

ORIGINAL ARTICLE

Colonoscopy in Colorectal-Cancer Screening for Detection of Advanced Neoplasia

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ABSTRACT

BACKGROUND

Recommendations for colorectal-cancer screening are based solely on age and family history of cancer, not sex.

METHODS

We performed a cross-sectional analysis of the data from a large colonoscopy-based screening program that included 50,148 participants who were 40 to 66 years of age. People 40 to 49 years of age were eligible only if they had a family history of cancer of any type. Of the 43,042 participants 50 to 66 years of age, 13.3% reported a family history of colorectal cancer, as did 66.3% of the 7106 participants who were 40 to 49 years of age. We defined advanced neoplasia as cancer or adenoma that was at least 10 mm in diameter, had high-grade dysplasia, or had villous or tubulovillous histologic characteristics, or any combination thereof. We used multivariate logistic regression to identify associations between participants' characteristics and advanced neoplasia in a primary (or derivation) data set, and we confirmed the associations in a secondary (or validation) data set.

RESULTS

Advanced neoplasia was detected in 2553 (5.9%) participants 50 to 66 years of age and in 243 (3.4%) participants 40 to 49 years of age. The rate of complications during colonoscopy was 0.1%, and no participants died. In the validation set, a logistic-regression model showed that male sex was independently associated with advanced neoplasia (adjusted odds ratio, 1.73; 95% confidence interval, 1.52 to 1.98; $P < 0.001$). In each age group (40 to 49 years, 50 to 54 years, 55 to 59 years, and 60 to 66 years), the number of persons who would have to undergo colorectal-cancer screening in order to detect one advanced neoplasia was significantly lower in men than in women (23 vs. 36, 17 vs. 28, 12 vs. 22, and 10 vs. 18, respectively).

CONCLUSIONS

We detected advanced neoplasia at a significantly higher rate in men than in women, which may warrant refinement of the screening recommendations for colorectal cancer.

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COLORECTAL CANCER IS THE MOST FREQUENT cancer in Europe¹ and the second leading cause of death related to cancer in the United States.² Screening can lead to decreased incidences of colorectal cancer and death owing to the detection of both precancerous lesions and cancers at early stages, respectively.³⁻⁵ Fecal occult-blood testing and flexible sigmoidoscopy can miss a substantial fraction of important lesions.⁶ Despite its risk, inconvenience, and cost, colonoscopy is a valid primary screening tool for colorectal cancer when performed every 10 years, beginning at 50 years of age in people who are at average risk.^{7,8}

Whatever method is chosen, screening is currently recommended to begin at 50 years of age in populations at average risk and at 40 years of age for populations at increased risk.⁹ Although it is generally accepted that the lifetime risk of colorectal cancer is similar among men and women, the prevalence of advanced neoplasia that is detected during colonoscopic screening has been found to be higher among men than among women.¹⁰⁻¹² Despite this fact, current recommendations for colorectal-cancer screening do not take sex into account.

We performed a cross-sectional analysis of data from a national colonoscopy-based screening program for colorectal cancer in Poland that included 50,148 participants. Our primary objective was to derive and validate a model for the detection of advanced neoplasia in the large bowel during screening colonoscopy. Our secondary objective was to determine the number of persons who would have to undergo colorectal-cancer screening in order to detect one advanced neoplasia — the number needed to screen — in various age groups and to compare these numbers in men and women. This information may be useful to refine future screening recommendations.

METHODS

SCREENING PROGRAM

A national screening program for colorectal cancer in Poland, launched in October 2000, used colonoscopy as the primary screening tool.^{13,14} The number of centers involved increased gradually from 6 in 2000 to 40 in 2004. Each participating center established an administrative office for the screening program, which was responsible for handling logistics, information, and data. The demographic data, participant questionnaires, results of colonoscopy and histopathological analysis, and

follow-up information were stored in a central database. The program was entirely financed by the Polish Ministry of Health, independently of the general health care system.

STUDY PROCEDURES

People were advised by their general or family practitioners to participate in the screening program. They were eligible if they were 50 to 66 years of age and in good general health and colorectal cancer was not suspected; people 40 to 49 years of age were also eligible if they had a family history of cancer of any type. Exclusion criteria were recent changes in bowel habits, anemia, unexplained weight loss, bleeding in the lower gastrointestinal tract not attributable to hemorrhoids (although people with small amounts of apparently fresh blood during defecation and known hemorrhoids were eligible), characteristics that met the criteria for hereditary nonpolyposis colorectal cancer or familial adenomatous polyposis,⁹ inflammatory bowel disease, and colonoscopy within the preceding 10 years. The recruitment method was the same for men and women. Written informed consent was obtained from each participant. The research was reviewed by an institutional ethics committee and was judged to be exempt from oversight.

