Low compliance with colonoscopic screening in first-degree relatives of patients with large adenomas.

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Abstract

Background: Little is known about compliance with colonoscopy as a screening method in first-degree relatives of patients with large adenomas.

Aims: To evaluate the compliance with screening colonoscopy among this population, and its determinants.

Methods: Data were obtained from the family part of the GEADE study, a study on genetic factors of colorectal adenomas. Index cases were 306 patients with adenomas ≥ 10mm. All living first-degree relatives aged 40-75 who could be contacted by the index case were invited to undergo a colonoscopy, unless they had had one in the previous 5 years.

Results: Among 674 eligible relatives, 56 had had a colonoscopy within the preceding 5 years and 114 underwent a screening colonoscopy resulting in a compliance with screening colonoscopy of 18%. This was not related to most characteristics of index cases. Compliance was significantly lower when the index case lived in the Greater Paris area than when he/she lived in other areas (12% *vs* 21%). It was higher in siblings (18%) and offspring (23%) than in parents (9%) and in relatives under 55 years old (22%) than in relatives aged 55 and over (15%).

Conclusions: Compliance with colonoscopy was low in first-degree relatives of patients with large adenomas. The reasons should be determined and appropriate strategies developed to increase compliance.

Colorectal cancer is one of the most frequent cancers in developed countries. In France, it ranks third with 36,250 new cases in 2000 (1). Most cancers arise from colorectal adenomas which have high malignant potential when they are ≥ 10mm in diameter and/or present severe dysplasia and villous component. Endoscopic detection and removal of adenomas is therefore recommended in order to reduce the risk of colorectal cancer in affected patients (2).

An increased risk of colorectal cancer and adenomatous polyps in the family members of patients with colorectal cancer has already been demonstrated (3,4). The association between the risk of developing colorectal tumours and family history of large adenomas in first-degree relatives has not been so extensively studied (5-8). A systematic review of 9 studies published between 1984 and 1998 estimated the relative risk of colorectal cancer associated with history of adenomas in relatives as 2 (95%CI=2-3) (3). All these studies used a case-control design and compared the frequency of family history of colorectal cancer in adenoma cases with polyp-free or population controls. These studies might be subject to recall biases and could not be used to quantify the risk of colorectal adenomas in relatives of adenoma patients.

Whereas professional bodies usually recommend colonoscopic screening in relatives of patients with colorectal cancer, screening modalities for relatives of patients with high-risk adenomas are debated. In 1998, the French consensus conference on colorectal cancer concluded that the scientific evidence was not sufficient to establish guidelines for these patients (9). According to more recent French recommendations, individuals with a family history of colon cancer or adenomas diagnosed in first-degree relatives under 60 years old should be advised to have screening colonoscopy from the age of 45, or 5 years younger than the earliest diagnosis in their family (10). No recommendations were proposed for individuals with first-degree relatives diagnosed with colorectal cancer after 60. In the same way, the American guidelines recommend colonoscopy at 40, or 10 years before the index case for individuals with a strong family history of colorectal cancer or polyps (11,12).

Colonoscopy is an expensive and invasive screening method which carries some risk for the patient and thus, may not be appropriate in populations with a moderately increased risk of colorectal cancer. Furthermore, its acceptability in such populations is debatable. From a public health point of view, participation rate is one of the key factors likely to affect the effectiveness of a screening method on the reduction of colorectal cancer mortality or incidence in a given population.

Because of the scarcity of data about this topic, the present analyses, based on the data from the GEADE study, aimed at assessing compliance with colonoscopy as a screening method among first-degree relatives of patients with large adenomas and at examining some determinants of the compliance.

Patients and Methods

The GEADE study is a French family and case-control study on genetic factors of colorectal adenomas. The primary aims were to compare the frequency of various susceptibility genes in patients with large adenomas (index cases) and in controls with small adenomas or free of adenomas, and to assess the risk of colorectal tumours in first-degree relatives of index cases compared to a reference population. The family part of this study gave us the opportunity of evaluating the compliance with colonoscopy in first-degree relatives with large adenomas and its determinants.

