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## Observational Study

## Colorectal cancer fecal screening test completion after age 74, sources and outcomes in French program

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**Abstract****BACKGROUND**

Elderly patients aged at least 75 years old (Elderly<sub>75</sub>), represent 45% of colorectal cancer (CRC) incidence. As others, the French Colorectal Cancer Screening Program (CRCSP) does not include Elderly<sub>75</sub>. To date, there is little evidence to justify stopping screening at 74 years of age.

requested by e-mail. However, each request will be processed in accordance with French legislation on the availability of research data.

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## AIM

To describe CRC fecal screening test completion after age 74, source (CRCSP/Provider ordered) and outcomes of these tests.

## METHODS

The study concerned 18704 Elderly\_75 residing in eleven French districts (Ain, Doubs, Essonne, Haute-Saone, Hauts-de-Seine, Jura, Seine-Saint-Denis, Territoire-de-Belfort, Val-de-Marne, Val-d'Oise, Yonne), having performed a CRC screening test between January 2008 and December 2017. The tests performed in a circumstance of delayed response to a solicitation (DRS) from the local cancer screening managing center (Managing-Center) were distinguished from the tests non-solicited by the Managing-Center, performed after a recommendation by a General Practitioner (GP) or other provider ordered (RGP). DRS was any test realized by an Elderly\_75 following an initial invitation from the Managing-Center with a maximum 24 mo after this invitation. Any Non-DRS test was considered RGP. The outcomes of these tests were described according to the circumstances of test completion.

## RESULTS

Of 18995 screening-tests were performed at ages: 75 (83.5%), 76-80 (13.4%) and > 80 (3.1%) years old. Elderly\_75 performed the screening test in a circumstance of DRS (71.9%) or RGP (28.1%). The proportion of the tests that could not be analyzed and not restarted was 13.2%. For these unanalyzed tests, the reason was age-related in 78.0% of cases, related to the laboratory's refusal to analyze the test of people aged  $\geq 77$ . Reported colonoscopy completion rate was 81.3%. For those 575 people with reported colonoscopy, no complication was listed. 18.0% of the 366 Elderly\_75 with lesions had no anteriority in the CRCSP. The neoplasia (124 Low-risk-polyps, 159 High-risk-polyps, 13 Unspecified-polyps and 70 CRCs) detection rate was 19.3/1000 Elderly\_75 screened and the CRC detection rate was 3.7/1000 Elderly\_75 screened.

## CONCLUSION

The high rate of colonoscopy completion after a positive test and the high proportion of screened lesions observed suggest that the lengthening of the screening period could allow significant detection of CRC and polyps that occur in Elderly\_75 excluded from CRCSP.

**Key words:** Colorectal cancer; Fecal screening test; Participation rate; Colonoscopy completion rate; Elderly

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**Core tip:** Reported colonoscopy completion rate was 81.3% and the neoplasia detection rate was 19.3 per 1000 Elderly screened and the colorectal cancer detection rate was estimated at 3.7 per 1000 Elderly screened. These results remain significantly higher than that usually found in the French Colorectal Cancer Screening Program (CRCSP). The motivation to participate including for colonoscopy and the high proportion of screened lesions sufficiently demonstrate that the lengthening of the follow-up period in a screening program, up to about 80 years of age, could make it possible to detect many cases that occur after the exclusion of Elderly\_75 from CRCSP.

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## INTRODUCTION

In addition to its high incidence and high mortality (around 42000 new cases and 18000 deaths per year), colorectal cancer (CRC) meets all the conditions to be screened in France<sup>[1-3]</sup>. Screening every two years, allows to obtain a reduction in CRC mortality in tested population<sup>[2,3]</sup>. In Burgundy, this decrease in mortality was of the order of 16% after 11 years of follow-up of a cohort of 45000 individuals<sup>[2]</sup>. European Commission recommended the implementation of the Colorectal Cancer Screening Program (CRCSP) by the search for occult bleeding in stool to face the high morbidity and mortality associated with CRC<sup>[4]</sup>. Following the recommendations, the screening of the CRC started in Germany in 1977<sup>[5]</sup>, was progressively implemented between 2000 and 2010 in other European countries, through CRC screening pilot programs, notably in England<sup>[6]</sup>, in Italy<sup>[7]</sup> in Holland<sup>[8,9]</sup> and in France<sup>[10]</sup>.