Video-assisted colonoscopy was performed after standard bowel preparation by participants at home with sennosides (X-Prep) or polyethylene glycol (Fortrans), followed by a cleansing phosphate enema 30 minutes before the procedure. Sedation was performed according to local practice. The colonoscopist recorded the extent of the examination and the quality of the bowel preparation. Polyps up to 10 mm in diameter were removed immediately, and larger ones were removed during a separate procedure. The size of polyps was estimated visually *in situ* with the use of the open biopsy forceps or was determined after removal. Biopsy specimens were evaluated locally by a pathologist using criteria established by the World Health Organization.¹⁵ The 30-day data for complications and death from colonoscopy were not collected systematically.

The findings on colonoscopy were categorized on the basis of the most advanced lesion identified.¹⁶ Advanced neoplasia was defined as cancer or adenoma that was at least 10 mm in diameter, had high-grade dysplasia, had villous or tubulovillous histologic characteristics, or any combination thereof.^{16,17}

Family history of cancer was self-reported by

Table 1. Demographic Characteristics and Characteristics of Colonoscopy for the 50,148 Participants.*

Characteristic	All (N=50,148)	Women (N=32,136)	Men (N=18,012)
Age — yr			
Range	40–66	40–66	40–66
Mean ±SD	55.2±5.8	55.2±5.7	55.2±5.9
Age group — no. (%)			
40–44 Yr	2,384 (4.8)	1,454 (4.5)	930 (5.2)
45–49 Yr	4,722 (9.4)	3,006 (9.4)	1,716 (9.5)
50–54 Yr	15,965 (31.8)	10,401 (32.4)	5,564 (30.9)
55–59 Yr	14,148 (28.2)	9,207 (28.7)	4,941 (27.4)
60–66 Yr	12,929 (25.8)	8,068 (25.1)	4,861 (27.0)
Family history of cancer — no. (%)			
Two first-degree relatives with CRC	455 (0.9)	304 (0.9)	151 (0.8)
One first-degree relative <60 yr of age with CRC	2,673 (5.3)	1,758 (5.5)	915 (5.1)
One first-degree relative ≥60 yr of age with CRC	7,315 (14.6)	4,770 (14.8)	2,545 (14.1)
Family history of other neoplasm	8,470 (16.9)	5,664 (17.6)	2,806 (15.6)
No family history of neoplasm	31,235 (62.3)	19,640 (61.1)	11,595 (64.4)
Intravenous sedation — no. (%)	14,922 (29.8)	10,074 (31.3)	4,848 (26.9)
Bowel preparation — no. (%) †			
Very good	18,270 (36.4)	11,578 (36.0)	6,692 (37.2)
Good	20,329 (40.5)	13,158 (40.9)	7,171 (39.8)
Sufficient	7,502 (15.0)	4,814 (15.0)	2,688 (14.9)
Poor	3,456 (6.9)	2,187 (6.8)	1,269 (7.0)
Very poor	360 (0.7)	243 (0.8)	117 (0.6)
Data missing	231 (0.5)	156 (0.5)	75 (0.4)
Cecal intubation — no. (%)	45,693 (91.1)	28,774 (89.5)	16,919 (93.9)

* Because of rounding, percentages may not total 100. CRC denotes colorectal cancer.

† Bowel preparation was assessed by endoscopists.

the participants. Initially, histories were classified into one of seven categories, but after statistical modeling, the following categories were found to be the most strongly associated with advanced neoplasia and were retained: two first-degree relatives who had colorectal cancer (but who did not meet the criteria for hereditary nonpolyposis colorectal cancer or familial adenomatous polyposis), one first-degree relative under 60 years of age with colorectal cancer, or one first-degree relative 60 years of age or older with colorectal cancer.

STATISTICAL ANALYSIS

We randomly partitioned the original data set in a ratio of 2:1 to create a derivation data set and a validation data set, respectively, while controlling for the distribution of the most advanced lesions.¹⁸

A multivariate logistic-regression model was applied to the derivation data set in order to investigate the relation between clinical factors and the odds of detecting advanced neoplasia.¹⁹ A backward-selection procedure, with a P value of less than 0.1 used for retention in the model, was performed in order to identify important factors at the 0.05 level of statistical significance. Predictions of the resulting model and estimated odds ratios were verified with the use of the validation data set. The Hosmer–Lemeshow test was used to check the goodness-of-fit of the model.¹⁹

Point estimates for the numbers needed to screen were derived from the inverse of the point estimates for the prevalence of the finding. We derived the confidence intervals (CIs) for the numbers needed to screen by inverting the values for the 95% CIs for the risk proportions. We compared

Table 2. Findings on Colonoscopy in the 50,148 Participants, According to the Most Advanced Lesion Found.*