The study was performed in 18 participating gastroenterology units in French non-university hospitals with mixed urban/rural recruitment. They were located in small to medium-sized towns (6 towns were on a large area around Paris called 'Greater Paris area', 3 on the Northeast, 2 on the southwest, 3 on the southeast and 4 on the centre of France). From September 1995 to March 2000, 306 consecutive patients with a newly diagnosed adenoma ≥ 10mm were enrolled and referred as index cases. Subjects with a history of colorectal cancer or other cancer, familial adenomatous polyposis syndrome, established hereditary non-polyposis colorectal cancer and inflammatory bowel disease were excluded. For all index cases, endoscopic and pathological records were obtained from participating centres. We also collected information about demographic data (age, gender, residence area), personal history of polyps, family history of colorectal cancer, indications of colonoscopy, completeness of colonoscopy and detailed characteristics of lesions removed (size, location, histologic type, histologic architecture, degree of dysplasia). Lesion location was defined as distal (including rectum, rectosigmoid, sigmoid, descending colon, and splenic flexure) and proximal (including transverse colon, hepatic flexure, ascending colon and caecum).

All index cases belonged to independent families. Two hundred and sixty-seven (89%) index cases consented to a family investigation. Information on all first-degree relatives (parents, siblings and offspring) was obtained during a face-to-face interview between the

gastroenterologist and the index cases. Family data included demographic and medical characteristics of each relative such as name, date of birth and/or age, residence area, vital status, cause and age at death if applicable, history of polyps or cancer.

As indicated in Figure 1, 1763 first-degree relatives were identified among whom 550 were deceased. According to French ethical rules, no direct contact between investigators and relatives of the patients is allowed. Thus, during a special consultation, the study was explained to the index cases who were asked to contact their relatives and to pass on an explanatory booklet. This contained a general introductory letter describing briefly the aims of the study and its implementation, a general leaflet about colorectal cancer (edited previously by the Ligue Nationale Contre le Cancer), an informed consent sheet explaining the advantages and potential drawbacks of colonoscopy and a health study questionnaire to return. Finally, information about the genetic part of the study was given together with a specific informed consent form, tubes for blood sampling and a letter for the customary laboratory used by the relative.

If the relatives were aged 40-75 and had not had an examination during the preceding 5 years, they were invited to consult their general practitioner in order to discuss the indications for colonoscopy, and to be addressed to a gastroenterologist of their choice to perform the examination, standard letters to them being attached to booklet. There was no a priori exclusion of patients with prior history of cancer or bowel resection.

Index cases refused to contact 85 relatives (7.0%) for the following reasons: old age (n=3) or poor health of the relatives (n=8), family dissensions (n= 38), relatives living too far away (n=34) or unknown reasons (n=2). Three hundred and twenty relatives out of 1120 living first-degree relatives who could be contacted, returned the health study questionnaire (29%), gathering information about possible previous colonoscopies and the name and address of the general practitioner. Whether colonoscopy was performed before or after that of the index case, details about endoscopic findings were obtained from the relative's

gastroenterologist for 94% of the participating subjects. No endoscopic report could be obtained for ten relatives: eight subjects declared that no lesion was discovered during their colonoscopy and two did not know the results of the colonoscopy.

All index patients and first-degree relatives gave their informed consent. The research protocol was approved by the ethics committee of Kremlin-Bicêtre hospital.

