

28,708 Were assigned to colonoscopy
916 Were not contacted
27,792 Were invited to undergo colonoscopy
472 Were permanently excluded
206 Had previous CRC or adenoma
56 Had inflammatory bowel disease
147 Had family history of CRC or polyposis
617 Were temporarily excluded
60 Had colorectal symptoms
557 Had previous screening test

28,696 Were assigned to FIT
1054 Were not contacted
27,642 Were invited to undergo FIT
431 Were permanently excluded
170 Had previous CRC or adenoma
60 Had inflammatory bowel disease
177 Had family history of CRC or polyposis
612 Were temporarily excluded
61 Had colorectal symptoms
551 Had previous screening test

26,703 Were eligible for colonoscopy
7368 Attended screening office
1706 Requested FIT
1628 Completed FIT
92 Had positive results on FIT
76 Completed colonoscopy
Results:
4 CRC
32 Advanced adenomas
9 Nonadvanced adenomas

26,599 Were eligible for FIT
9512 Attended screening office
9353 Accepted FIT
8983 Completed FIT
675 Had positive results on FIT
587 Completed colonoscopy
Results:
26 CRC
482 Advanced adenomas
1100 Nonadvanced adenomas

Figure 1. Enrollment and Outcomes.
A total of 1970 subjects were not contacted after being randomly assigned to undergo either colonoscopy or fecal immunochemical testing (FIT) because they had died or had an inaccurate mailing address, which resulted in the return of the invitation letters. Criteria for permanent exclusion were a personal history of inflammatory bowel disease, colorectal polyps, or colorectal cancer (CRC) and a family history of CRC or polyposis syndromes. Temporary exclusion criteria were the presence of symptoms suggestive of colorectal disease and occult blood testing within the previous 2 years or sigmoidoscopy or colonoscopy within the previous 5 years. The subjects with previous screening tests became eligible when sufficient time had elapsed since the tests, and those with symptoms became eligible if the results of the clinical workup were negative.
the numbers of subjects who needed to undergo colonoscopy to find one colorectal cancer were 191 in the colonoscopy group and 18 in the FIT group; to find any advanced neoplasm, the numbers were 10 and 2, respectively (Table 3 in the Supplementary Appendix).

Complications

Major complications occurred in 24 subjects (0.5%) in the colonoscopy group (12 subjects with bleeding, 10 subjects with hypotension or bradycardia, 1 subject with perforation, and 1 subject with desaturation) and in 10 subjects (0.1%) in the FIT group (8 subjects with bleeding and 2 subjects with hypotension or bradycardia, all of whom required colonoscopy because of a positive result on FIT). Accordingly, the complication rate was higher in the colonoscopy group than in the FIT group (odds ratio, 4.81; 95% CI, 2.26 to 10.20; P<0.001).

Discussion

In this trial, participation rates were low in both groups of subjects who were invited to undergo colorectal-cancer screening, but subjects in the FIT group were more likely to agree to participate than those in the colonoscopy group. The number of patients in whom colorectal cancer was detected was similar in the two study groups, but more patients with adenomas were identified in the colonoscopy group. Since the primary outcome of this trial is the reduction in the rate of death from colorectal cancer at 10 years, the relative benefits and risks of the two strategies will be assessed at the end of the trial.

Our study has a number of strengths. We used a randomized design to compare a sensitive, semiquantitative FIT with colonoscopy. The study design accepts crossover between groups and includes intention-to-screen and as-screened analyses. Our analyses incorporated stratification of results according to the location of detected lesions, thus allowing assessment of differences in procedure performance in both the proximal and distal colon, a critical issue that has become controversial in recent years. However, the study also has a number of limitations. First, the generalizability of the study findings is limited because participation in each screening strategy, a critical aspect with a direct effect on the diagnostic yield, depends on several factors and varies geographically. To overcome this limitation, we also evaluated the rate of detection of the screening procedure that was actually performed in order to establish the intrinsic efficacy of both strategies. Second, although recruitment was encouraged, the rate of participation was lower than expected according to European population-based screening programs and American colonoscopy-based strategies. However, it is important to note that our participation rate did not differ from the corresponding rates in other trials that were performed in a similar setting.

