Cancer Screening and Prevention **2023** vol. 2(4) | 204–213
DOI: 10.14218/CSP.2023.00024S

Original Article

Colorectal Cancer Screening in Araba (Basque Country)

Jesús Iturralde-Iriso[1,2*], Carmen Orcajo-Bermúdez[3], Javier Guinea-Castañares[1] and Eugenia Campo-Cimarras[3,4]

[1]*La Habana-Cuba Health Center, Vitoria-Gasteiz, Spain;* [2]*Department of Preventive Medicine and Public Health, University of the Basque Country, Leioa, Spain;* [3]*University of the Basque Country, Leioa, Spain;* [4]*General Surgery Service, University Hospital of Alava, Vitoria-Gasteiz, Spain*

Received: October 30, 2023 | **Revised:** November 26, 2023 | **Accepted:** December 06, 2023 | **Published online:** December 25, 2023

Abstract

Background and objectives: Colorectal cancer (CRC) is the third most common malignancy worldwide. The average age at diagnosis of CRC is around 70 years old. This study aimed to assess the prevalence of asymptomatic CRC and premalignant lesions in the colon in OSI Araba.

Methods: This study included individuals aged 50–69 who were admitted to OSI Araba Health Centers. It spanned from the start of CRC screening through fecal occult blood test immunological analysis in 2009 to the publication of the latest updated data in 2021.

Results: An average of 90.98% of participants obtained a definitive result. Specifically, 31.71% were normal, 1.22% had relevant non-neoplastic pathology, 5.49% had non-neoplastic polyps, 15.93% had low-risk adenomas, 22.26% had medium-risk adenomas, 17.65% had high-risk adenomas and 5.02% had CRC.

Conclusions: CRC screening is an effective strategy for reducing incidence and mortality rates, preventing new cases, and minimizing disease burden in the future.

Introduction

Colorectal cancer (CRC) ranks as the third most common neoplasia globally and the second leading cause of cancer-related death.[1,2] In the Basque Country, located in the north of Spain, CRC accounted for 15.26% of all malignant tumors detected in men and 13.48% in women during 2013–2017. Regarding mortality, these tumors represented 12.27% of the men and 13.07% of the women in the Basque Country during 2013–2017 (https://www.euskadi.eus/contenidos/informacion/registros_cancer/es_def/adjuntos/Cancer-CAE-2001-2021.pdf).

The average age at diagnosis of CRC is approximately 70 years old in both sexes (https://seom.org/info-sobre-el-cancer/colon-recto, https://www.cancer.net/cancer-types/colorectal-cancer/risk-factors-and-prevention).[1] The risk starts to increase at the age of 50, when the incidence of early-onset sporadic CRC increases, primarily in the left colon. However, there is a higher mortality rate observed in cases with tumors in the right colon[1,3] and a noticeable increase in cases with tumors in the rectum (https://www.cancer.net/cancer-types/colorectal-cancer/risk-factors-and-prevention). Notably, patients with tumors located in the colon have a higher survival rate than those with tumors located in the rectum.[1]

Seventy to eighty-five percent of CRC cases are sporadic, with adenomatous polyps or serrated lesions being the precursors. They progress to CRC slowly, with the majority being adenocarcinomas.[1,4]

Although several risk factors and lifestyles can be modified, the greatest decrease in the incidence and mortality of CRC lies in improving screening methods (https://seom.org/info-sobre-el-cancer/colon-recto).[1,5] The survival rate is related to the stage at diagnosis, as premalignant lesions can be detected and eliminated early (https://seom.org/info-sobre-el-cancer/colon-recto).[1,6,7] Currently, several intervention options are available for secondary prevention, but there is no consensus regarding the type, age of onset, or frequency of screening.[1]

The Program of Preventive Activities and Health Promotion (PAPPS) 2022 recommends the following CRC screening strategies for individuals aged 50–74 years old, with moderate evidence and a weak recommendation in favor: perform fecal occult blood test immunological analysis (FOBTi) annually or biennially, and

Keywords: Colorectal cancer; Prevention program; Fecal occult blood test; Immunological analysis.

Abbreviations: CRC, colorectal cancer; FOBTi, fecal occult blood test immunological analysis; HRA, high risk adenoma; LRA, low risk adenoma; MRA, medium risk adenoma; PPV, positive predictive value.

***Correspondence to:** Jesús Iturralde-Iriso, La Habana-Cuba Health Center, Vitoria-Gasteiz 01012, Spain; Department of Preventive Medicine and Public Health, University of the Basque Country, Leioa 48940, Spain. ORCID: https://orcid.org/0000-0002-7800-3928. Tel/Fax: +34-945006785, E-mail: jesusmaria.iturraldeiriso@osakidetza.eus

How to cite this article: Iturralde-Iriso J, Orcajo-Bermúdez C, Guinea-Castañares J, Campo-Cimarras E. Colorectal Cancer Screening in Araba (Basque Country). *Cancer Screen Prev* 2023;2(4):204–213. doi: 10.14218/CSP.2023.00024S.