Age of the index case and of relatives was considered as a two-category variable. Because French guidelines recommend a colonoscopy for first-degree relatives of patients affected before 60 years, a cut-off of 60 years was used for the index case. A cut-off of 55 years corresponding to the approximate median was used for the first-degree relatives. Residence proximity between the index case and relatives was defined as residence in the same administrative area or in bordering areas. Associations between compliance with colonoscopy among first-degree relatives and the characteristics of index case or the characteristics of relatives were evaluated by population-averaged logit models using generalized estimating equations (13). The generalized estimating equations method allows simultaneous analysis of data regarding index cases and relatives, and takes into account both intra-familial correlations and family size. The exchangeable correlation structure was the most appropriate for such clustered observations, because there was no logical ordering for family members within a family cluster. Moreover, it was the most neutral option. All variables related to colonoscopy compliance with a significance level < 0.15 were considered in the multivariate analysis. All statistical analyses were performed using STATA software (StataCorp: Stata Statistical Software: Release 7.0. College Station, TX, Stata Corporation, 2001). Odds ratios (OR) are presented with their corresponding 95% confidence intervals (95% CI). Intra-familial correlation of acceptance for screening was investigated by comparing the expected distribution of the number of colonoscopies performed among families under the assumption of absence of intra-familial correlation (equal probability of acceptance among all relatives) to the observed one. Under this assumption, the distribution

of colonoscopies within families is simply a binomial one depending only on compliance rate and family size, and the number of expected colonoscopies can be computed for each family size from the average compliance rate, and then summed over all families.

Results

Three hundred and six eligible patients with an adenoma ≥ 10mm were enrolled as index cases. Colonoscopy was complete in 301 of them (98%), did not reach the caecum in 3 cases, and was completed by a double-contrast barium enema in 2 cases. The main characteristics of index cases are indicated in Table 1. The mean age of the patients was 62 years (standard deviation=13), and 63% were men. Forty-two (14%) had a personal history of polyps and 65 (21%) had a family history of colorectal cancer. Index cases presented large adenomas on the distal colon in 83.3% of the cases, on the proximal colon in 11.4% and 5.2 % had on both locations. Most index cases (67.6%) had at least one adenoma with villous component and/or severe dysplasia or intramucosal carcinoma.

As summarised in Figure 1, 39 of the 306 index cases did not have any family investigation. Characteristics of the index cases with and without family investigations were similar, except for gender. The family tree was more frequently drawn up for women than for men (93% vs. 84%, p=0.03).

Among the 674 first-degree relatives eligible for screening colonoscopy, 170 relatives from 97 families underwent this examination, resulting in an overall proportion of subjects with colonoscopy of 25%. Fifty-six relatives had had a colonoscopy over the previous 5 years whereas 114 underwent a screening colonoscopy after the index case. Patients who had a screening colonoscopy were examined after a mean time period of 10.6 months (standard deviation=11.4). Among them, 49% and 74% underwent their colonoscopy respectively within 6 months and one year following the examination of the index case. None of the characteristics of first-degree relatives or index cases influenced this time period, except for

residence proximity. The time period for colonoscopy was longer for relatives residing near the index case than for those residing far away (p=0.02).

After exclusion of 56 first-degree relatives who had had a colonoscopy within the preceding 5 years, the compliance rate for screening colonoscopy was 18% (114/618). Associations between first-degree relative's characteristics and compliance are shown Table2. The compliance rate for colonoscopy was significantly higher in first-degree relatives under 55 than in older subjects, in siblings and offspring than in parents of index cases, and tended to be higher in women than in men, but not significantly so.

The Table 3 describes associations between index cases characteristics and compliance. The residence area of index cases was the only characteristic that significantly influenced the compliance of relatives with screening colonoscopy. Compliance was lower when the index cases lived in the Greater Paris area than when they lived in other areas. Compliance of relatives was not related to age, gender, family history of colorectal cancer, personal history of polyps and the presence of advanced adenomas among index cases.