The most relevant result of this interim analysis is that the FIT group had a lower incidence of colorectal cancer than the colonoscopy group. This finding is consistent with previous studies that have shown a lower incidence of cancer in FIT-detected lesions than in colonoscopy-detected lesions. These findings suggest that FIT may be a more effective screening tool than colonoscopy for the early detection of colorectal cancer.
is that one-time screening with FIT was very similar to one-time colonoscopy with respect to the rate of detection of colorectal cancer, and there was no significant difference in the stage of tumors detected by the two strategies. Additional cases of colorectal cancer might be detected during ongoing biennial FIT screening, and this could lead to an increased rate of cancer detection and a decreased rate of death in this group. On the other hand, more tumors might have been prevented in the colonoscopy group owing to the larger number of adenomas detected and removed, in comparison with the FIT group.

The higher detection rate and diagnostic yield of colonoscopy with respect to premalignant lesions also warrant comment. First, since advanced adenomas are usually considered a surrogate marker for colorectal cancer, the superiority of colonoscopy for detecting such lesions should be considered a potential advantage of this strategy in terms of reducing not only the rate of death from colorectal cancer but also the incidence of disease. However, this effect was diminished in our study by the lower participation rate in the colonoscopy group than in the FIT group. Moreover, the first round of FIT screening detected about half the number of advanced adenomas that were detected by colonoscopy. The lower participation rate in the colonoscopy group and the recurrent nature of FIT screening may reduce the apparent advantage of colonoscopy. The lower participation rate in the colonoscopy group and the recurrent nature of FIT screening may reduce the apparent advantage of colonoscopy. On the other hand, the remarkably high detection rate with colonoscopy for patients with nonadvanced adenomas is more difficult to interpret. Most of these lesions correspond to low-risk adenomas, with a natural history that is more unpredictable but unquestionably less prone to progression to colorectal cancer than the natural history of advanced adenoma.

| Table 2. Diagnostic Yield of Colonoscopy and Fecal Immunochemical Testing (FIT), According to the Intention-to-Screen Analysis and the Location of the Colorectal Lesion.* |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Colorectal Lesion               | Colonoscopy     | FIT             | Odds Ratio      | P Value         |
|                                 | (N = 26,703)    | (N = 26,599)    | (95% CI)†       |                 |
|                                 | Subjects Rate   | Subjects Rate   |                 |                 |
| Subjects No.                   | Rate %          | Subjects No.    | Rate %          |                 |
| Cancer                         |                 |                 |                 |                 |
| Proximal                       | 6 <0.1          | 11 <0.1         | 0.56 (0.21–1.53) | 0.26            |
| Distal                         | 25 0.1          | 23 0.1          | 1.22 (0.69–2.16) | 0.49            |
| Advanced adenoma‡              |                 |                 |                 |                 |
| Proximal                       | 199 0.7         | 51 0.2          | 4.06 (2.98–5.53) | <0.001          |
| Distal                         | 365 1.4         | 206 0.8         | 1.82 (1.53–2.16) | <0.001          |
| Advanced neoplasia§            |                 |                 |                 |                 |
| Proximal                       | 205 0.8         | 62 0.2          | 3.44 (2.58–4.57) | <0.001          |
| Distal                         | 390 1.5         | 229 0.9         | 1.76 (1.49–2.08) | <0.001          |
| Nonadvanced adenoma            |                 |                 |                 |                 |
| Proximal                       | 608 2.3         | 62 0.2          | 10.06 (7.74–13.08) | <0.001          |
| Distal                         | 677 2.5         | 85 0.3          | 8.21 (6.55–10.29) | <0.001          |
| Any neoplasia                  |                 |                 |                 |                 |
| Proximal                       | 813 3.0         | 124 0.5         | 6.84 (5.65–8.27) | <0.001          |
| Distal                         | 1067 4.0        | 314 1.2         | 3.58 (3.15–4.07) | <0.001          |