Most Advanced Lesion	40–49 Years of Age				50–66 Years of Age					
	No. of Participants (N=7106)	Women with Family History of CRC (N=2957)	Women with No Family History of CRC (N=1503)	Men with Family History of CRC (N=1757)	Men with No Family History of CRC (N=889)	No. of Participants (N=43,042)	Women with Family History of CRC (N=3875)	Women with No Family History of CRC (N=23,801)	Men with Family History of CRC (N=1854)	Men with No Family History of CRC (N=13,512)
Main findings										
Cancer	31 (0.4)	7 (0.2)	7 (0.5)	8 (0.5)	9 (1.0)	385 (0.9)	25 (0.6)	143 (0.6)	30 (1.6)	187 (1.4)
Advanced neoplasia†	243 (3.4)	95 (3.2)	29 (1.9)	89 (5.1)	30 (3.4)	2,553 (5.9)	220 (5.7)	1,023 (4.3)	227 (12.2)	1083 (8.0)
Any adenoma or cancer	674 (9.5)	260 (8.8)	95 (6.3)	255 (14.5)	64 (7.2)	6,396 (14.9)	572 (14.8)	2,700 (11.3)	506 (27.3)	2618 (19.4)
Detailed findings										
None	3764 (53.0)	1689 (57.1)	792 (52.7)	843 (48.0)	440 (49.5)	19,720 (45.8)	1828 (47.2)	11,502 (48.3)	695 (37.5)	5695 (42.1)
Nonneoplastic abnormalities	2044 (28.8)	771 (26.1)	532 (35.4)	433 (24.6)	308 (34.6)	12,669 (29.4)	1082 (27.9)	7,481 (31.4)	407 (22.0)	3699 (27.4)
Hyperplastic polyps	569 (8.0)	223 (7.5)	67 (4.5)	212 (12.1)	67 (7.5)	3,778 (8.8)	348 (9.0)	1,888 (7.9)	218 (11.8)	1324 (9.8)
Nonepithelial polyps (submucosal lesions), including carcinoids	19 (0.3)	4 (0.1)	9 (0.6)	5 (0.3)	1 (0.1)	142 (0.3)	14 (0.4)	80 (0.3)	6 (0.3)	42 (0.3)
Small polyps removed but not assessed histologically	36 (0.5)	10 (0.3)	8 (0.5)	9 (0.5)	9 (1.0)	337 (0.8)	31 (0.8)	150 (0.6)	22 (1.2)	134 (1.0)
Tubular adenoma										
<10 mm in diameter										
1 or 2	399 (5.6)	152 (5.1)	64 (4.3)	151 (8.6)	32 (3.6)	3,374 (7.8)	310 (8.0)	1,512 (6.4)	233 (12.6)	1319 (9.8)
3 or more	32 (0.5)	13 (0.4)	2 (0.1)	15 (0.9)	2 (0.2)	469 (1.1)	42 (1.1)	165 (0.7)	46 (2.5)	216 (1.6)
≥10 mm in diameter	63 (0.9)	28 (0.9)	6 (0.4)	24 (1.4)	5 (0.6)	671 (1.6)	61 (1.6)	256 (1.1)	61 (3.3)	293 (2.2)
Tubulovillous adenoma (25–75% villous)										
<10 mm	54 (0.8)	18 (0.6)	7 (0.5)	25 (1.4)	4 (0.4)	525 (1.2)	47 (1.2)	232 (1.0)	42 (2.3)	204 (1.5)
≥10 mm	49 (0.7)	24 (0.8)	3 (0.2)	14 (0.8)	8 (0.9)	473 (1.1)	52 (1.3)	187 (0.8)	43 (2.3)	191 (1.4)
Villous adenoma (>75% villous)‡										
<10 mm in diameter	4 (0.1)	0	1 (0.1)	3 (0.2)	0	44 (0.1)	2 (0.1)	21 (0.1)	7 (0.4)	14 (0.1)
≥10 mm in diameter	6 (0.1)	3 (0.1)	3 (0.2)	0	0	67 (0.2)	8 (0.2)	26 (0.1)	7 (0.4)	26 (0.2)
High-grade dysplasia§										
<10 mm in diameter	18 (0.3)	6 (0.2)	2 (0.1)	7 (0.4)	3 (0.3)	171 (0.4)	10 (0.3)	71 (0.3)	12 (0.6)	78 (0.6)
≥10 mm in diameter	18 (0.3)	9 (0.3)	0	8 (0.5)	1 (0.1)	217 (0.5)	15 (0.4)	87 (0.4)	25 (1.3)	90 (0.7)
Cancer in adenoma	8 (0.1)	1 (0.0)	2 (0.1)	2 (0.1)	3 (0.3)	80 (0.2)	6 (0.2)	26 (0.1)	6 (0.3)	42 (0.3)
Endoscopically evident tumors¶	23 (0.3)	6 (0.2)	5 (0.3)	6 (0.3)	6 (0.7)	305 (0.7)	19 (0.5)	117 (0.5)	24 (1.3)	145 (1.1)

* Because of rounding, percentages may not total 100. Family history of colorectal cancer (CRC) was defined as the presence of one or two first-degree relatives with CRC.
 † Advanced neoplasia was defined as a cancer or adenoma that was at least 10 mm in diameter, had high-grade dysplasia, or had a villous component, or any combination thereof.
 ‡ Of the 121 participants whose most advanced lesion was a villous adenoma, 22 (18.2%) had lesions that were 5 mm or less in diameter.
 § Of the 424 participants whose most advanced lesion was high-grade dysplasia, 76 (18.0%) had polyps that were 5 mm or less in diameter.
 ¶ Tumors evident on endoscopy were present in 147 of the 1,367 women with advanced neoplasia (10.8%) and in 181 of the 1,429 men with advanced neoplasia (12.7%) (P=0.12).