To date, most of the CRCSP policies target a medium risk population of CRC, defined on the age criterion with considerable variability from one program to another<sup>[11]</sup>. Since the effectiveness of screening depends on its application in an appropriate setting and at an appropriate frequency<sup>[12]</sup>, most European programs, observe an interval of 2 years between two screenings campaign. The test was offered to people (all gender) aged between 40 and 60 in Bulgaria, between 50 and 74 in France, England and Belgium; between 50 and 70 in Italy, between 55 and 75 in Holland<sup>[13]</sup>. The justification of these age groups remains controversial in the current state of knowledge. Indeed, there is little objective data to justify discontinuation of screening at 75 years. Recent Modeling was proposed to estimate from what age it was desirable to no longer invite to do the screening. They estimate screening up to age 82 as relevant<sup>[14,15]</sup>.

In France, as in other countries, the CRCSP does not include people aged  $\geq 75$  years, despite the high incidence of CRC after 74 years<sup>[16]</sup> and the constant increase in life expectancy since 2000<sup>[17]</sup>. It seems necessary to guide the debate on the problem of screening among the elderly. Indeed, in each French district, the sporadic participation of elderly patients aged at least 75 years old (Elderly\_75), out of the national CRCSP's recommendation, is recorded every year. We describe here, these CRC fecal screening test completion after age 74, the source (screening program or provider ordered) and outcomes.

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## MATERIALS AND METHODS

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### **Ethical considerations**

Before analysis, all data were anonymized. The screening database had a favorable opinion from the institution that oversees the ethics of data collection ("Commission nationale de l'informatique et des libertés": CNIL). According to the current French legislation, a study that does not change the care of patients did not require the opinion of the Clinical Research Centers Ethics Committee. This article does not contain any studies with human participants performed by any of the authors. This study does not involve human participants and informed consent was therefore not required. This article does not contain any studies with animals performed by any of the authors.

### **Study design**

A descriptive study of 18704 Elderly\_75s, residing in eleven French districts (Ain, Doubs, Essonne, Haute-Saone, Hauts-de-Seine, Jura, Seine-Saint-Denis, Territoire-de-Belfort, Val-de-Marne, Val-d'Oise, Yonne), having performed a CRC screening test between January 1, 2008 and December 31, 2017. The circumstances of performing this test (source of the test, previous behavior in the CRCSP) and the outcome (test result, colonoscopy completion and detected lesions) were described.

### **Distribution of screening tests in the districts**

On a voluntary basis, the eleven districts were chosen in three French regions (Bourgogne-Franche-Comté, Ile-de-France, Rhône-Alpes-Auvergne), among those using the same screening database management's materials. With a population (50-74 years) of 2355240 persons targeted by the 2015-2016 screening campaign, these eleven districts totaled 554294 participants in this campaign, with an average participation rate estimated at 23.5%<sup>[18]</sup>.

In France, a nationwide population based CRCSP was rolled out from January 2008 to December 2009. The program was based on a biennial guaiac faecal occult blood test distributed to men and women aged 50-74 at average risk of developing CRC. If positive, the test was followed by a total colonoscopy<sup>[19,20]</sup>. CRCSP was organized at a district level by the local cancer screening managing center (Managing-Center), in accordance with CRCSP's national specifications<sup>[19,20]</sup>. Each year, people targeted by

the campaign receive a letter inviting them to take a free screening test from their General Practitioner (GP). The pattern of distribution of the screening test recommends that the GP gives the screening test to any person aged 50 to 74 years, provided with an invitation letter. In the absence of this letter, the GP may give the test after establishing the eligibility of the person, using a connection made available to doctors or by calling to the Managing-Center. Until July-November, 2014, people who did not tested after the first recall letter, received the test kit at home, six months after the initial solicitation. The only organizational change (related to the objective of the study) imposed by the introduction of a new screening test *i.e.*, OC-sensor© fecal immunochemical test (FIT) replacing guaiac test in May 2015, was the supplying mode of GPs in screening tests kit, the classic pattern of kit distribution remaining unchanged.

### **Operational definition of variables and descriptive analysis**

For each Elderly\_75 having performed a test out of recommendation, solicitation/participation data from previous campaigns were extracted from the Managing-Centers databases. These databases were regularly enriched by socio-demographic data (gender, age), colonoscopy, histopathology and follow-up data provided by partners (Health Insurance Plan, Medical Information Services, Gastroenterologists, Surgeons, GP, *etc.*). The tests performed in a circumstance of delayed response after a solicitation (DRS, initial or recall letter existing) from the Managing-Center, done before 75 years were distinguished from the tests non-solicited by the Managing-Center, performed after a recommendation by a GP or other provider ordered (RGP). DRS was any test realized by an Elderly\_75 following an initial invitation from the Managing-Center with a maximum 24 months after this invitation. Any Non-DRS test was considered RGP.