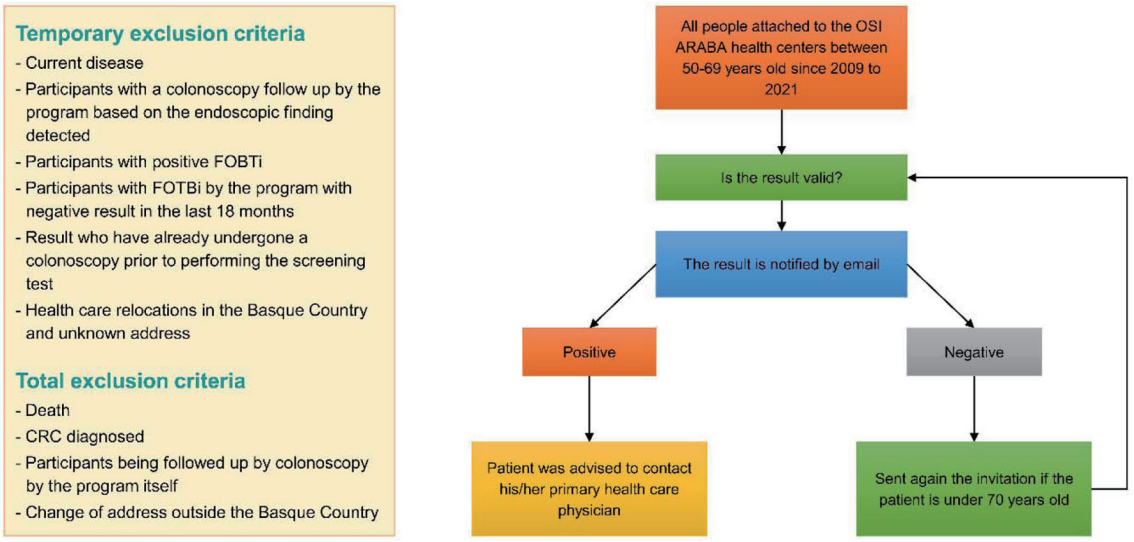

Fig. 1. The process of enrolling participants, with the temporary exclusion criteria and the total exclusion criteria. CRC, colorectal cancer; FOBTi, fecal occult blood test immunological analysis.

undergo sigmoidoscopy and/or colonoscopy every 15 years or only at the peak risk age of 55 to 64 years old.[1]

Since polyps tend to bleed, the use of FOBTi as a screening method has been shown to be a positive intervention for reducing CRC-related mortality as evidenced by controlled studies conducted in both Europe and the USA.[2] The reduction in mortality varies between 14 and 18% when colonoscopy is used as a confirmatory test in those with a positive FOBTi result. When together with colonoscopic polypectomies, this combination suggests a 53% reduction in mortality.[7] Over time, immunological FOBTi has become the most widely accepted screening method, due to its high sensitivity (79%) and specificity (94%) in detecting CRC in asymptomatic subjects, owing to its superior capability in detecting human hemoglobin.[6–10] In the Basque Country, this screening method was approved in 2008, adopting a biennial schedule with a fecal blood threshold offset at 20 μ/g. The decision to utilize a single sample for the FOBTi, in contrast to other autonomous communities, and the biennial screening interval align with the recommendations of Levis and van Rossum. This approach is designed to enhance participation rates and achieve an optimal balance between sensitivity and specificity.[11] The diagnostic confirmation test and the gold standard for this screening is colonoscopy in positive FOBTi, since it allows visualization of the most proximal lesions (unlike sigmoidoscopy) and allows removal of premalignant lesions (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).[12]

Population screening is also cost-effective since it generates net cost savings, and 90% of the total cost is derived from CRC treatment.[9,13]

Screening by colonoscopy and polypectomy has proven to be a diagnostic and therapeutic procedure that effectively reduces the incidence and mortality of CRC. It is considered the gold standard in the detection of CRC. Once suspicion is raised, colonoscopy is the primary screening method for CRC and premalignant lesions across all screening strategies.[5]

Our objectives involved assessing the prevalence of asymptomatic colorectal cancer and premalignant lesions in the colon. This assessment contributed to the establishment of the Colorectal Cancer Screening Program by the Basque Health Service-Osakidetza since its implementation in 2009 across various primary care units of our region's integrated health organization, OSI Araba.

Methods

The study enrolled all individuals aged 50–69 who were admitted to the OSI Araba Health Centers. It spanned from the start of CRC screening through FOBTi in 2009 to the publication of the latest updated data in 2021. Individuals within the target population who, due to specific temporary or total exceptions, were not involved in the initial invitation to participate, will be excluded. The temporary exclusion criteria include current disease, participants who had undergone a colonoscopy/sigmoidoscopy in the past 4 years, participants who had undergone colonoscopy follow-up within the Program based on endoscopic finding, participants who had a negative FOBTi screening result in the last 18 months, participants with a positive FOBTi screening result who have already undergone a colonoscopy before the screening test, healthcare relocations in the Basque Country and unknown address. Total exclusion criteria included death, diagnosis of CRC, participants under colonoscopy follow-up within the program (according to the findings), and changes in address outside the Basque Country (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/). It should be noted that only those with a valid test result, whether positive or negative, were included. Participants were notified of the result and subsequent steps by mail. For those under 70 years old with a negative result, a new invitation will be sent within 2 years. If there are signs of blood in the stool (positive FOBTi: ≥20 μg/g stool and/or ≥100 ng/100 mL), the participant is advised to contact their primary care physician, who will then determine the necessity of a confirmatory colonoscopy. This process is shown in Figure 1.

The variables were as follows: Percentage of individuals (50 to 69 years old) to the target population (the population registered in the National Institute of Statistics of individuals between the ages of 50 and 69 and residents of the autonomous community under study on December 31 of the evaluated year) who were invited to participate in the Program.

Participation rate: Percentage of participants who underwent quantitative FOBTi out of the total number of individuals invited.

Positivity rate: Percentage of individuals with positive quantitative FOBTi results among those who underwent the test.

Colonoscopy acceptance and rejection rates.

Percentage of valid colonoscopies.

Percentage of colonoscopies according to the type of preparation.

Percentage of colonoscopies according to the type of complication (bleeding, perforation, post-polypectomy, mild sedation, severe sedation, death, and others).