Table 3. Associations between Patient Characteristics and Advanced Neoplasia in the Large Bowel.*

Covariate in the Model for Detection of Advanced Neoplasia†	Odds Ratio (95% CI) from Derivation Data Set	P Value	Odds Ratio (95% CI) from Validation Data Set	P Value
Age — yr				
50–54 vs. 40–49	1.64 (1.35–1.99)	<0.001	1.82 (1.38–2.40)	<0.001
55–59 vs. 40–49	2.39 (1.97–2.89)	<0.001	2.38 (1.81–3.14)	<0.001
60–66 vs. 40–49	2.95 (2.44–3.57)	<0.001	2.91 (2.21–3.83)	<0.001
Family history of CRC (vs. no family history)				
Two first-degree relatives with CRC	2.10 (1.41–3.13)	<0.001	2.49 (1.42–4.38)	0.002
One first-degree relative <60 yr of age with CRC	1.87 (1.53–2.30)	<0.001	1.33 (0.96–1.85)	0.09
One first-degree relative ≥60 yr of age with CRC	1.43 (1.24–1.64)	<0.001	1.41 (1.16–1.71)	0.001
Male sex (vs. female sex)	2.08 (1.89–2.28)	<0.001	1.73 (1.52–1.98)	<0.001

* The initial list of covariates included male and female sex, five age groups (40 to 44, 45 to 49, 50 to 54, 55 to 59, and 60 to 66 years), and seven family-history subcategories: two first-degree relatives who had colorectal cancer (CRC) but did not meet the criteria for hereditary nonpolyposis colorectal cancer (HNPCC) or familial adenomatous polyposis, one first-degree relative under 60 years of age with CRC, one first-degree relative 60 years of age or older with CRC, one or more second-degree relatives with CRC, one or more first-degree relatives with HNPCC-related neoplasms (in the endometrium, ovary, stomach, pancreas, small bowel, hepatobiliary tract, ureter, or renal pelvis), one or more first-degree relatives with neoplasms not related to HNPCC, and no family history of cancer.

† The model was created with the use of the derivation data set (33,431 participants) and checked in the validation data set (16,717 participants). The Hosmer–Lemeshow test confirmed the goodness-of-fit of the model, with a P value of 0.42 for the derivation data set and 0.99 for the validation data set (with a P value >0.05 considered to indicate that there was no significant lack of fit).

the numbers needed to screen for two separate subgroups by calculating the natural logarithm of the ratio of the two numbers needed to screen and the appropriate 95% CIs, followed by back-exponential transformation.

All the tests performed as part of the univariate and multivariate analyses were two-sided. A P value of less than 0.05 was considered to indicate statistical significance. The analyses were computed with the use of Stata statistical software, version 8 (StataCorp).

RESULTS

A total of 50,148 persons — 32,136 women (64.1%) and 18,012 men (35.9%) — met the eligibility criteria and underwent screening colonoscopy between October 2000 and December 2004. Of the 43,042 participants who were 50 to 66 years of age, 5728 (13.3%) had a family history of colorectal cancer, as did 4714 of the 7106 participants (66.3%) who were 40 to 49 years of age. The characteristics of the study population are listed in Table 1. Intravenous sedation was used during 29.8% of the colonoscopies. Colonoscopy was completed to the cecum in 91.1% of the participants. Sedation was

used more often in women, and cecal intubation was achieved more often in men (Table 1). Polypectomy was performed in 11,913 participants (23.8%). Findings on colonoscopy are presented separately for participants 50 to 66 years of age and 40 to 49 years of age (Table 2). A total of 2796 participants (5.6%) had advanced neoplasia (5.9% of those 50 to 66 years of age and 3.4% of those 40 to 49 years of age), including 416 (0.8%) with adenocarcinoma (stage I in 169 participants [40.6%], stage II in 91 participants [21.9%], stage III in 111 participants [26.7%], and stage IV in 36 participants [8.7%]; the stage was undetermined in 9 participants [2.2%]).

Clinically significant complications requiring medical intervention (including complications from polypectomy) occurred in 51 participants (0.1%) and included 5 cases of perforation (1 of which occurred after polypectomy), 13 episodes of bleeding, 22 cardiovascular events, and 11 other events. No deaths occurred as a result of screening colonoscopy or its complications.