**Previous behavior in the CRCSP:** Anteriority in the CRCSP was defined by the existence of at least one solicitation to participate in a CRCSP campaign between 50 and 74 years of age. The previous behavior in terms of the outcome of these earlier solicitations was described.

For each solicitation, the participation was defined as carrying out a fecal occult blood test according to the specifications of the French CRCSP<sup>[19,20]</sup>. For each person, the adherence to testing was evaluated as frequency of participation in previous campaigns. This frequency was expressed by the ratio between the observed number of participations in previous campaign and the expected number of participations in these previous campaigns. Considering the bi-annual organization of screening campaigns and a person age (X) at the date of first invitation in the district, the expected number of participation for a person aged Y year old, was  $(Y-X)/2$ . It was coded as a discrete variable: Without anteriority (The person was never solicited in the district program); Never participated (The person has not participated in any of the previous campaigns to which it was solicited); Participated with frequency < 30% of campaigns; frequency between 30 and 50%; frequency > 50% to 75% and frequency > 75%.

For Elderly\_75 with a history of solicitation, the presence of a history of NLAI (Does Not Live at the Address Indicated) or refusal to participate in a campaign was collected and coded as a binary variable (No/Yes). Similarly, the presence of a history of colonoscopy, reported by a mailing response after solicitation, was described as a binary variable (No/Yes). If the person participated in at least one campaign, history of positive test and colonoscopy performed after this positive test was collected and coded as a discrete variable: No history of positive test, positive test without colonoscopy, positive test with normal colonoscopy, positive test with positive colonoscopy.

**CRC fecal screening test completion after age 74:** The outcome of screening test performed after 74 years was analyzed in terms of test quality (non-analyzable test proportion) and test result (Negative, Positive). In the event of a positive result, the diagnostic course has been analyzed in terms of frequency of colonoscopy completion and in terms of frequency and types of diagnosed lesions including: Low-risk-polyps, High-risk-polyps, Unspecified-polyp and CRC. High-risk-polyps included, Adenomas  $\geq 10$  mm (except hyperplastic polyps), Serrated adenomas, Adenomas with high grade dysplasia, Villous or Tubulo-villous adenomas. The diagnoses associated with CRC and polyps were those related to the C18-C20 and D12 codes of the 10th version of the WHO International Classification of Diseases<sup>[21]</sup>. The positive predictive value (PPV) of the test was estimated as the proportion of lesions among the Elderly\_75 who completed a colonoscopy after a positive test.

### **Statistical analysis**

Qualitative variables were described in frequency and quantitative variables were described in mean  $\pm$  SD. Frequencies were compared between groups by a Pearson  $\chi^2$  test or Fisher's exact test. Means were compared between two groups by Student's *T* test. All the analyzes were carried out with version 13 of STATA software (College Station, Texas, United States) and  $P < 0.05$  was considered for statistical significance.

## RESULTS

### **Modality of participation**

Of 18704 Elderly\_75 (56.3% female), performed 18995 tests between January 1, 2008 and December 31, 2017. These 18995 screening-tests were performed at ages: 75 (83.5%), 76-80 (13.4%) and  $> 80$  (3.1%) years old. Over this period, 250 Elderly\_75 out of 18704 completed at least 2 tests after the age of 74. On average, over one year of campaign, 7 out of 1000 tests were realized by people aged  $\geq 75$  years. This proportion reached 15 per 1000 in 2015 (Table 1). 13442 people (71.9% of the sample), performed the first test after the age of 74, in a circumstance of DRS of the Managing-center. This response delayed by  $7.8 \pm 5.3$  mo after the initial solicitation. For those who have performed a test under recommendation and have an anteriority in CRCSP, the delay between the last test in the CRCSP and this test was  $37.6 \pm 18.9$  mo.

Mean age at the time of the test was  $75.7 \pm 1.4$  years with extremes between 75 and 91 years ( $75.3 \pm 0.3$  years in the DRS group *vs*  $76.9 \pm 2.3$  years in the RGP group,  $P = 0.00001$ ). In the DRS group, 98.2% were 75 years old at the time of the test and 1.8% were 76-80 years. In the RGP group, 49.8% were 75 years old at the time of the test, 40.0% were 76-80 years and 10.2% were  $> 80$  years ( $P = 0.00001$ ). The proportion of females was not significantly different between DRS (56.5%) and RGP (56.0%,  $P = 0.52$ ).