Percentage of colonoscopies according to endoscopic findings (inconclusive, normal/irrelevant findings, relevant non-neoplastic pathology, non-neoplastic polyps, low-risk adenomas (LRA), medium-risk adenomas (MRA), high-risk adenomas (HRA) and invasive cancer).

Detection rates.

Likewise, several positive predictive values (PPVs) were calculated for FOBTi (screening program quality indicator), LRA, MRA, HRA, CRC and any type of adenoma, including CRC.

A retrospective cross-sectional observational study was designed to analyze the descriptive variables collected by the Program for patients at OSI Araba who agreed to participate in the CRC screening program during specific years. Comparisons were made with results observed in other integrated health organizations of the Basque Country. The results were analyzed using the statistical software STATA/IC 15.0.

The standardized and validated Boston Scale (BBPS) was used. This scale evaluates each of the three colonic segments, assigning them a score of 0–3 based on the observed degree of cleanliness (20).

Post-colonoscopy complications were defined as those occurring within 0–30 days after the colonoscopy procedure (https://www.euskadi.eus/contenidos/informacion/registros_cancer/es_def/adjuntos/Cancer-CAE-2001-2021.pdf).

Participants whose diagnostic process was completed with a high-quality colonoscopy (ensuring good preparation and completeness) were assigned based on the most severe histological lesion found. Following the completion of FOBTi diagnostic confirmation, the endoscopic findings were categorized as follows:

Normal: Absence of pathological findings or presence limited to hemorrhoids or diverticula, or cases of melanosis coli.

Hyperplastic polyps: Exclusion of adenomatous and/or serrated components.

LRAs: 1–2 adenomas <10 mm and tubular adenomas with low-grade dysplasia. MRA: When any of the following circumstances occur: 3 to 4 adenomas, one adenomas ≥10 mm and <20 mm, one with villous or tubulovillous components, or one with high-grade dysplasia or non-hyperplasic serrated polyps.

HRA: Sessile or flat lesion ≥20 mm with fragmented resection, presence of more than 5 adenomas, or some with a length ≥20 mm.

Carcinoma: Lesions that invade the submucosa with different degrees of infiltration into adjacent structures

Relevant non-neoplastic pathology: Endoscopic findings generally related to inflammatory bowel disease (ulcerative colitis, Crohn's disease); cases involving polyposis or conditions that required a genetic or hereditary study and follow-up by a digestive specialist.

Inconclusive: Positive findings without a definitive diagnosis.

The result of the colonoscopy (depending on the histological results, the degree of dysplasia and the size of the polyps/adenomas) will determine the subsequent follow-up of the participant, who may continue in the screening program or be excluded (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

In the case of malignant neoplastic pathology (carcinoma), tumor staging followed the TNM classification system.[14]

This study was carried out in accordance with the recommendations of the ethical guidelines of the Helsinki Declaration. The protocol was approved by the OSI Araba Research Ethics Committee, which provided favorable support for its implementation on March 24, 2023 (No. 2023-006). The data collected were aggregated and anonymized. The individual consent for this retrospective analysis was waived.

Results

Invitations and participation in the screening program

A total of 360,724 valid personalized invitations were sent to the patients' home addresses during the six rounds of CRC screening conducted from 2009 to 2021. The participation rate varied from 67.14% in 2010 to a maximum of 74.43% in 2017, maintaining around 70%, as shown in Figure 2.

With regard to the differences between the sexes, women showed higher participation rates than men in all years. Women's participation rates ranged from 69.9% in 2010 to 76.3% in 2017, while men's participation rates ranged from 64.2% in 2010 to 72% in 2017, as shown in Figure 3.

Feces occult blood test immunological analysis

Positivity.

Of the 251,687 individuals who underwent FOBTis, the average positivity rate was 4.97%, showing a declining trend over the years, as shown in Table 1.

Positive predictive value.

The overall PPV for the FOBTi was 61.48%, as shown in Table 2.

Colonoscopy

The acceptance and the rejection

Among the patients with a positive FOBTi, 93.9% agreed to undergo screening colonoscopy, as shown in Table 3.

The complete colonoscopies and the level of preparation

A total of 90.8% of participants completed colonoscopies, and 90.4% were adequately prepared, as shown in Table 3.

Complications

During the study period, colonoscopy resulted in a 0.488% incidence of serious complications: perforations were reported in 0.2%, 0.1% bleeding that required transfusion, 0.01% severe sedation, 0.07% mild sedation, 0.1% post-polypectomy syndromes, and one death (mortality rate per colonoscopy 0.008%), as shown in Table 3.

Endoscopic findings.

There 69.77% (251,687 individuals) underwent FOBTi testing, with 90.98% (11,378 individuals) obtaining definitive results. The distribution of findings included 31.71% with normal results, 1.22% with relevant non-neoplastic pathology, 5.49% with non-neoplastic polyps, 15.93% with LRA, 22.26% with MRA, 17.65%