The derivation and validation data sets consisted of 33,431 and 16,717 participants, respectively. Logistic-regression modeling performed on the derivation data set allowed us to create a

Table 4. Numbers Needed to Screen with Colonoscopy to Detect Advanced Neoplasia in the Large Bowel, According to Age, Sex, and the Presence or Absence of a Family History of Colorectal Cancer.*

Subgroup	Percentage of Participants with a Family History of CRC	No. Screened (%)	No. Needed to Screen to Detect Advanced Neoplasia in the Large Bowel (95% CI)
Age			
40–49 Yr			
Men	66.4	2,646 (5.3)	23 (19–27)
Women	66.3	4,460 (8.9)	36 (31–44)
50–54 Yr			
Men	14.1	5,564 (11.1)	17 (15–19)
Women	15.6	10,401 (20.7)	28 (26–32)
55–59 Yr			
Men	11.9	4,941 (9.9)	12 (11–13)
Women	14.1	9,207 (18.4)	22 (20–25)
60–66 Yr			
Men	10.0	4,861 (9.7)	10 (9–11)
Women	11.8	8,068 (16.1)	18 (17–20)
Family history of CRC			
40–49 Yr			
Men		1,757 (3.5)	20 (17–25)
Women		2,957 (5.9)	32 (26–39)
50–54 Yr			
Men		783 (1.6)	13 (10–16)
Women		1,624 (3.2)	20 (17–26)
55–59 Yr			
Men		587 (1.2)	8 (7–10)
Women		1,296 (2.6)	18 (15–23)
60–66 Yr			
Men		484 (1.0)	6 (5–8)
Women		955 (1.9)	16 (13–20)

model for detecting advanced neoplasia in the large bowel (Table 3). The modeling indicated the following independent predictors of advanced neoplasia: an age of more than 49 years, family history of colorectal cancer, and male sex. Hosmer–Lemeshow goodness-of-fit testing of the model in the derivation and validation data sets confirmed its validity. Male sex was independently associated with advanced neoplasia (adjusted odds ratio in the validation data set, 1.73; 95% CI, 1.52 to 1.98; $P < 0.001$). After adjustment for colonoscopic factors (presence or absence of cecal intubation and sedation, and adequacy of bowel preparation) as well as for family history and age, the Mantel–Haenszel

odds ratios for the detection of advanced neoplasia in men, as compared with women, was 1.98 (95% CI, 1.83 to 2.14).

Table 4 shows the numbers needed to screen to detect advanced neoplasia, calculated for the whole data set. We defined the subgroups using combinations of predictors of advanced neoplasia (age, sex, and presence or absence of a family history of colorectal cancer). Details of the statistical comparisons between the subgroups in Table 4 are presented in the Supplementary Appendix, available with the full text of this article at www.nejm.org. Figure 1 shows the major differences between men and women of various ages.

Table 4. (Continued.)

Subgroup	Percentage of Participants with a Family History of CRC	No. Screened (%)	No. Needed to Screen to Detect Advanced Neoplasia in the Large Bowel (95% CI)
No family history of CRC			
40–49 Yr			
Men		889 (1.8)	30 (22–46)
Women		1,503 (3.0)	52 (39–82)
50–54 Yr			
Men		4,781 (9.5)	18 (16–20)
Women		8,777 (17.5)	31 (28–35)
55–59 Yr			
Men		4,354 (8.7)	12 (11–14)
Women		7,911 (15.8)	23 (21–26)
60–66 Yr			
Men		4,377 (8.7)	10 (10–11)
Women		7,113 (14.2)	19 (17–21)
Participants 40–49 yr of age with a family history of CRC			
Two first-degree relatives with CRC			
Men		54 (0.1)	11 (6–66)
Women		92 (0.2)	16 (9–68)
One first-degree relative <60 yr of age with CRC			
Men		532 (1.1)	17 (13–25)
Women		916 (1.8)	27 (20–39)
One first-degree relative ≥60 yr of age with CRC			
Men		1,171 (2.3)	23 (19–32)
Women		1,949 (3.9)	37 (29–49)

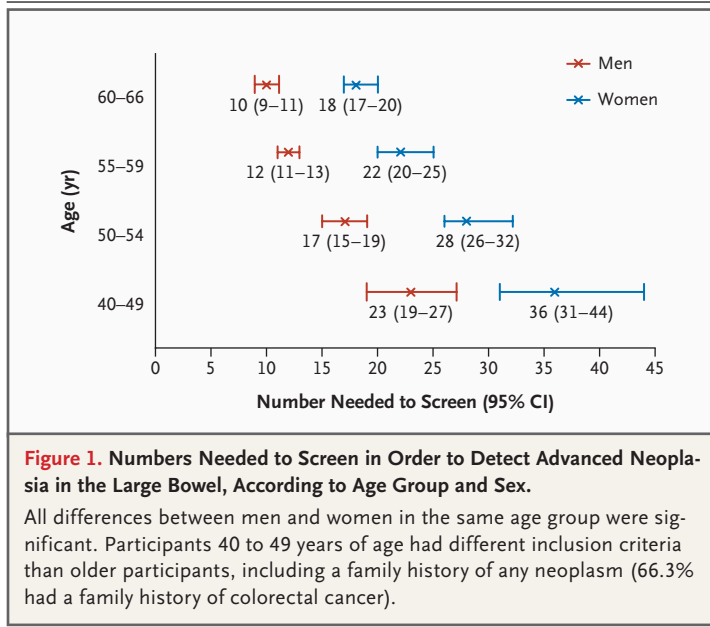
* In each subgroup of age, the number needed to screen was significantly lower in men than women (details are shown in the Supplementary Appendix). Unless otherwise specified, a family history of colorectal cancer (CRC) was defined as the presence of one or two first-degree relatives with CRC. Because of rounding, percentages may not total 100.