### **Previous behavior in the CRCSP**

Seventy-nine point five percent of this population (76.9% of the 13442 DRSs *vs* 86.3% of the 5262 RGPs,  $P = 0.60$ ) had an anteriority, i.e. at least one previous invitation in the CRCSP. Among these 14875 Elderly\_75 with an anteriority (10336 in DRS and 4539 in RGP), 12678 had at least one previous screening test between 50 and 74 years old (9119 in DRS and 3559 in RGP) and they participated in 73.6% (77.2% in DRS *vs* 65.4% in RGP,  $P = 0.00001$ ) of the campaigns to which they were solicited. Average number of this previous solicitations was  $2.5 \pm 1.3$  ( $2.4 \pm 1.2$  in DRS *vs*  $2.7 \pm 1.3$  in RGP,  $P = 0.00001$ ). 11.8% of the Elderly\_75 with an anteriority never participated in a previous CRCSP campaign (9.1% in DRS *vs* 18.6% in RGP,  $P = 0.00001$ ) and 9.3% had a reported history of colonoscopy (8.0% DRS *vs* 12.1% RGP,  $P < 0.001$ ). Only 1.9% (1.7% in DRS *vs* 2.1% in RGP,  $P = 0.1$ ) had a reported history of NLAI or sent previously a form indicating their refusal to participate in the CRCSP. The frequency of participation in previous campaign and the results of previous tests by campaign year are summarized in Table 2. The proportion of Elderly\_75 with a previous positive test in CRCSP among these with an anteriority was 1.1% (200 Elderly\_75/18704). This proportion was higher in RGP (1.1% in DRS *vs* 2.8% in RGP,  $P = 0.00001$ ). Whatever the source of the test and the year of screening, the frequency of participation in previous campaign was at least 60.0%. Peoples who performed the test under recommendation in 2012 were less regular in the CRCSP than those who performed the test the same year, in a context of DRS (Figure 1). Before 2010, the screening test was performed mostly by people without any anteriority (1339 out of 1721 Elderly\_75 in 2009) in the CRCSP or having never participated in a campaign (157/1721 tests in 2009). From 2011 to 2017, the test was mostly performed by people who participated in at least 70% of campaigns.

### **CRC fecal screening test completion after age 74**

Overall, 3.7% (3.7% in DRS *vs* 3.7% in RPD,  $P = 0.79$ ) of the 18995 tests performed were positive (Table 3). The proportion of the tests that could not be analyzed and not restarted was 13.2%. For these unanalyzed tests, the reason was age-related in 78.0% of cases, related to the laboratory's refusal to analyze the test of people aged  $\geq 77$ . 18.0% of the 366 Elderly\_75 with lesions had no anteriority in the CRCSP and 10.4% had never participated. Reported colonoscopy completion rate was 81.3%. For those 575 people with reported colonoscopy, no complication was listed. 124 Low-risk-polyps, 159 High-risk-polyps, 13 Unspecified-polyps and 70 CRCs were detected, with an average neoplasia's PPV estimated at 0.64. This PPV varied from 0.46 (16 neoplasia out of 35 colonoscopy) in 2008 to 0.67 in 2017 (40 neoplasia out of 60 colonoscopy) (Table 4). The neoplasia detection rate was 19.3 per 1000 Elderly\_75 screened and the CRC detection rate was estimated at 3.7 per 1000 Elderly\_75

**Table 1** Total tests performed in the ten districts and part of tests performed by elderly aged  $\geq 75$  years (elderly  $\geq 75$ ), by year of campaign

Campaign year	Total tests performed in the districts	Tests performed by elderly $\geq 75$			
		75 yr	76-80 yr	> 80 yr	Total (Part in %)
2008	230467	1172	113	13	1298 (5.6)
2009	343468	1588	141	3	1732 (5.0)
2010	289120	1119	147	14	1280 (4.4)
2011	313982	1659	166	18	1843 (5.9)
2012	287818	1478	158	17	1653 (5.7)
2013	302392	1815	166	16	1997 (6.6)
2014	267342	1557	122	25	1704 (6.4)
2015	163976	2039	435	100	2574 (15.7)
2016	399039	1992	728	225	2945 (7.4)
2017	286039	1436	369	164	1969 (6.9)
Total	2883643	15855	2545	595	18995 (6.6)

screened. An increased detection rate (all neoplasia) was observed after the immunochemical test introduction in 2015 (Table 5). The mean age at neoplasia diagnosis was  $75.7 \pm 1.2$  years ( $75.2 \pm 0.2$  years in DRS *vs*  $77.1 \pm 1.8$  years in RGP,  $P < 0.001$ ). This mean age was  $75.4 \pm 0.7$  years when the lesion was a low risk polyp,  $75.4 \pm 0.5$  years when it was a high-risk polyp and  $77.0 \pm 2.1$  years when it was a CRC.

