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Abstract
Study objective. The present study tested whether the surveillance behavior of women with a family history of colorectal cancer (CRC) differed from that of women without such a history.
Design. The study includes 72,710 subjects from the population of E3N, a cohort study, part of the European Prospective Investigation on Cancer, investigating risk factors for cancer among women.
Results. Fecal occult-blood testing (FOBT) was reported by 19.4% of the women with no CRC in their family and by 21.8% of those with one or more CRC (Frequency Odds Ratio (FOR)=1.01; ns). The degree of kinship did not influence FOBT. Colonoscopy was reported by 10.9% of women with no CRC in their family; its frequency increased with increasing number of subjects affected by CRC in the family, in particular when it concerns first-degree relatives. Colonoscopy was reported almost four times more frequently by subjects having two or more first-degree relatives with CRC (FOR=3.55; 95%CI:2.47-5.10) than by those without any affected member; the frequency of colonoscopy increased, though less sharply among women with second-degree affected relatives, as compared to those without any affected relative in their family.
Conclusion. In conclusion, whereas FOBT was unaffected by family history of CRC, screening colonoscopy was more frequent among women with a reported family history and differed with the degree of kinship of the affected relatives. The high rate of colonoscopy observed among subjects with first- and second-degree relatives is likely due to physician participation in screening decisions.
Key words: Colorectal cancer, family history, colonoscopy.

Introduction

Colorectal cancer (CRC) is among the leading cause of cancer deaths in most occidental countries. Family history is one of the best documented risk factors for this cancer. Thus it is important that individuals with such a history undergo rigourous screening procedures, though we do not know the appropriate management of first-degree relatives of people who have had colorectal cancer (1). The existing literature on the surveillance behavior of subjects with a family history of CRC is very scarce. A recent Medline search revealed six papers having analysed whether a family history influenced screening behaviors (2-7). Based on the population of participants in a cohort study, a prospective study on risk factors for female cancers, undertaken in France in 1990 (8), we analysed whether women with a family history of CRC had a surveillance behavior different from those with no family history. Moreover, the sample size of our population made it possible to examine the effect on screening behavior of the number of family members with CRC and of their relationship to the participant (i.e. first degree relative versus other).

Subjects and methods

The "E3N" study (Etude Epidémiologique de femmes de la Mutuelle Générale de l'Education Nationale) is a prospective cohort study, part of the European Investigation on Cancer (EPIC) (9). E3N is conducted in France and investigates risk factors for cancer in women. The cohort comprises women aged 40 to 65 years at baseline in 1990. Some demographic characteristics of the population are described in Table 1. The women had a mean age of 48.8 (SD=6.6), and were reasonably well educated (over 80% had completed secondary school). One third were post-menopausal. Concerning tobacco use, 66.3% were never smokers and

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21.1% were ex-smokers. Oral contraceptives had been ever used by 57.1% and intra-uterine devices by 11.4%. A description of the dietary habits of a representative sample of 5,623 subjects is given in Table 2.

Table 1. **Description of some demographic characteristics of the E3N population (n=72,710)**

Characteristic	
Age [mean (SD)]	48.8 (6.6)
40-44	34.3%
45-49	24.2%
50-54	19.5%
55-59	13.1%
60+	8.9%
Educational level	
University degree	18.0%
College degree	18.7%
High school	49.9%
Junior high school or lower	13.4%
Smoking habits	
Non-smokers	66.3%
Ex-smokers	21.1%
Current smokers	12.6%
Age at menarche [mean (SD)]	12.8 (1.5)
Number of pregnancies	
0	12.5%
1	10.8%
2	28.7%
3	24.2%
4	13.4%
5+	10.4%
Age at first pregnancy	
15-19	5.4%
20-24	50.0%
25-29	33.1%
30-34	8.5%
35-39	2.3%
40-44	0.4%
Other	0.3%
Contraception : ever use of	
Oral contraceptives	57.1%
Intra-uterine device	11.4%
Menopausal status	
Premenopausal	52.7%
Postmenopausal	34.4%
Natural	24.6%
Artificial*	9.8%
Perimenopausal	12.9%
Height (cm) [mean (SD)]	160.6 (11.0)
<150	0.8
150-154	8.5
155-159	22.8
160-164	35.4
165-169	22.8
170-174	8.4
175+	1.3
Weight (kg) [mean (SD)]	59.2 (10.3)
<45	3.3
45-49	8.9
50-54	22.1
55-59	25.4
60-64	19.1
65-69	11.3
70-74	5.5
75-79	2.8
80+	1.6
Body mass index (kg/m^2)	
<17.0	0.6
17.0-18.4	3.8
18.5-19.9	14.2
20.0-24.9	64.4
25.0-29.9	13.9
30.0+	3.0

**includes women with a history of hysterectomy without ovariectomy*

Table 2. **Description of some dietary habits of the E3N population (representative sample of 5,623 subjects)**