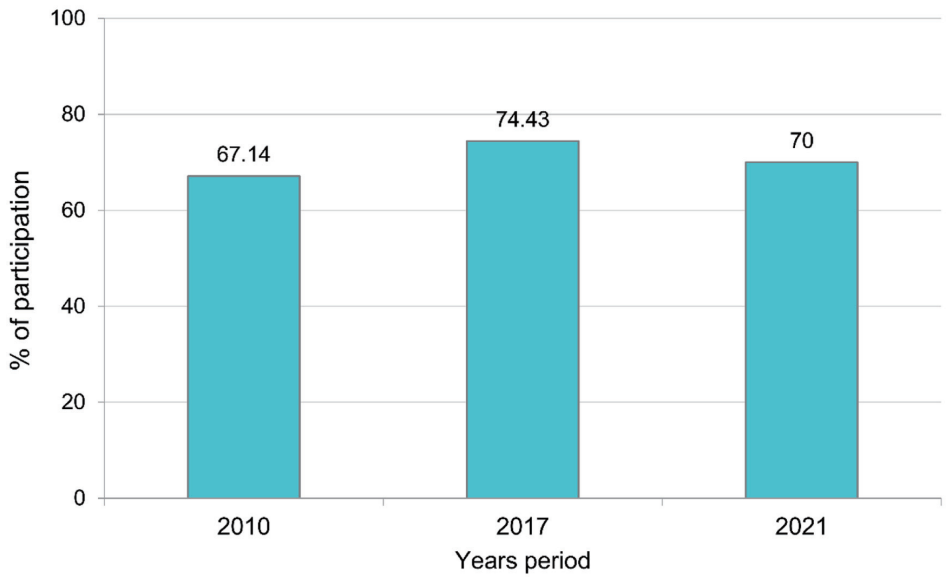

Fig. 2. The participation rate.

with HRA, and 5.02% with CRC. Table 4 shows a detailed breakdown by year in OSI Araba. To analyze the differences between the sexes in endoscopic findings, we relied on the elaborated data provided by the program, as raw numbers are unavailable. Among women, 43.5% were normal, 1.4% had relevant non-neoplastic pathology, 6.3% had non-neoplastic polyps, 15.7% had LSA, 28.9% had advanced lesions (MRA + HRA), and 4.3% had CRC. Among men, 22.5% of the conclusive colonoscopies were normal, 1% had relevant non-neoplastic pathology, 5% had non-neoplastic polyps, 16.6% had LRA, 48.5% had advanced lesions, and 5.5% had CRC.

Detection rate

The detection rates of CRC and advanced lesions were higher in males (5.5% and 48.5%, respectively) compared to females. The detection rate of any type of adenoma, including CRC, was higher in men (70.6%), while women presented 43.5% of normal colonoscopies, and men presented only 22.5%.

The non-neoplastic polyp detection rate was 2.48‰, the LRA detection rate was 7.2%, the MRA was 10.06%, the HRA was 7.98%, and the CRC detection rate was 2.27%. Therefore, the detection rate for CRC and any type of adenoma was 25.25‰, the detection rate for advanced adenomas (AA: MRA+HRA) was 18.04%, and the detection rate for advanced neoplasia (AA+CRC) was 20.31%, as shown in Table 5.

Positive predictive values

The PPV for LRA was 14.5%, for MRA was 20.25%, for HRA was 16.06% and for CRC was 4.57%. Consequently, the PPV for

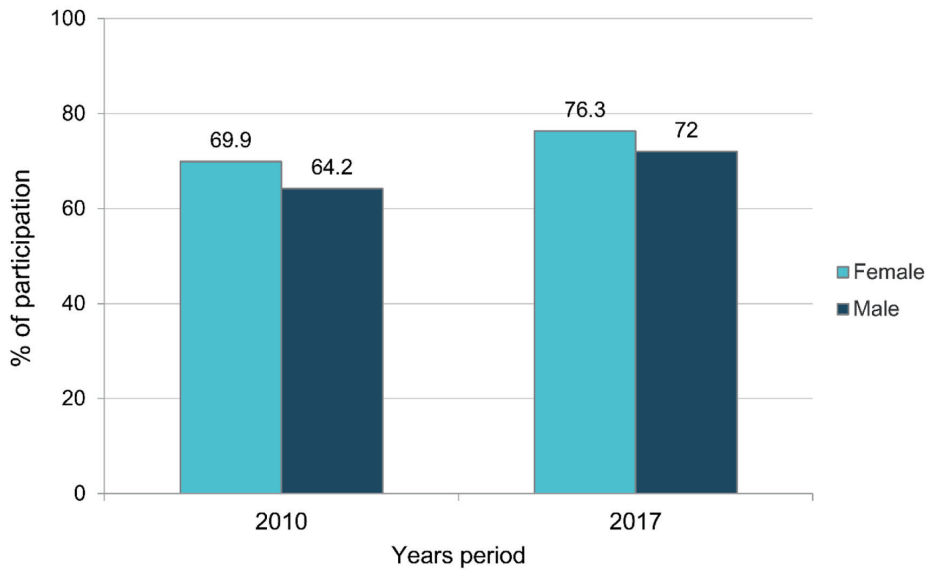

Fig. 3. The difference in participation between the sexes and the trend by year.

Table 1. Results of the Program during the period 2009–2021 at OSI Araba

OSI Araba	Invitations (n)	Participation (%)	Participation (n)	Positives (%)	Positives (n)	People with definitive colonoscopy (%)	People with definitive colonoscopy (n)	Inadequate preparation
2009	4217	58,98%	2487	6,47%	161	91,35%	147	6%
2010	41241	67,14%	27689	6,09%	1686	91,92%	1550	20,67%
2011	19671	67,07%	13193	6,29%	830	94,47%	784	10,23%
2012	40687	68,26%	27773	4,33%	1203	89,72%	1079	9,03%
2013	20468	69,28%	14180	5,9%	837	92,16%	771	7,27%
2014	40633	70,56%	28671	4,79%	1373	93,86%	1289	8,28%
2015	21777	72,15%	15712	5,24%	823	93,28%	768	11,1%
2016	30695	70,32%	21585	4,68%	1010	90,88%	918	9,63%
2017	30358	74,43%	22595	4,86%	1098	90,97%	999	8,21%
2018	20760	71,96%	14939	4,3%	642	92,63%	595	4,04%
2019	39305	70,62%	27757	4,7%	1305	83,09%	1084	6,27%
2020	15163	68,63%	10406	4,6%	479	88,37%	423	8,09%
2021	35749	69,09%	24699	4,29%	1060	91,64%	971	5,06%
TOTAL	360724	69,77%	251687	4,97%	12506	90,98%	11378	8,76%

The data are presented in absolute form as the number of people (n) and percentages (%). The titles of the following table are invitations (n), participation (%), participation (n), positives %, positives (n), people with complete colonoscopy (%), people with complete colonoscopy (n) and inadequate preparation.

any type of adenoma, including CRC, was 50.81%, the PPV for advanced adenomas (AA: MRA+HRA) was 36.31%, and the PPV for advanced neoplasia (AA+CRC) was 40.87%.