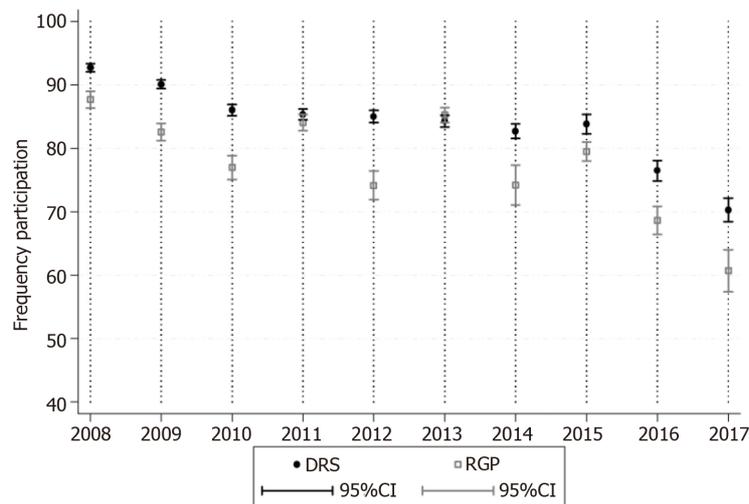
## DISCUSSION

Few results of CRC fecal screening in elderly are available. This study presents results of out of recommendation screening in 18704 elderly over 74 years of age. The results observed appear to be beyond expectations. Indeed, the proportion (3.7%) of positive tests remains significantly higher than that found (2.9) in these districts in the same period or that usually found (2.6%) in the CRCSP program<sup>[20]</sup>. In the national program, reported colonoscopy completion rate after a positive test was 76.9% with approximately major incidents, including perforation in 3 in 1000 colonoscopies<sup>[20]</sup>. In addition to a similar even higher rate of colonoscopy completion observed in this study (81.3%), no major incident was recorded in this elderly population. In France, the detection rate of CRC was estimated at 1.6/1000 in CRCSP<sup>[20]</sup>, which is only half of the rate observed in this study. Certainly, the high detection rate observed could be explained, at least in part, by age. Indeed, the increase in the incidence of CRC with age has been well documented<sup>[1,22,23]</sup>. Between 40 and 80 years of age, the incidence doubles almost every ten years<sup>[24]</sup> and 45% of CRCs are diagnosed in people aged at least 75 years in Burgundy<sup>[16]</sup>. In this population, CRC were diagnosed on average age at 77 years. Considering these findings, it could be argued that extending the duration of CRCSP in healthy people up to 80 years, could allow the screening of the many cases that occur after the exclusion of the Elderly\_75 from CRCSP.

The sample described in this analysis consisted mainly of people regularly invited by the local cancer screening managing center with delayed answer. Although the age group concerned by the CRCSP is 50 to 74 years old, the logistic approach implemented for the last invitation challenges this approach. Indeed, people receive their last invitation until the eve of the 75th birthday. This timing inevitably has the consequence of carrying out a screening test beyond the extreme ages recommended in CRCSP.

The motivation of people previously devoted in the CRCSP, to continue the screening after 74 years has been previously discussed and ending screening at 75 years is a real ethical issue<sup>[25]</sup>. Previous modeling studies have recommended screening up to 82 years, however, heterogeneity of the Elderly\_75 population limit this implementation<sup>[14,15]</sup>. Indeed, in addition to the fact that the gain in years of life remains very modest, heterogeneity of the population with both healthy subjects and subjects in precariousness or with comorbidities makes it difficult to choose the type of appropriate screening<sup>[25]</sup>. The United States Preventive Services Task Force advocated screening for CRC in healthy people up to age 84. Beyond this age, it suggested that the disadvantages of screening outweigh profits<sup>[22,26]</sup>.