Nutrient	Quantity (SD)	
Energy (kcal)	2,365	(802)
Carbohydrates (g)	241	(87)
Proteins (g)	95	(31)
Lipids (g)	104	(51)
Saturated (g)	43	(22)
Monounsaturated (g)	32	(18)
Polyunsaturated (g)	18	(13)
Cholesterol (mg)	442	(203)
Fibers (g)	21	(8)
Vitamin C (mg)	139	(76)
Retinol (μg)	981	(954)
β-Carotene (μg)	7,745	(4,192)
Vitamin E (mg)	15	(11)
Alcohol (g)	13	(16)
Calcium (mg)	1,044	(522)
Iron (mg)	14	(4)

Since that date, participants have been asked to complete questionnaires every 18 months. Information on colorectal cancer in the family (parents, grand-parents, siblings, children, uncles and aunts) was recorded in the initial questionnaire. Also recorded in the same questionnaire was the information on the practice of screening tests for colorectal cancer, i.e. colonoscopy and fecal occult-blood testing (FOBT). As women of the cohort belong to the health insurance plan, they have complete reimbursement of all examinations.

Frequency Odds Ratios (FOR), i.e. ratios of the frequency of the screening test for each category of family history, compared with no family history were computed. Multiple logistic regression was used to obtain adjusted FOR estimates together with their 95% confidence intervals. Included in the regression equation were terms for age, personal history of intestinal problems, educational level, geographic region and the other test (colonoscopy or FOBT). The present study was undertaken on the whole E3N population, after exclusion of women with a history of CRC or Crohn's disease. Also excluded were those without valid data concerning colonoscopy, FOBT, or family history. The study population was thus composed of 72,710 women.

Results

A description of their screening practices is shown in Table 3. Of the women, 12.7% had ever had a colonoscopy and 20.1% had ever had a FOBT; the FOBT was positive for 1.5% of the women of our study. Five percent (5.2%) reported to have had both tests.

Table 3. **Screening practices in the E3N population**

Screening test	(*n*=72,710)	%
Colonoscopy	9,265	12.7
And FOBT with positive result	858	1.2
with negative result	2,785	3.8
with unknown result	125	0.2
And no FOBT	5,497	7.6
No colonoscopy	63,445	87.3
And FOBT with positive result	253	0.3
with negative result	10,100	13.9
with unknown result	396	0.5
And no FOBT	52,696	72.5

A history of colorectal cancer in the family was reported by 22.8% of the E3N participants. FOBT was reported by 19.4% of the women with no CRC in their family and by 21.8% of those with one or more CRC in their family (adjusted FOR equal to 1.01; ns). FORs were all close to unity, whatever the family history of CRC. The degree of kinship did not significantly affect FOBT (Table 4).

Table 4: **Distribution of fecal occult-blood test according to history of CRC in the family.**

Number of CRC in the family	**(*n*=72,710)**	**Fecal occult-blood test**			
		%	**CrudeFOR[a]**	**Adjusted FOR[a,b]**	**95%CI**
Any degree					
0	56,143	19.4	1.00[c]	1.00[c]	
1	13,343	21.2	1.11	1.00	0.95-1.05
2	2,576	24.4	1.35	1.08	0.98-1.19
3+	648	24.2	1.32	0.97	0.80-1.18
First-degree[d]					
0	56,143	19.4	1.00[c]	1.00[c]	
1	4,132	23.9	1.30	0.98	0.90-1.06
2+[e]	176	22.7	1.17	0.75	0.51-1.11
Second-degree[f]					
0	56,143	19.4	1.00[c]	1.00[c]	
1	9,211	20.0	1.04	1.01	0.95-1.07
2	1,391	23.0	1.25	1.14	1.00-1.30
3+	256	21.5	1.16	1.00	0.73-1.37

[a]FOR: Frequency Odds Ratio, i.e. ratio of the frequency of the test for each category compared with the reference category.
[b]FOR ajusted for age (<45, 45-49, 50-54, 55-59, 60+), personal history of hemorroïds (yes/no), personal history of polyps, intestinal biopsy and other intestinal problems (yes/no), educational level (3 categories), geographic region (12 categories) and for the other test (colonoscopy).
[c]Reference category.
[d]All with no second-degree relative affected.
[e]Only 20 subjects had 3+ first-degree affected relatives.
[f]All with no first-degree relative affected.

A description of screening by colonoscopy according to the number of CRC in the family is shown in Table 5. Among women with no CRC in their family, 10.9% reported colonoscopy. This percentage was 17.4, 23.5 and 30.1 for women with respectively one, two and three or more members of their family affected. The corresponding FORs were 1.68 (95%CI:1.59-1.77), 2.36 (95% CI:2.17-2.65) and 3.57 (95%CI:2.98-4.27) compared with women without affected members in their family. The test of increasing FOR with increasing number of affected relatives was significant ($P<10^{-4}$) with a slope of 1.58 (95%CI:1.52-1.63).

The degree of kinship was also considered. The FOR increased with increasing number of CRC among first-degree members of the family (trend test $P<10^{-4}$; slope: 2.38 (95%CI:2.22-2.56).). An FOR of 2.56 (95% CI:2.36-2.77) was found for women with one and of 3.55 (95% CI:2.47-5.10) for those with two or more first-degree relatives with CRC compared with those without any family member affected.