Colorectal cancer stage

Of the CRC cases detected during the period 2009–2021 at OSI Araba, 67.5% were in the early stage (stages I-II), 32% were in the advanced stage (stages III-IV), and 0.5% were in an unknown stage. The detection rate of CRC in the early stages was slightly higher in men than in women (68% *vs.* 66.7%), while the detection rate of CRC in the advanced stages was marginally higher in women than in men (32.3% *vs.* 31.8%).

Table 2. PPVs of FOBTi, LRA, MRA, HRA, CRC, adenomas (LRA+MRA+HRA), AA and NA during the 2009–2021 period at the OSI Araba

OSI Araba	PPV FOBTi	PPV LRA	PPV MRA	PPV HRA	PPV CRC	PPV of all adenomas	PPV AA	PPV MA
2009	70,22%	11,19%	0,62%	47,85%	4,97%	64,63%	48,47%	53,44%
2010	69,32%	12,33%	0,59%	43,47%	6,88%	63,28%	44,06%	50,94%
2011	66,76%	8,68%	25,18%	20,97%	7,23%	62,06%	46,15%	53,38%
2012	56,55%	11,39%	22,45%	12,97%	5,65%	52,47%	35,42%	41,08%
2013	58,09%	12,55%	24,02%	9,68%	5,38%	51,64%	33,71%	39,09%
2014	61,24%	15,95%	24,98%	9,76%	3,79%	54,47%	34,73%	38,52%
2015	57,45%	15,43%	24,17%	8,62%	3,16%	51,38%	32,79%	35,95%
2016	57,61%	13,17%	23,36%	9,11%	4,45%	50,09%	32,47%	36,92%
2017	60,65%	18,49%	22,04	10,29%	3,37%	54,18%	32,33%	35,7%
2018	60,40%	16,81%	24,75%	9,18%	3,58%	54,33%	33,94%	37,52%
2019	59,48%	15,41%	22,92%	11,73%	2,68%	52,74%	34,65%	37,33%
2020	58,7%	15,88%	22,14%	10,65%	4,18%	52,85%	32,8%	36,98%
2021	64,18%	19,44%	24,35%	10,76%	3,4%	57,95%	35,11%	38,51%
TOTAL	61,48%	14,5%	20,25%	16,06%	4,57%	50,81%	36,31%	40,87%

The data are presented as percentages and are translated into the probability that a person with a positive FOBTi result actually has the lesion studied. The different PPVs for FOBTi, adenomas (LRA+MRA+HRA), CRC: colorectal cancer, LRA: low-risk adenoma, MRA: medium-risk adenoma, HRA: high-risk adenoma, AA: advanced adenoma (MRA+ HRA) and NA: advanced neoplasia (AA+CRC) are presented. Abbreviations: CRC, colorectal cancer; FOBTi, fecal occult blood test immunological analysis; LRA, low-risk adenoma; MRA, medium-risk adenoma; HRA, high-risk adenoma.

Table 3. Quality of screening colonoscopy at OSI Araba and Osakidetza during the period 2009–2021

Invitations (2009–2011)	OSI Araba (2009–2021)	Osakidetza (2009–2021)	P
Complications	%	%	
Hemorrhage with transfusion	0,1	0,1	0,661
Drilling	0,2	0,2	0,769
Severe sedation	0,01	0,02	0,798
Mild sedation	0,07	0,17	0,007
Post polypectomy syndrome	0,1	0,12	0,925
Death	0,008	0,002	0,249
Quality of colonoscopy preparation	%	%	P
Adequate (e. Boston ≥ 6)	90,4	91,1	0,591
Bad (e. Boston <6)	9,6	8,9	0,024
Colonoscopies	%	%	P
Complete colonoscopies	90,8	91,5	0,548
Rejection of colonoscopy	6,1	5,3	0

The colonoscopy rejection rates were 6.1%, 90.4% of the preparations were adequate, and the complication rates were similar. (P: level of significance).

Discussion

Participation

It should be noted that the participation rate increased over the years in the OSI Araba from 2009 to 2017 (59%; 67.2%; 67%; 68.2%; 69.3%; 70.8%; 72.2%; 71.8%; 74.4%), followed by a decrease in subsequent years (72% in 2018, 70% in 2019, 71.3% in 2020 and 69% in 2021). Similarly, in the Basque Country, the participation rate increased since the screening implementation from 2009–2018 (58.1%; 65.5%; 65.8%; 67 0.7%; 69.7%; 70.7%; 70.3%; 72.4%; 72.3%; 72.5%), but a decline began thereafter. Regarding gender in OSI Araba and Osakidetza, the participation rate is higher in women (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/). Sex should be considered one of the main factors determining participation rates in cancer screening programs. Our results are consistent with the vast majority of studies that have shown a higher participation rate in CRC screening programs among women than among men worldwide. The literature suggests that men could be less active in prevention and health promotion activities. However, older men (60–69 years) participate more often, possibly reducing the differences in participation rate between the sexes in successive rounds

Table 4. Findings of the colonoscopies with a definitive diagnosis carried out at the OSI Araba in the period 2009–2021