* The diagnostic yield was calculated as the number of subjects with true positive results divided by the number of subjects who were eligible to undergo testing. Subjects were classified according to the most advanced lesion that was proximal or distal to the splenic flexure. The total number of subjects with proximal and distal lesions may exceed the total number of subjects because subjects could have lesions in both locations.
† Odds ratios were adjusted for age, sex, and participating center.
‡ Advanced adenoma was defined as an adenoma measuring 10 mm or more in diameter, with villous architecture (>25%), high-grade dysplasia, or intramucosal carcinoma.
§ Advanced neoplasia was defined as either advanced adenoma or cancer.
recent European guidelines for quality assurance in colorectal-cancer screening consider patients with only one or two small adenomas (<10 mm in diameter) to be at low risk and thus to be appropriate candidates for the same screening strategy that is recommended for patients without adenomas. Accordingly, the lower rate of detection of these lesions among patients who underwent screening by means of FIT might be seen as an additional advantage of this strategy, since it would reduce the number of patients who would need to undergo colonoscopy, with consequent reductions in costs and colonoscopy-related complications. This issue will be assessed at the end of the trial.

An interesting aspect of our study is the differential performance of screening strategies according to the location of the neoplasm. This aspect of colorectal-cancer screening is controversial since it has been suggested that both colonoscopy and FIT are less effective for detecting lesions located in the proximal colon than in the distal colon. Precise explanations for these differential findings or how they may influence long-term results are unclear.

In summary, in this interim analysis, subjects in the FIT group were more likely to participate in colorectal-cancer screening than subjects in the colonoscopy group. On the baseline screening examination, the number of subjects in whom colorectal cancer was detected was similar in the two study groups, but more adenomas were detected in the colonoscopy group. The comparative effectiveness of FIT and colonoscopy for preventing death from colorectal cancer will be assessed at the completion of this 10-year trial.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

### Table 3. Detection Rate for Colonoscopy and Fecal Immunochemical Testing (FIT), According to the As-Screened Analysis.

| Colorectal Lesion | Colonoscopy (N = 5059) | FIT (N = 10,507)† | Odds Ratio (95% CI)‡ P Value |
|-------------------|------------------------|------------------|-----------------------------|-----------------|
|                   | Subjects no. | Rate %     | Subjects no. | Rate %     |  (95% CI)‡ P Value   |
| Cancer            | 27          | 0.5        | 36           | 0.3        | 1.56 (0.93–2.56) 0.09 |
| Advanced adenoma§ | 493         | 9.7        | 252          | 2.4        | 4.32 (3.69–5.07) <0.001 |
| Advanced neoplasia¶ | 520         | 10.3       | 288          | 2.7        | 4.01 (3.45–4.67) <0.001 |
| Nonadvanced adenoma | 1116        | 22.1       | 112          | 1.1        | 25.98 (21.27–31.74) <0.001 |
| Any neoplasia     | 1636        | 32.3       | 400          | 3.8        | 12.28 (10.89–13.84) <0.001 |

* The detection rate is the comparison between the number of positive results and the number of subjects who actually underwent testing. Subjects were classified according to the most advanced lesion.
† A total of 104 subjects with positive results on FIT did not undergo colonoscopy.
‡ Odds ratios were adjusted according to age, sex, and participating center.
§ Advanced adenoma was defined as an adenoma measuring 10 mm or more in diameter, with villous architecture (>25%), high-grade dysplasia, or intramucosal carcinoma.
¶ Advanced neoplasia was defined as advanced adenoma or cancer.


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