The frequency of colonoscopy increased less sharply among women with second-degree affected relatives, compared with those without any member affected by CRC in their family. The value of the slope was lower, equal to 1.27 (95% CI:1.21-1.33).

Discussion

This study reveals different screening behaviors within our population. Screening colonoscopy was more frequent among women with a reported family history and differed with the degree of relationship of the affected relatives. FOBT was unaffected by family history of CRC.

In the literature, a family history influenced screening behavior in most but not all studies. McCarthy and Moscowitz (2) reported on attitudes and compliance with screening sigmoidoscopy using a patient survey at the time sigmoidoscopy was ordered and again one week after the procedure was performed. They studied 105 subjects, 25 with a family history of CRC. Seventy-five of the one hundred five actually reported

sigmoidoscopy. Compliance with screening sigmoidoscopy was higher among those with family history of first-degree relatives with CRC (92% vs 70%; *P*=0.03) than among those without.

Table 5. **Distribution of colonoscopy according to history of CRC in the family.**

Number of CRC in the family	**(*n*=72,710)**	**Colonoscopy**			
		%	**FOR[a]**	**FOR[a,b]**	**95%CI**
Any degree					
0	56,143	10.9	1.00[c]	1.00[c]	
1	13,343	17.4	1.71	1.68	1.59-1.77
2	2,576	23.5	2.49	2.36	2.17-2.65
3+	648	30.1	3.62	3.57	2.98-4.27
First-degree[d]					
0	56,143	10.9	1.00[c]	1.00[c]	
1	4,132	25.3	2.72	2.56	2.36-2.77
2+[e]	176	30.7	3.37	3.55	2.47-5.10
Second-degree[f]					
0	56,143	10.9	1.00[c]	1.00[c]	
1	9,211	13.9	1.32	1.32	1.23-1.41
2	1,391	16.8	1.64	1.56	1.34-1.81
3+	256	17.6	1.75	1.70	1.21-2.39

[a]FOR: Frequency Odds Ratio, i.e. ratio of the frequency of the test for each category compared with the reference category.
[b]FOR ajusted for age (<45, 45-49, 50-54, 55-59, 60+), personal history of hemorroïds (yes/no), personal history of polyps, intestinal biopsy and other intestinal problems (yes/no), educational level (3 categories), geographic region (12 categories) and for the other test (FOBT).
[c]Reference category.
[d]All with no second degree relative affected.
[e]Only 20 subjects had 3+ first-degree affected relatives.
[f]All with no first degree relative affected.

Macrae et al (3) studied 581 subjects and found that those with one or more first degree relatives with CRC were more likely to accept than refuse the offer of FOBT ($P<0.05$). This factor did not discriminate between compliers and non-compliers within the group of accepters. However, no data were provided on those with no affected relative.

Morrow et al. (4) studied 1,200 subjects for compliance with FOBT. The percentage of compliers was higher, though not significantly, in those with colon cancer in their family (83%) compared with those without (77%). The reasons for refusal of FOBT was studied by Hynam et al (5) on 81 subjects from a random sample of people who wrote declining the offer. No history of bowel cancer in the family was one of the 11 possible reasons for rejection, mentionned by one subject in this sample of 81 subjects.

Sandler et al (6-7) compared participation in an FOBT screening program of 193 siblings of colon cancer patients to 526 control siblings. Compliance was higher ($P<0.005$) among the cancer siblings (52.2%) than the control siblings (37.7%). The authors then attempted by interview to identify those factors that affected compliance with the test. Only 24.8% of the cancer siblings thought they were more likely to get colon cancer compared with others of their own age and 27.8% thought they were less likely. Thus perceived risk did not predict compliance beyond membership in the high-risk group.

Our results are in general agreement with the literature which, however, concerns almost exclusively first-degree relatives.

We assessed internal validity of our results by adjusting for all possible factors which could have interfered with the screening practices under study. Adjustment for a history of benign intestinal problems is of particular importance since such a history is related to familial history of CRC in our study ($P<10^{-3}$) and in others (10). Moreover evidence strongly suggests that most CRC arise from preexisting adenomas (1).

Participation in screening is apparently high in our study population although comparison is impossible as we could not succeed in finding data on the general population of French women of the same age. Several possible explanations exist for the participation in colorectal screening in our study. Our sample is not representative of the general French population since it is more highly educated and health conscious. Additionnally, our study adressed mainly breast and colorectal cancer epidemiology, and thus responders

were possibly more likely women with heightened consciousness of these cancers. However differences observed among subgroups can hardly be affected by this selection. Finally, it is probable that the percentage reporting colonoscopy included both total colonoscopy and sigmoidoscopy.

The high rate of colonoscopy observed in subjects with first- and second-degree relatives is likely due to physician participation in screening decisions, since colonoscopy is generally recognised as the definitive procedure for detection of CRC. Our study, however, did not determine reasons for screening behavior. Further investigation in this area would be useful in designing future screening programs.

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