Because the age of relatives and their blood relationship with the index case were strongly related, these variables were separately introduced in two distinct multivariate regression models. Thus, in the first model, variables entered were residence area of index case, gender and age of relatives. The compliance with screening colonoscopy was lower for relatives of index case from Greater Paris area than for relatives of index cases from other areas (OR=0.5, 95% CI: 0.3-0.9, *p=0.03*). Although not significantly, women had a better compliance with colonoscopy than men, (OR=1.4, 95% CI: 0.9-2.2, p=0.10). The compliance was lower for relatives older than 55 years than for younger relatives (OR=0.6, 95% CI: 0.4-1.0, p=0.03). A second model including relationship with index case instead of relative's age showed very close results regarding the effect of residence area of index case and relative's gender. In comparison with parents, the OR for siblings was 2.9 (95% CI: 0.9-9.1, p=0.06) and for offspring, 3.5 (95% CI: 1.1-11.4, p=0.04).

The 618 first-degree relatives eligible for screening colonoscopy were members of 218 families. Among 73 families, one relative at least underwent the examination. As shown in table 4, there is a strong excess of families with no colonoscopy and with 2 or more colonoscopies and a consequent deficit of families with only one colonoscopy, which means that there is a high degree of intra-familial correlation of acceptance for screening ($\chi^2 = 68$; $p<0.001$).

Colonoscopic findings could be obtained in 168 out of 170 first-degree relatives who participated in the study. Colorectal tumours were detected in 38 first-degree relatives (23%). The prevalence of cancers and adenomas was respectively 3 % and 20%. All cancers were found in relatives of index cases who presented advanced adenomas (villous component and/or severe dysplasia) of which two were also ≥ 20 mm in diameter.

Discussion

To our knowledge, this study was the first prospective study to examine compliance with colonoscopy among first-degree relatives of patients with large adenomas. The study showed that, in clinical practice, it was possible to contact, through the index case, the great majority of eligible relatives, in order to encourage them to have a colonoscopy. However, it also revealed a low compliance with screening colonoscopy, around 18%, among these subjects.

Several strengths and limitations of the study should be emphasised. This study was performed in a large number of endoscopy units within general hospitals throughout the country. Eligible patients with large adenomas were prospectively and consecutively recruited after a complete colonoscopy was obtained. Thus, it is unlikely that major selection biases may have affected our study sample. Indeed, the distribution of age, gender and family history of colorectal cancer among patients with large adenomas was very close to that found in a previous French study (6). Furthermore, the family information was carefully collected

through a face-to-face interview by well-trained and motivated investigators according to a protocol similar to that used in a previous study carried out by our group (14). For the vast majority of relatives (94%) who participated in the study, colonoscopic findings were confirmed through endoscopic and pathological reports. These procedures give some guarantee about the reliability of information recorded for family members. The main limitation of the study lies in the fact that physicians were unable to directly contact patient's relatives. According to French ethical rules, relatives can only be contacted by the index case. Although index cases were well aware of the importance for their relatives to undergo a colonoscopy, we cannot be sure that family members were really informed about the study and received the information booklet and consent form.

Although investigators were highly motivated and, often, solicited index cases again when their relatives were non-compliant, the low rate of colonoscopy among relatives (18%) was disappointing. This suggests that compliance would be even lower in routine clinical practice. Compliance was lower than that found in a previous French study (39%) using the same design among relatives of patients with colorectal cancer (14). Other studies performed among relatives of patients with colorectal cancer showed large variations in compliance rates with colonoscopy ranging from 30% in Italy (15), 42% in United States (16), and 82% in Norway (17). The occurrence of colorectal cancer in first-degree relatives is probably a more worrying event than the occurrence of large adenomas probably considered as harmless lesions by most people. In this study, one third of the relatives had already undergone a colonoscopy over the previous 5 years. They were more often parents of the index case and presented a higher proportion of colorectal cancer (7%) than relatives who were examined after the index case (1%). It is possible in fact, that the cancer discovery in the first-degree relative led the index case to have an examination.