In order to sustain the CRCSP extension after 74 years, the availability of the



**Figure 1** Frequency of participation in previous campaigns, by circumstances and by screening year. DRS: Delayed response after solicitation; RGP: Recommendation of a General Practitioner/Provider ordered; CI: Confidence interval.

medical profession must be acquired for medical monitoring and a continuous evaluation of the disadvantages and benefits of screening. It has been documented that the adherence of the GP is a determining factor in the acceptability and effectiveness of a screening campaign<sup>[27]</sup>. Although the inequalities in access to cancer care are still visible in France<sup>[28,29]</sup>, the results of this study show the possible availability of GPs to do a shared decision making process with patients regarding the pros and cons, and individualized risk assessments. Indeed, more than a quarter of the test were performed under medical recommendation which would testify not only an adherence of GPs but especially their concern for the follow-up of patient excluded from CRCSP. However, two major hypotheses could explain the test delivery to the Elderly\_75 by the GPs. The hypothesis of a catch-up for the less regular persons in the CRCSP between 50 to 74 years, is concordant with the low frequency of participation in previous campaign of the people having performed a test after provider ordered recommendation (compared to the DRS). It is not excluded that GPs also use the screening test as an additional means of diagnosis. The bond in Elderly\_75 participation after FIT introduction (in 2015), which is more sensitive and more user-friendly (only one sample) is also an essential point to be mentioned.

The proportion of non-analyzable tests remains abnormally high, especially among those who have taken the test under provider recommendation and after the introduction of FIT. Indeed, the proportion of non-analyzable tests was 1.6% in the CRCSP<sup>[19,20]</sup>. When we subtract these numerous cases related to the refusal of the laboratory, the elderly could have a rate of non-analyzable tests lower than that observed in the CRCSP. The fundamental question with this main reason could be: "How many cancers have not been detected because of this age-based refusal of the person who made the tests"? The answer to this question is predicted by the high incidence of CRC (0.6/1000 Person-years) among people performing their last screening tests (between 70 and 74 years) in the CRCSP<sup>[23]</sup>.

The study sample consisted mainly of 83.4% of tests performed at the age of 75, which could lend interpretation almost exclusively to this age. In addition, outside of the hypotheses evoked, the study could not bring more precise details on the real circumstances of realization of the test after 74 years. Indeed, a major concern regarding the RGP group is the possible self-selection bias: The considered population could have been motivated to participate in the screening by high risk factors or symptoms. In this group, screening test could have been used as a diagnostic tool. However, performing a colonoscopy after a positive screening test is a classic pattern in the French organized screening program. Certainly, the obtained results do not provide enough evidence on the benefits of screening in this age group, i.e. decrease in mortality from CRC if screening would be recommended above the currently accepted age limit. The results could, however, constitute a starting point (or even a reference) for a possible experimentation of the screening program for CRC in the elderly, in France.

In conclusion, despite a regulatory framework that is not favorable to their participation in CRCSP campaigns, a motivation to continue CRCSP after 74 years of

**Table 2** Distribution of 18704 elderly aged  $\geq 75$  years, according to the test performing contexts and history in Colorectal Cancer Screening Program, by year of campaign

Test achieving contexts	Campaign year										
	Total	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total	18704	1298	1721	1264	1815	1627	1966	1687	2525	2882	1919
Circumstances											
Delayed response to solicitation	13442	1108	1509	982	1548	1363	1689	1496	814	1645	1288
Recommendation of a GP	5262	190	212	282	267	264	277	191	1711	1237	631
Average number of previous solicitation <sup>1</sup>	2.5 $\pm$ 1.3	1.2 $\pm$ 0.4	1.2 $\pm$ 0.5	1.3 $\pm$ 0.6	1.4 $\pm$ 0.8	1.8 $\pm$ 0.9	2.3 $\pm$ 0.9	2.5 $\pm$ 1.0	3.1 $\pm$ 1.1	3.2 $\pm$ 1.2	3.5 $\pm$ 1.3
Fidelity in CRCSP											
Without anteriority	3829	1174	1339	417	164	114	80	76	99	212	154
Never participated	2197	57	157	278	384	212	200	143	183	330	253
< 30%	248	0	0	1	3	5	17	24	34	74	90
30%-50%	1824	4	28	50	130	205	312	268	236	324	267
50%-75%	1573	0	1	27	53	64	145	180	357	431	315
75%-100%	9033	63	196	491	1081	1027	1212	996	1616	1511	840
NLAI/refusal history <sup>1</sup>	277	3	5	8	25	25	28	32	40	59	52
Colonoscopy history in mailing response <sup>2</sup>	1378	10	22	44	106	97	138	155	271	300	235
History of positive test [T(+)] <sup>2</sup>											
T(+) without colonoscopy	22	1	0	0	0	2	4	0	8	5	2
T(+) with normal colonoscopy	3	0	0	0	0	1	0	2	0	0	0
T(+) with colonoscopy (+)	175	0	0	0	4	3	16	19	39	51	43

This was about the first test for people who performed at least 2 tests after 74 years.