DISCUSSION

In our study of 50,148 persons who participated in a colorectal-cancer screening program involving colonoscopy, the large number of participants in the study allowed us to derive and validate a model to identify characteristics that were independently associated with advanced neoplasia. We identified male sex as an independent predictor of advanced neoplasia. We were also able to determine the numbers needed to screen in order to detect advanced neoplasia in subgroups defined according to age, sex, and the presence or absence of a family history of colorectal cancer. Advanced neoplasia, not just cancer, was chosen

for analysis, because this target has been suggested as the most appropriate for colorectal-cancer screening.^{6,11,12,16,20-24}

Although sex has not been included in published screening guidelines,^{9,25,26} our study indicates that the numbers needed to screen in order to detect advanced neoplasia are significantly lower in men than in women of similar age and with a similar family history of colorectal cancer. This finding suggests that the screening recommendations should be modified in order to ensure the maximal diagnostic yield of the screening and the optimal use of resources. The numbers needed to screen, as calculated from our data, can be used as a basis for such modifications; however, we did not



evaluate the effect of potential changes in screening recommendations on the cost-effectiveness of screening or on the incidence of colorectal cancer or death. A practical approach might be to recommend screening only in groups with numbers needed to screen that are below a certain threshold. For example, it may not be prudent to exclude from screening men 40 to 49 years of age without a family history of colorectal cancer and, at the same time, include women 50 to 54 years of age without a family history of colorectal cancer, because our data show that these two groups have very similar numbers needed to screen (Table 4 and Supplementary Appendix). Alternatively, if the recommended age at first screening is 50 years for men, the age for women may be 60 years, since the number needed to screen among women 60 to 66 years of age is similar to that among men 50 to 54 years of age. Our data also reinforce the recommendation that men who are 40 to 49 years of age and have one first-degree relative older than 60 years of age with colorectal cancer should be screened, since the number needed to screen in this group is as low as 23.

Another approach to reduce the demand for colonoscopy driven by colorectal-cancer screening is to perform colonoscopies only in people who are at risk for proximal advanced neoplasia and to perform flexible sigmoidoscopy in others. The results of studies addressing this issue are not unequivocal. Imperiale et al. proposed an index to stratify the risk of proximal advanced neoplasia,²¹

and male sex was among the important risk factors. A disadvantage of this index is that performing flexible sigmoidoscopy is a prerequisite. In addition, a recent study found that women should be screened with the use of colonoscopy, because advanced neoplasia would have been missed in 65% of women if they had undergone sigmoidoscopy alone.¹² Anderson et al. suggested that an age greater than 60 years and smoking are predictors of isolated proximal advanced neoplasia.²³

Our results suggest that a national program offering patients colonoscopy in order to screen for colorectal cancer is feasible. The cecal intubation rate of 91.1% was somewhat lower than expected for expert colonoscopists.²⁷ However, the screening colonoscopy program is a large-scale operation that cannot be limited to expert centers (only about one quarter of the 40 centers involved in our program would have been considered expert). Consequently, a less-than-expert rate of intubation probably has to be accepted in a mass-screening setting, although improvements are likely to occur over time, as the participating endoscopists become more experienced. Bowel preparation was sufficient, good, or very good for 91.9% of participants. Sedation was necessary for only 29.8% of the participants. No participants died, and the rate of complications was only 0.1%. Along with data from other studies,^{6,11,12,16,21-24,28} the results of our screening study indicate that colonoscopy in this setting is safe.

Our findings should be interpreted in the context of the limitations of our study. We analyzed data from a screening program that included only people who were offered and agreed to colonoscopy; our results cannot be generalized to population-based screening programs. However, this limitation is shared among the colonoscopic-screening studies published previously,^{6,11,12,16,21-24} except one.²⁹

Although the men and women were recruited according to the same method, women outnumbered men in the study group by three to two. This disproportion may reflect the sex structure of the population asked to undergo screening (patients visiting general or family practitioners for various reasons) or may be due to sex-related differences in agreeing to undergo screening. Assuming that women are more likely than men to accept an offer of screening, it cannot be ruled out that more men than women entered the program owing to unreported subtle symptoms potentially related to colorectal cancer. Although possible, such a recruit-

ment bias seems to be unlikely, because the fraction of cancers evident on endoscopy, and which are thus potentially symptomatic, among all participants with advanced neoplasia was similar in both sexes (Table 2). Similarly, the slightly higher rate of cecal intubation in men, and the higher proportion of examinations requiring sedation in women, had little effect on the odds ratio for the detection of advanced neoplasia. The quality of bowel preparation was similar in men and women.