OSI Araba	Normal	Non-neoplastic polyp	LRA	MRA	HRA	CRC	Non neoplastic relevant pathology
2009	23,13% (34)	4,76% (7)	12,24% (18)	0,68% (1)	52,38% (77)	5,44% (8)	1,36% (2)
2010	23,03% (357)	4,9% (76)	13,42% (208)	0,65% (10)	47,29% (733)	7,48% (116)	1,68% (25)
2011	27,68% 217)	4,08% (32)	9,18% (72)	26,66% (209)	22,19% (174)	7,65% (60)	0,89% (7)
2012	36,14% (390)	2,69% (29)	12,7% (137)	25,02% (270)	14,46% (156)	6,3% (68)	1,85% (20)
2013	36,58% (282)	5,71% (44)	13,62% (105)	26,07% (201)	10,51% (81)	5,84% (45)	1,3% (10)
2014	34,45% (444)	6,13% (79)	16,99% (219)	26,61% (343)	10,4% (134)	4,03% (52)	1,09% (14)
2015	38,15% (293)	5,6% (43)	16,54% (127)	25,91% (199)	9,24% (71)	3,39% (26)	0,91% (7)
2016	36,6% (336)	7,3% (67)	14,49% (133)	25,71% (236)	10,02% (92)	4,9% (45)	0,98% (9)
2017	33,13% (331)	5,81% (58)	20,32% (203)	24,22% (242)	11,31% (113)	3,70% (37)	1,3% (13)
2018	34,79% (207)	5,88% (35)	18,15% (108)	26,72% (159)	9,92% (59)	3,87% (23)	0,67% (4)
2019	30,26% (308)	7,21% (76)	16,3% (201)	26,81% (299)	14,54% (153)	3,91% (35)	0,98% (12)
2020	31,6% (135)	4,97% (23)	18,67% (76)	24,41% (106)	12,74% (51)	4,8% (10)	1,38% (5)
2021	28,71% (274)	5,71% (56)	21,44% (206)	26,64% (258)	11,6% (114)	3,25% (36)	0,96% (10)
TOTAL	31,71% (3608)	5,49% (625)	15,93% (1813)	22,26% (2533)	17,65% (2008)	5,02% (571)	1,22% (139)

The data are presented in absolute form as the number of people (n) and percentages (%). Abbreviations: CRC, colorectal cancer; LRA, low-risk adenoma; MRA, medium-risk adenoma; HRA, high-risk adenoma.

Table 5. Detection rate per 1000 people for GNP (GROSS NATIONAL PRODUCT), adenoma, CRC, LRA, MRA, HRA, AA and NA during the period 2009–2021 at OSI Araba

OSI Araba	Adenoma detection rate 1000p	CRC detection rate 1000p	AA detection rate 1000 p	NA detection rate 1000p	LRA detection rate 1000p	MRA detection rate 1000p	HRA detection rate 1000p
2009	38,6	3,22	3,36	34,58	7,24	0,4	30,96
2010	34,35	4,19	26,83	31,02	7,51	0,36	26,47
2011	34,49	4,55	29,03	33,58	5,46	15,84	13,19
2012	20,27	2,45	15,34	17,79	4,93	9,72	5,62
2013	27,29	3,17	19,89	23,06	7,4	14,17	5,71
2014	24,28	1,81	16,64	18,45	7,64	11,96	4,67
2015	25,27	1,65	17,18	18,84	8,08	12,67	4,52
2016	21,36	2,08	15,2	17,28	6,16	10,93	4,26
2017	24,7	1,64	15,71	17,35	8,98	10,71	5
2018	21,82	1,54	14,49	16,13	7,23	10,64	3,95
2019	23,53	1,26	16,28	17,55	7,24	10,77	5,51
2020	22,39	1,92	15,09	17,01	7,3	10,19	4,9
2021	23,4	1,46	15,06	16,52	8,34	10,45	4,62
TOTAL	25,25	2,27	18,04	20,31	7,2	10,06	7,98

The different detection rates per 1000 people calculated for GNP are presented: Non-neoplastic polyps, adenomas (LRA+MRA+HRA), CRC: colorectal cancer, LRA: low-risk adenoma, MRA: medium-risk adenoma, HRA: adenoma of high risk, AA: advanced adenoma (MRA+HRA) and NA: advanced neoplasms (AA+CRC). CRC, colorectal cancer; LRA, low-risk adenoma; MRA, medium-risk adenoma; HRA, high-risk adenoma; AA: advanced adenoma.

of screening.[15,16] While population screenings aim to promote equality, there is an observed tendency for lower participation rates in extreme social positions.[17] This might be attributed to lower-class individuals prioritizing other health concerns or higher-class individuals relying on private healthcare.[15,16,18] On the one hand, factors such as age under 60 years old, inadequate control of risk factors, or lack of active engagement in preventive activities contribute to non-participation.[15,18] Translating informative materials and training professionals in prevention programs and service delivery facilities at all primary care points would help reduce these inequalities.[17]

On the other hand, the invitation method also influences the participation rate. Prior informative letters, souvenir letters and sending the FOBTi kit directly to homes increased the participation rate. Even so, the factor that has the greatest positive impact on the participation rate is the active engagement of primary care physicians in promoting and recommending screening.[19]

Positivity of FOBTi

The average FOBTi positivity in OSI Araba users was 4.97%, which decreased until 2021. The PPV ranged from 56.55% to 61.24% between 2012 and 2020, with an increase in 2021 up to 64.18%, probably related to the diagnostic delay caused by the pandemic the previous year.