<sup>1</sup>Persons without anteriority are excluded;

<sup>2</sup>Persons without anteriority or who have never participated in the previous Colorectal Cancer Screening Program are excluded. NLAI: Does Not Live at the Address Indicated; CRCSP: Colorectal Cancer Screening Program; GP: General Practitioner.

age was observed. To optimize CRC fecal screening for these Elderly\_75, in addition to existing communication tools, the implementation of other means to better select patients and minimize the proportion of non-analyzable tests could be beneficial. The motivation to participate including the high colonoscopy participation rates and the high proportion of screened lesions demonstrate eloquently that the lengthening of the follow-up period in a screening program, up to about 80 years of age, could make it possible to detect many cases that occur after the exclusion of Elderly\_75 from CRCSP. In a period of implementation of proposals for improving national program of CRCSP, it seems necessary to feed the debate on screening of the elderly to alert decision-making bodies. More in-depth studies on the feasibility of organized screening in Elderly\_75 seem necessary to confirm or not, the current screening age limit.

**Table 3** Distribution of the 18995 tests performed by elderly aged  $\geq 75$  years, according to the circumstances of realization (It was about the circumstances of the first test for people who performed at least 2 tests after 74 years) and the results of the test

Results	Circumstances of realization		
	Delayed response after solicitation	Reco- mme- n- dation of a pre- scriber doctor	Total
Total tests performed after 74 yr	13596	5399	18995
Negative test	12529	3262	15791
Non-analyzable and non-restated test	559	1938	2497
Positive without colonoscopy	107	25	132
Positive with normal colonoscopy	147	62	209
Positive with colonoscopy (+)	254	112	366
Total lesions screened	254	112	366
Unspecified polyps	8	5	13
Low risk polyps	94	30	124
High risk polyps	109	50	159
Colorectal cancer	43	27	70

**Table 4** Distribution of 18995 tests performed by elderly aged  $\geq 75$  years (elderly  $\geq 75$ ), according to the results of the test and year of screening

Results	Screening year										
	Total	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total test performed by elderly $\geq 75$	18995	1298	1732	1280	1843	1653	1997	1704	2574	2945	1969
Test results											
Negative test	15791	1227	1600	1204	1720	1549	1855	1590	1878	1837	1331
Non-analyzable and non-restated	2497	23	70	23	69	70	89	82	544	972	555
Positive without colonoscopy	132	13	13	11	5	7	10	9	16	25	23
Positive with normal colonoscopy	209	19	20	15	15	7	22	5	49	37	20
Positive with colonoscopy (+)	366	16	29	27	34	20	21	18	87	74	40
Type of lesions screened											
Unspecified polyps	13	0	2	0	1	0	0	0	6	1	3
Low risk polyps	124	6	7	11	12	7	10	6	24	29	12
High risk polyps	159	5	13	10	16	7	5	7	44	33	19
Colorectal cancer	70	5	7	6	5	6	6	5	13	11	6

**Table 5** Colorectal cancer detection rate in the 11 districts and part of tests performed by elderly aged  $\geq 75$  years (elderly  $\geq 75$ ), by year of campaign

Campaign year	Tests performed in the 11 districts				Tests performed by elderly $\geq 75$ in the 11 districts			
	No. of tests (% of T+)	No. of colonoscopy (Completion rate in %)	No. of neoplasia (Detection rate in %)	No. of CRC (Detection rate in %)	No. of tests (% of T+)	No. of colonoscopy (Completion rate in %)	No. of neoplasia (Detection rate in %)	No. of CRC (Detection rate in %)
2008	230467 (2.7)	5392 (85.0)	3020 (13.1)	420 (1.8)	1298 (3.7)	35 (72.9)	16 (12.3)	5 (3.9)
2009	343468 (2.5)	7324 (83.7)	4025 (11.7)	609 (1.8)	1732 (3.6)	49 (79.0)	29 (16.7)	7 (4.0)
2010	289120 (2.5)	6117 (85.4)	3250 (11.2)	473 (1.6)	1280 (4.1)	42 (79.3)	27 (21.1)	6 (4.7)
2011	313982 (2.3)	6283 (86.9)	3327 (10.6)	458 (1.5)	1843 (2.9)	49 (90.7)	34 (18.4)	5 (2.7)
2012	287818 (2.1)	5010 (84.5)	2618 (9.1)	355 (1.2)	1653 (2.1)	27 (79.4)	20 (12.1)	6 (3.6)
2013	302392 (1.8)	4646 (84.7)	2420 (8.0)	325 (1.1)	1997 (2.7)	43 (81.1)	21 (10.5)	6 (3.0)
2014	267342 (1.9)	4146 (81.0)	2153 (8.1)	238 (0.9)	1704 (1.9)	23 (71.9)	18 (10.6)	5 (2.9)
2015	163976 (4.4)	6222 (85.8)	4107 (25.0)	474 (2.9)	2574 (5.9)	136 (89.5)	87 (33.8)	13 (5.1)
2016	399039 (4.7)	155109 (80.9)	9993 (25.0)	1126 (2.8)	2945 (4.6)	111 (81.6)	74 (25.1)	11 (3.7)
2017	286039 (4.4)	8928 (71.5)	5764 (20.2)	632 (2.2)	1969 (4.2)	60 (72.3)	40 (20.3)	6 (3.0)
Total	2883643 (2.9)	69177 (81.9)	40677 (14.1)	5110 (1.8)	18995 (3.7)	575 (81.3)	366 (19.3)	70 (3.7)