In our study, the prevalence of advanced neoplasia in participants 50 to 66 years of age was 5.9%, whereas studies performed in the United States typically report values ranging from 5.6 to 10.6%.^{6,11,16,21,23} Three issues may have contributed to the lower prevalence observed in our study than in most other studies. First, the incidence of colorectal cancer is lower in Poland than in the United States. However, according to the Globocan 2002 database, the age-standardized incidences are similar in proportion between men and women in both countries: 44.6 and 33.1, respectively, in the United States and 31.9 and 23.5, respectively, in Poland.¹ Second, we did not study people older than 66 years of age. Third, women were predominant in our study, unlike in other colonoscopic screening studies.^{6,11,16,21-23} The study by Schoenfeld et al., which included only women, reported a prevalence of advanced neoplasia as low as 4.9%.¹² In our study, 10.0 to 15.6% of the participants (depending on their age) had a family history of colorectal cancer, values similar to those reported in studies from the United States (13.4 to 15.7%).^{12,16,23}

We enrolled people who were 40 to 49 years of

age and who had a family history of any cancer, including colorectal cancer (in 66.3%) and other neoplasms (in 33.7%). The prevalence of advanced neoplasia in this particular group was 3.4% (0.4% had cancer). A similar prevalence (3.5%) was found among participants in this age group by Imperiale et al., although no data on their family history of cancer were available.²² Our results confirm that having a first-degree relative with colorectal cancer is an important predictor of advanced neoplasia and that the age at which the cancer was diagnosed in the index patient is also important. A family history of cancers other than colorectal cancer was not a significant predictor in the multivariate analysis.

In summary, we found that sex is an independent predictor of the detection of advanced neoplasia during colonoscopic screening. The numbers needed to screen in order to detect advanced neoplasia were significantly lower in men than in women, both in general and after adjustment for subgroups of similar age and similar family histories of colorectal cancer. Different rates of detection of advanced neoplasia during colonoscopic screening of men and women may warrant a refinement of the screening recommendations to include sex along with age and family history of colorectal cancer. Our data can be used to design future screening programs; however, studies evaluating their cost-effectiveness and their effect on the incidence of colorectal cancer and death are warranted.

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APPENDIX

The following endoscopists and histopathologists participated in the Polish national colorectal cancer screening program: *Białystok* — E. Wroblewski, A. Baniukiewicz, C. Poplawski, A. Dabrowski, A. Kemonia, M. Barwijuk-Machala, and M. Sobaniec-Lotowska; *Bielsko-Biala* — K. Beszter, M. Konop, J. Dobrzanska, P. Wandzel, and A. Jurczyk; *Bydgoszcz* — Z. Kula, M. Klopocka, K. Tojek, Z. Banaszekiewicz, M. Swiatkowski, C. Swiatczak, M. Rydzkowski, P. Jarmocik, D. Bujalski, J. Budzynski, L. Sobczynski, M. Switonski, M. Jankowski, D. Sosnowski, J. Piech, D. Bala, A. Weishof, J. Koremkiewicz, and K. Ryc; *Bytom* — W. Cebula, W. Latos, K. Niepsuj, W. Zielesnik, M. Gruk, A. Gadowska-Cicha, K. Majewski, A. Gabriel, K. Steplewska-Mazur, and A. Ziolkowski; *Ciechanow* — R. Jocz, A. Kostrubala, and R. Oczkowski; *Czestochowa* — R. Paczkowski, K. Janik, L. Franusiak, L. Gostkowski, J. Mizerski, and A. Bednarczyk; *Elblag* — S. Ligaj, K. Niezgoda, K. Filipiuk, and W. Dudek; *Gdansk* — B. Korybalski, G. Rompa, A. Jasinski, K. Adrych, K. Kawecki, A. Wytoski, M. Dubownik, M. Chelstowska, M. Orlowski, J. Wroblewska-Stankiewicz, B. Janicka, M. Madalinski, A. Babicki, S. Hac, M. Smoczynski, D. Dymecki, S. Dobrowolski, R. Gawlik, M. Horynski, D. Kleczkowski, A. Karmolinski, K. Jaskiewicz, M. Kaminski, G. Kobierska-Gulida, R. Rzepko, I. Sliwinska, A. Antolak, L. Pikiel, K. Winogradow, U. Smialek, B. Maniszewska, E. Izycka-Swieszevska, and T. Wrzolkowa; *Gorzow Wielkopolski* — P. Szulc, M. Buszkiewicz, Z. Samulski, P. Dunowski, J. Stanczyk, and J. Mietkiewski; *Kielce* — E. Mazur-Retmanska, T. Wollny, W. Korejba, A. Chil, M. Ostrowski, S. Strojnowski, J. Sygut, J. Kopczyński, and I. Komorowska; *Konin* — S. Kielek, M. Andrzejczak, T. Dudzik, M. Ostrowska, and B. Kaszuba; *Kraków* — M. Szura, R. Solecki, J. Krzak, J. Krzeszowiak, J. Ejma-Multanski, U. Blaut, J. Gniady, A. Matyja, W. Kostarczyk, C. Osuch, J. Marecik, P. Richter, K. Czajewski, K. Galazka, and L. Rudnicka; *Krosno* — K. Skrzypiec, K. Krzyzak, and B. Bialas; *Lublin* — H. Cichoż-Lach, W. Kosikowski, A. Wysokinski, R. Grodziński, J. Drabko, W. Juszkiewicz, T. Skoczylas, M. Szczerbinski, P. Bury, B. Kasztelam-Szczerbinska, G. Rybak-Drabik, K. Zinkiewicz, J. Furtak, W. Zgodzinski, K. Celinski, U. Radwanska-Konarzewska, D. Skomra, and J. Sierocinska-Sawa; *Lomza* — B. Opyrchal, R. Lowczak, A. Sobanski, and K. Dach; *Lodz* — B. Wozniak, W. Walent, M. Pazurek, A. Gasiorowska, D. Szymanski, A. Eichelkraut, T. Krawczyk, and R. Danilewicz; *Nowa Sol* — P. Hasik; *Nowy Sacz* — H. Kaczmarek and W. Frasik; *Nysa* — G. Ruszecki, K. Kaminski, B. Blonski, Z. Mielcarzewicz, D. Lange, and A. Smok-Ragankiewicz; *Opole* — W. Beker, J. Biernat, J. Struzik, and Z. Szudrowicz; *Pabianice* — D. Fisiak,