Colonoscopy

Acceptance and rejection

Among OSI Araba users, 93.9% agreed to undergo a colonoscopy as recommended by the Coordinating Center of the program. The rejection rate of colonoscopy was 6.1%, which presents a statistically significant difference (p = 0.000) compared to that in the Basque Country (5.3%), although this difference is only one percentage point (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

Complete colonoscopies

The percentage of complete colonoscopies performed in the OSI Araba program was slightly lower than the average percentage of complete colonoscopies performed in the Basque Country during the same period (90.8% *vs*. 91.5%) (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

Colonoscopy preparation level

From 2009 to 2021, the rate of inadequate colonic preparation for screening colonoscopy in OSI Araba was 9.6%, exceeding the average rate for inadequate preparation registered in the Basque Country (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/), which was 8.9%, with a Boston Scale score of less than 6. Analyzing the rates of adequate colonic preparation (Boston ≥6) during the 2009–2018 period revealed that OSI Araba consistently exhibited a higher rate of adequate preparations compared to the Basque Country in most years; but starting from 2019, it began to present lower rates of adequate preparations compared to the Basque Country. The possible causes of this difference should be investigated (such as changes in preparation methods or clarity of the procedure explanation by nurses). Although the differences did not exceed 5% in any given year, notably, in 2020, only 91.2% of the preparations at the OSI Araba were adequately prepared, whereas 96% of them were prepared at the Osakidetza level (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

Complications

From 2009 to 2021, the complication rates associated with colonoscopies at OSI Araba were reported as follows: 0.1% for bleed-

ing requiring transfusion, 0.2% for perforation, 0.01% for severe sedation, 0.07% for mild sedation, 0.1% for post polypectomy syndromes, and a mortality rate of 0.008%. Comparing with the respective complication rates registered in Osakidetza in the same period, we found that the complication rates in OSI Araba were equal to or lower than those registered in Osakidetza (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/) (0.1% bleeding requiring transfusion, 0.2% perforations, 0.02% severe sedation, 0.17% mild sedation, 0.12% post polypectomy syndromes), except for the mortality rate. The mortality rate of OSI Araba was 0.008%, and it was 0.002% at the community level (Osakidetza), as shown in Table 3.

Endoscopic findings

Among the total number of colonoscopies, 31.5% were found to be normal, 5.5% were non-neoplastic polyps, 1.2% were non-neoplastic relevant pathology, 17.8% were LRA, 22.3% were MRA, 17.6% were HRA, 0.2% were fragmented advanced lesions (FAL) and 5.1% were CCR. Among these findings, 38.2% were neither adenomatous nor cancerous, 57.7% were adenomatous lesions and 5.1% were cancerous lesions. All this information is detailed in Table 4. OSI Araba has higher detection rates than the Basque Country, (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/) for normal colonoscopies (31, 5% *vs.* 30.9%), while rates for non-neoplastic polyps was similar (5.5% *vs*. 5.6%), as was the rates for relevant non-neoplastic pathology (1.2% *vs*. 1.1%). However, OSI Araba had lower detection rates for LRA (17.8% *vs*. 18.9%) and higher detection rates for advanced lesions(MRA and HRA) (39.9% *vs.* 38.4%), fragmented advanced lesions (0.2% *vs*. 0.17%), and CRC (5.1% *vs*. 4.6%) compared to the Basque Country (https://www.osakidetza.euskadi/eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/). The proportions of these findings were similar in both regions.

In OSI Araba, the detection of neither adenomatous nor cancerous lesions presents a higher proportion in females than in males (51.2% *vs*. 28.5%), and the finding of adenomatous pathology (65.1% *vs*. 44.6%) and cancerous (5.5% *vs*. 4.3%) is more frequent among men than among women. If we compare these results with those of the colonoscopy findings in the Basque Country for the period 2009–2021, we observe similar results (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/). These data indicate that, in the Basque Country (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/), among women who underwent screening colonoscopy, 1 in 93 had advanced lesions or CRC, with 1 in 900 having CRC. In contrast, among men who underwent colonoscopy, 1 in 43 had an advanced lesion or CRC, with 1 in 590 having CRC. The detection rate of advanced lesions and CRC is approximately double in men than in women.

The proportion of benign findings in women is higher in the OSI Araba than in the Basque Country (51.2% *vs*. 49.2%), and more advanced adenomatous lesions were detected in men in the OSI Araba than in the Basque Country (54.2% *vs*. 51.4%). However, the detection rate of non-advanced lesions (LRAs) is higher in the Basque Country than in the OSI Araba for both sexes (18.9% *vs.* 17.8%). These differences in these findings do not exceed 5%, suggesting a similar distribution of the findings according to sex in the OSI Araba and the Basque Country, with men presenting a higher detection of advanced lesions than women in both (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

The main current interest is focused on ensuring the quality and safety of the screening process adhering to the criteria and indicators recommended by the European guidelines regarding the accuracy of the FOBTi and colonoscopy without underestimating the possible negative effects derived from this type of procedure, such as colonoscopy complications, false negatives, and false positives. It has been suggested that adjustments should be made in the fecal hemoglobin (HBf) concentration cut-off points, considering factors such as gender, age, family history, and comorbidities, to better predict CRC risk. This is because a higher FOBTi positivity index and a higher detection rate of CRC and advanced neoplasms are detected in men with the use of a single cut-off point for HBf, while women are mostly affected by a higher rate of false positives when colonoscopy is performed. This pattern has been detected in the OSI Araba and the Basque Country. These results are consistent with those of other studies indicating that the FOBTi has greater sensitivity and less specificity for CRC detection in men. Variations in the distribution of HBf concentration according to sex and age suggest the need for individualized cut-off points to improve the precision of the FOBTi in screening programs. On the other hand, some studies do not support the change, stating that the use of different cut-off points could influence the effectiveness of the screening, considering that the PPV in both sexes should be the same. Any variation in these cut-off points would lead to different consequences, either an increase in the sensitivity for the detection of advanced tumors and an increase in false positives when the cut-off point is increased or the demand for colonoscopies when the cut-off point is decreased, which would imply an economic challenge for any screening program. For these reasons, further studies should be carried out to determine the optimal cut-off point for the HBf concentration for specific populations based on sex, age and other related factors, to enhance the identification of true-positive cases.[7,13]

CRC detection

The average CRC detection rate in OSI Araba users was 5% for both sexes. Over the years, the detection rate increased since screening (2009–2011), and the CRC detection rate has gradually decreased since 2012, presenting certain fluctuations but showing a slightly decreasing trend.