Our study did not reveal any strong determinants of compliance with colonoscopy among relatives who underwent an examination after the index case. As observed in our

previous study among first-degree relatives of patients with colorectal cancer, our results suggest a lower acceptability of colonoscopy when the index case lived in the Greater Paris area (14). Both studies were based on patients recruited in French non-university hospitals. Thus, the extrapolation of our finding to subjects recruited in other clinical settings is uncertain. We have no reasons to suspect that investigators from this area were less actively involved in the study or less convincing among their patients than other investigators. Inhabitants of the Greater Paris area are known to be more highly mobile, to have a more stressful life with less free time, and family ties are probably less close than in other regions. Living conditions may partly explain the difficulty of obtaining the adherence of relatives to a screening programme in the Greater Paris area. In accordance with our previous observations among relatives of patients with colorectal cancer, age and blood relationships were the main characteristics for predicting their participation in screening colonoscopy. Compliance of relatives under 55 was better than that of older subjects and, accordingly, offspring and, to a lesser extent, siblings were more compliant than parents. Interestingly, this study showed the existence of a strong intra-familial correlation of acceptance for screening. This finding subsequently justifies the use of generalized estimation equations for the evaluation of determinants of compliance. Such a correlation may be the result of a higher motivation of individuals whose relative(s) already underwent screening colonoscopy, and/or familial characteristics, including educational and socioeconomic factors that could not be investigated in this study.

The reasons why 80% of first-degree relatives did not participate in the study may be multiple. As less than 30% of the living relatives returned the questionnaire, it is possible that some of the remaining relatives were not informed by the index case. It is also possible that the information booklet was too complicated and could have discouraged the relatives from participating in the study. In addition, a previous study which focused on health beliefs suggested that first-degree relatives of patients with colorectal cancer did not perceive

themselves as being at risk for colorectal cancer (18). This behaviour is likely to be more pronounced in relatives of patients with pre-malignant colorectal lesions. The necessity of consulting a gastroenterologist in order to undergo embarrassing and uncomfortable procedures, the risk and cost of colonoscopy although it is almost totally reimbursed by the French health insurance system, and the fear of a lesion being discovered may also have discouraged family members. A thorough evaluation of sociological and psychological barriers in France would be necessary to understand the resistance of relatives to participation in screening programmes, and to improve their awareness about the seriousness of colorectal cancer and the benefits of screening. Potential targets for interventions to encourage relatives of colorectal cancer patients to have a colonoscopy have been identified in other countries (19,20). Interventions that aim at modifying perceived barriers and benefits of screening, that use family influences, particularly the affected member as a source of support, as well as physician influence may be possible ways to increase screening. Whether such interventions may be effective among relatives of patients with large adenomas in a European cultural background remains to be determined.

The yield of colorectal tumours in first-degree relatives of patients with large adenomas seems to be comparable to that observed in relatives of patients with colorectal cancer. Using a similar design, our previous study showed a prevalence of cancer and adenomas of respectively 3% and 23% instead of 3% and 20% in the present study, suggesting that a family history of large adenomas carries a risk in first-degree relatives which is close to that conferred by a family history of colorectal cancer (14).

The low compliance rate with colonoscopy in the context of a family study leads to questioning about the most appropriate screening method in first-degree relatives of patients with large adenomas. The prevalence of large adenomas in the population is much higher than that of cancer so that a non-negligible proportion of the population may be concerned by screening measures. Faecal occult blood (FOB) testing is currently the only screening method

for which controlled trials demonstrated a reduction in colorectal cancer mortality in Europe (21-23) and the USA (24). Although the FOB test is well accepted in the population, its low sensitivity (around 60%) suggests that it is not very appropriate in a family context, except for subjects who refused colonoscopic screening (25). In populations at average or moderate risk, newer FOB immunochemical tests and computed tomographic virtual colonoscopy may be alternative techniques that require careful evaluation.

In conclusion, the acceptability of colonoscopy is low in first-degree relatives of patients with large adenomas and only marginally influenced by the characteristics of relatives and index cases. Further studies are needed to better understand the reasons why members of some families are less compliant than others and to develop appropriate interventions to improve the acceptability of colonoscopy.