J. Daszuta, P. Mrozowski, J. Alwasiak, and M. Radynski; *Poznan* — C. Lozinski, J. Swirkowicz, U. Skowronska-Piekarska, A. Dryjas, J. Herman, J. Paszkowski, S. Malinger, P. Pyda, R. Marciniak, T. Banasiewicz, H. Klincewicz, D. Breborowicz, E. Nyczak, S. Lazowski, and P. Paprzycki; *Przemysl* — R. Sapula, J. Pilecki, M. Zubrzycki, M. Kosicka, A. Horeglad, M. Trzcinska, H. Lebek-Bielecka, and A. Woloszyn; *Rybnik* — S. Skupien, P. Czank, G. Gojny, and M. Panasiewicz; *Sosnowiec* — M. Gonciarz, D. Gil, A. Michalski, A. Stadnicki, G. Bierzynska-Macyszyn, E. Zielinska-Pajak, M. Kajor, P. Palen, J. Pajak, J. Wolanska-Karut, A. Wodolazski, and D. Golka; *Tarnow* — S. Lakoma, K. Aloksa, and R. Dziekan; *Szczecin* — A. Bialek, D. Bielicki, K. Boer, A. Kozłowska, A. Dlugosz, K. Niedzielin, M. Wieski, W. Bojullo, M. Kujawiak, J. Gibaszek, D. Pilecka, H. Jaroszewicz-Heigelman, R. Kosik-Warzynska, R. Mazuryk, S. Titti, K. Sycz, W. Dobrzycki, B. Kolodziej, S. Olewniczak, J. Lubinski, A. Kram, M. Chosia, and E. Bedner; *Warsaw* — M. Rupinski, W. Zych, A. Bielasik, K. Przytulski, M. Cwikla, J. Pachlewski, J. Pietrzak, E. Czackowska, A. Regula, A. Tilszer, J. Zurakowski, J. Regula, J. Basaj, T. Szwed, M. Degowska, W. Kosmala, D. Baczewska-Mazurkiewicz, T. Blazejczyk, I. Madejska, T. Wocial, J. Milewski, A. Blaszk, M. Pawlik, W. Rozanski, E. Wronska, D. Jaklewicz, K. Kosik, S. Wojtun, L. Jalocho, W. Gietka, A. Grabowski, B. Zysko, G. Grabowska, M. Wojtkowiak, P. Babski, G. Stanski, J. Orłowska, A. Nasierowska-Guttmejer, K. Bardadin, D. Jarosz, K. Filipowicz, B. Ziarkiewicz-Wroblewska, and M. Kalczak; *Wroclaw* — J. Langowski, J. Lewera, A. Gebuza, I. Lebski, M. Kondusz-Szkłarz, K. Pasko, E. Poniewierka, R. Massopust, M. Skoczylas, M. Skula, R. Zimoch, M. Jelen, E. Prudlak, and J. Kubacki; and *Zgorzelec* — S. Czekalowski, E. Suder, and J. Rabczynski.

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