T+: Positive test; CRC: Colorectal cancer.

## ARTICLE HIGHLIGHTS

### Research background

In France, as in other countries, the Colorectal Cancer (CRC) Screening Program (CRCSP) does not include people aged  $\geq 75$  years, despite the high incidence of CRC after 74 years and the constant increase in life expectancy since 2000. Indeed, elderly patients aged at least 75 years old (Elderly<sub>75</sub>), represent 45% of CRC incidence. To date, there is little evidence to justify stopping CRC screening at 74 years of age.

### Research motivation

In this period of implementation of the proposals for reform of the National CRCSP, our motivation was to feed the debate on the problem of screening in the elderly, in order to alert the decision-making bodies. By noting that in each French district, the sporadic participation of Elderly<sub>75</sub>, out of the national CRCSP's recommendation, is recorded every year.

### Research objectives

Our objective was to describe the sources and outcomes of these screening test performed out of recommendation. Indeed, in the absence of a CRC screening program involving this age group, the elderly and/or their attending physicians decide sporadic participation in the campaigns organized by the local cancer screening managing center. The analysis of these sources and outcomes could argue the need for the implementation of an experimental program on the benefits and risk of CRC screening after the age of 75 years.

### Research methods

The study concerned 18704 Elderly<sub>75</sub> residing in eleven French districts (Ain, Doubs, Essonne, Haute-Saone, Hauts-de-Seine, Jura, Seine-Saint-Denis, Territoire-de-Belfort, Val-de-Marne, Val-d'Oise, Yonne), having performed a CRC screening test between January 2008 and December 2017.

### Research results

Of 18995 screening-tests were performed by these 18704 Elderly<sub>75</sub> at ages: 75 (83.5%), 76-80 (13.4%) and  $> 80$  (3.1%) years old. Elderly<sub>75</sub> performed the screening test in a circumstance of delayed response to a solicitation from the local cancer screening managing center (71.9%) or following a recommendation by a General Practitioner or other provider ordered (28.1%). The proportion (3.7%) of positive tests remains significantly higher than that found (2.9) in these districts in the same period or that usually found (2.6%) in the CRCSP program. It's obvious that the high risk of colonoscopy complication after 75 years is a barrier to screening CRC in the elderly. With a reported colonoscopy completion rate estimated at 81.3%, this study recorded no complications. On reminder, in the national program, reported colonoscopy completion rate after a positive test was 76.9% with approximately major incidents, including perforation in 3 in 1000 colonoscopies. The neoplasia (124 Low-risk-polyps, 159 High-risk-polyps, 13 Unspecified-polyps and 70 CRCs) detection rate was 19.3/1000 Elderly<sub>75</sub> screened and the CRC detection rate was 3.6/1000 Elderly<sub>75</sub> screened. In this population, CRC were diagnosed on average age

at 77 years.

### Research conclusions

Despite a regulatory framework that is not favorable to their participation in CRCSP campaigns, a motivation to continue CRCSP after 74 years of age was observed. Considering these findings, it could be argued that extending the duration of CRCSP in healthy people up to 80 years, could allow the screening of the many cases that occur after the exclusion of the Elderly\_75 from CRCSP.

### Research perspectives

We are confident that more in-depth studies on the feasibility of CRC screening in Elderly are needed to confirm or not, the current age limit of screening at 74 years. Our perspectives converge in this direction because a pilot project for the implementation of CRC-screening after the age of 75, is currently in the process of identifying strategic and financial partners. One of the main objectives of this study will be to assess the risk associated with performing colonoscopy. Awaiting the implementation of this project, we intend to open the debate in France with the results of this study.

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