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References

1 Bouvier AM, Remontet L, Jougla E, et al. Incidence of gastrointestinal cancers in France. *Gastroenterol Clin Biol* 2004;**28**:877-81.

2 Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 1993;**329**:1977-81.

3 Johns LE, Houlston RS. A systematic review and meta-analysis of familial colorectal cancer risk. *Am J Gastroenterol* 2001;**96**:2992-3003.

4 Butterworth AS, Higgins JP, Pharoah P. Relative and absolute risk of colorectal cancer for individuals with a family history: a meta-analysis. *Eur J Cancer* 2006;**42**:216-27.

5 Ahsan H, Neugut AI, Garbowski GC, et al. Family history of colorectal adenomatous polyps and increased risk for colorectal cancer. *Ann Intern Med* 1998;**128**:900-5.

6 Boutron MC, Faivre J, Quipourt V, et al. Family history of colorectal tumours and implications for the adenoma-carcinoma sequence: a case control study. *Gut* 1995;**37**:830-4.

7 Nakama H,Fukazawa K. Colorectal cancer risk in first-degree relatives of patients with colorectal adenomatous polyp. *Hepatogastroenterology* 2002;**49**:157-9.

8 Winawer SJ, Zauber AG, Gerdes H, et al. Risk of colorectal cancer in the families of patients with adenomatous polyps. National Polyp Study Workgroup. *N Engl J Med* 1996;**334**:82-7.

9 *[Consensus conference: Prevention Screening and Management of the Colonic Cancers. Paris, France, January 29-30, 1998. Proceedings]*. 1998. Paris, France. Gastroenterol Clin Biol;22:S1-295.

10 Endoscopie digestive basse: Indications en dehors de dépistage en population. Recommendations pour la pratique clinique. 2004 http://www.anaes.fr/anaes/presse.nsf/(ID)/F4776FAB76041931C1256EC8005003B2?opendocument.

11 Smith RA, Cokkinides V,Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2004. *CA Cancer J Clin* 2004;**54**:41-52.

12 Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. *Gastroenterology* 2003;**124**:544-60.

13 Zeger SL, Liang KY,Albert PS. Models for longitudinal data: a generalized estimating equation approach. *Biometrics* 1988;**44**:1049-60.

14 Pariente A, Milan C, Lafon J, et al. Colonoscopic screening in first-degree relatives of patients with 'sporadic' colorectal cancer: a case-control study. The Association Nationale des Gastroenterologues des Hopitaux and Registre Bourguignon des Cancers Digestifs (INSERM CRI 9505). *Gastroenterology* 1998;**115**:7-12.

15 Colombo L, Corti G, Magri F, et al. Results of a pilot study of endoscopic screening of first degree relatives of colorectal cancer patients in Italy. *J Epidemiol Community Health* 1997;**51**:453-8.

16 Guillem JG, Forde KA, Treat MR, et al. Colonoscopic screening for neoplasms in asymptomatic first-degree relatives of colon cancer patients. A controlled, prospective study. *Dis Colon Rectum* 1992;**35**:523-9.

17 Sauar J, Hausken T, Hoff G, et al. Colonoscopic screening examination of relatives of patients with colorectal cancer. I. A comparison with an endoscopically screened normal population. *Scand J Gastroenterol* 1992;**27**:661-6.

18 Jacobs LA. Health beliefs of first-degree relatives of individuals with colorectal cancer and participation in health maintenance visits: a population-based survey. *Cancer Nurs* 2002;**25**:251-65.

19 Madlensky L, Esplen MJ, Gallinger S, et al. Relatives of colorectal cancer patients: factors associated with screening behavior. *Am J Prev Med* 2003;**25**:187-94.

20 Manne S, Markowitz A, Winawer S, et al. Understanding intention to undergo colonoscopy among intermediate-risk siblings of colorectal cancer patients: a test of a mediational model. *Prev Med* 2003;**36**:71-84.

21 Faivre J, Dancourt V, Lejeune C, et al. Reduction in colorectal cancer mortality by fecal occult blood screening in a French controlled study. *Gastroenterology* 2004;**126**:1674-80.

22 Hardcastle JD, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet* 1996;**348**:1472-7.

23 Kronborg O, Fenger C, Olsen J, et al. Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet* 1996;**348**:1467-71.

24 Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med* 1993;**328**:1365-71.

25 Jouve JL, Remontet L, Dancourt V, et al. Estimation of screening test (Hemoccult) sensitivity in colorectal cancer mass screening. *Br J Cancer* 2001;**84**:1477-81.

Figure1: Study profile

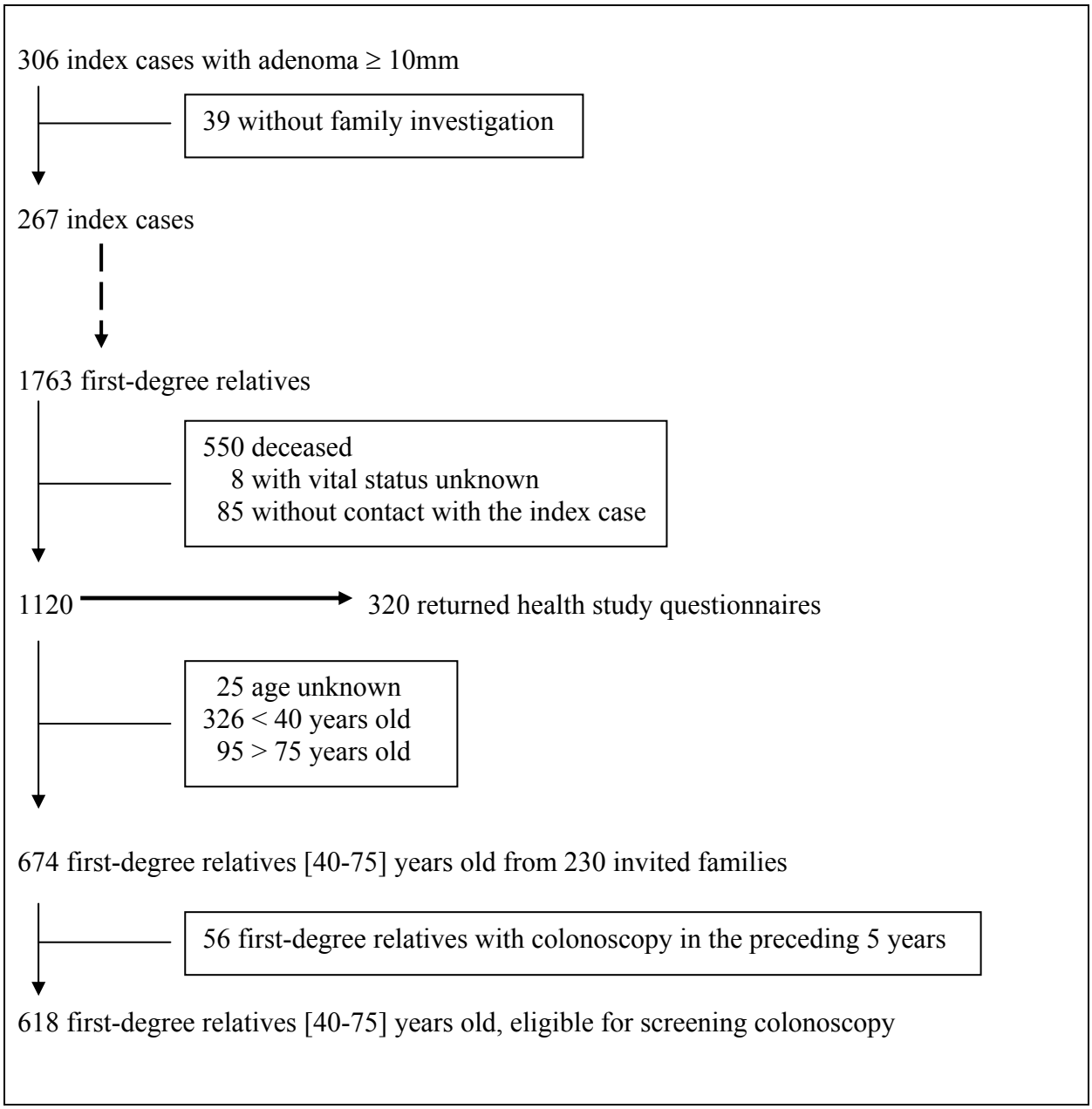

Table 1: Characteristics of 306 patients with large adenoma (index cases).

		n	%
Gender	women	113	*(36.9)*
	men	193	*(63.1)*
Age	< 60 years	123	*(40.2)*
	≥ 60 years	183	*(59.8)*
Residence area	Greater Paris area	80	*(26.1)*
	other regions	226	*(73.9)*
Family history of colorectal cancer †	yes	65	*(21.4)*
	no	239	*(78.6)*
Personal history of polyps	yes	42	*(13.7)*
	no	264	*(86.3)*
Rectal adenomas	yes	71	*(23.2)*
	no	235	*(76.8)*
Distal adenomas	yes	231	*(75.5)*
	no	75	*(24.5)*
Proximal adenomas	yes	84	*(27.4)*
	no	222	*(72.6)*
Advanced adenomas *	yes	207	*(67.6)*
	no	99	*(32.4)*

†2 missing values

*Adenomas with villous component and/or severe dysplasia or carcinoma *in situ*

Table 2: Univariate analysis of compliance with colonoscopy among first-degree relatives of patients with large adenoma according to characteristics of first-degree relatives.

	Number of relatives	Colonoscopies after index case diagnosis		
		n	***(%)***	***p****
Gender				
men	306	49	*(16)*	
women	312	65	*(21)*	***0.08***
Age				
<55 years	305	67	*(22)*	
≥55 years	313	47	*(15)*	***0.02***
Relationship with index case				
parents	47	4	*(9)*	
siblings	390	69	*(18)*	***0.08***
offspring	181	41	*(23)*	***0.03***
Residence proximity with index case†				
Same area or bordering	323	76	*(24)*	
Other areas	214	38	*(18)*	***0.36***
Total	**618**	**114**	***(18.4)***	

*: Obtained by Population Averaged logit models using Generalized Estimating Equations

†: 81 missing values

Table 3: Univariate analysis of compliance with colonoscopy among first-degree relatives of patients with large adenoma according to characteristics of index cases*.

	Number of relatives	Colonoscopies after index case diagnosis		
		n	*(%)*	*p*†
Gender				
men	338	67	*(20)*	
women	280	47	*(17)*	***0.35***
Age				
< 60 years	219	34	(16)	
≥ 60 years	399	80	(20)	***0.29***
Residence area				
Greater Paris area	167	20	*(12)*	
other areas	451	94	*(21)*	***0.03***
Family history of colorectal cancer				
yes	135	30	*(22)*	
no	483	84	*(17)*	***0.36***
Personal history of polyps				
yes	90	23	*(26)*	
no	528	91	*(17)*	***0.30***
Advanced adenomas ‡				
yes	445	80	*(18)*	
no	173	34	*(20)*	***0.56***
Total	**618**	**114**	***(19)***	

* The characteristics of the index case were reported to all first-degree relatives of his/her family.

† Obtained by Population Averaged logit models using Generalized Estimating Equations

‡ Adenomas with villous component and/or severe dysplasia or carcinoma in situ

Table 4: Comparison of observed and expected colonoscopies among families under the assumption of absence of intra-familial correlation for acceptability

Number of colonoscopies among families	Number of families	
	Expected	Observed
0	93	145
1	104	44
2 or more	21	29
Total	218	