At OSI Araba in the period 2009–2021, the CRC diagnoses were distributed as follows: 67.5% in the early stages I-II, 32% in the advanced stages III-IV and 0.5% in an unknown stage. The distribution of CRC stages in the Basque Country (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/) in the same period indicates that 70.6% were in the early stages I-II, 28.4% were in the advanced stages III-IV, and 1% were in an unknown stage. As we can see, both in the OSI Araba and in the Basque Country, most of the CRCs detected through the program were in the early stages, differing in the advanced stages III-IV, with 32% in OSI Araba and 28.4% in the Basque Country (https://www.osakidetza.euskadi.eus/programa-cribado-cancer-colorrectal/webosk00-oskenf/es/).

Limitations and strengths of the study

This study has certain limitations. The data obtained may not be readily applicable to the entire Basque Country population, where the CRC Prevention Program of the Department of Health of the Basque Government is established, nor to other populations in other autonomous communities. However, the results of this study have been compared with the Basque Country population data provided by the program, allowing comparison between OSI Araba

and the network. Another limitation could be that individuals at a high risk of developing CRC were included in the same detection program as those without such risk of CRC development. Additionally, participants spanning different social positions could present another limitation due to their different participation rates. Nevertheless, given the large sample size and sociodemographic characteristics similar to those of the Basque Country, we believe that the results could be reasonably extrapolated.

One of the main strengths of this study is the large number of participants evaluated. Due to the large amount of information obtained over the years, this population screening program has been validated and has a consistently high participation rate.

Conclusions

CRC screening is an effective strategy in reducing the incidence and mortality rates, preventing new cases and minimizing the disease burden in the future.

The possibility of implementing improved or complementary strategies that improve the efficiency of current measures should be assessed, such as the introduction of risk algorithms, differentiating between genders, assessing family susceptibility, or adjusting the cut-off points of the FOBTi.

Finally, it is crucial to highlight the importance of primary care physicians, as they are in charge of informing the population about the program, promoting secondary prevention, and carrying out daily work in primary prevention.

Acknowledgments

We thank Colon Cancer Prevention Program of the Basque Government for supporting this project.

Funding

None.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Contributed to the study concept and design (JI, CO, JG and ECC), acquisition of data (JI), assay performance and data analysis (JI, CO, JG and ECC), drafting of the manuscript (CO and JG), critical revision of the manuscript (ECC), and supervision (JI).

Ethical statement

This study was carried out in accordance with the recommendations of the ethical guidelines of the Helsinki Declaration. The protocol was approved by the OSI Araba Research Ethics Committee, which provided favorable support for its implementation on March 24, 2023 (No. 2023-006). The data collected were aggregated and anonymous. The individual consent for this retrospective analysis was waived.

Data sharing statement

No additional data are available.

References

[1] Marzo-Castillejo M, Bartolomé-Moreno C, Bellas-Beceiro B, Melús-Palazón E, Vela-Vallespín C. PAPPS Expert Groups. Cancer prevention recommendations: Update 2022. Aten Primaria 2022;54(Suppl 1):102440. doi:10.1016/j.aprim.2022.102440, PMID:36435580.

[2] Jodal HC, Helsingen LM, Anderson JC, Lytvyn L, Vandvik PO, Emilsson L. Colorectal cancer screening with faecal testing, sigmoidoscopy or colonoscopy: a systematic review and network meta-analysis. BMJ Open 2019;9(10):e032773. doi:10.1136/bmjopen-2019-032773, PMID:31578199.

[3] Tom CM, Mankarious MM, Jeganathan NA, Deutsch M, Koltun WA, Berg AS, *et al*. Characteristics and Outcomes of Right- Versus Left-Sided Early-Onset Colorectal Cancer. Dis Colon Rectum 2023;66(4):498–510. doi:10.1097/DCR.0000000000002273, PMID:35001052.

[4] Gutierrez-Stampa MA, Aguilar V, Sarasqueta C, Cubiella J, Portillo I, Bujanda L. Impact of the faecal immunochemical test on colorectal cancer survival. BMC Cancer 2020;20(1):616. doi:10.1186/s12885-020-07074-y, PMID:32611328.

[5] Arana-Arri E, Imaz-Ayo N, Fernández MJ, Idigoras I, Bilbao I, Bujanda L, *et al*. Screening colonoscopy and risk of adverse events among individuals undergoing fecal immunochemical testing in a population-based program: A nested case-control study. United European Gastroenterol J 2018;6(5):755–764. doi:10.1177/2050640618756105, PMID:30083338.

[6] Zubero MB, Arana-Arri E, Pijoan JI, Portillo I, Idigoras I, López-Urrutia A, *et al*. Population-based colorectal cancer screening: comparison of two fecal occult blood test. Front Pharmacol 2014;4:175. doi:10.3389/fphar.2013.00175, PMID:24454288.

[7] Arana-Arri E, Idigoras I, Uranga B, Pérez R, Irurzun A, Gutiérrez-Ibarluzea I, *et al*. Population-based colorectal cancer screening programmes using a faecal immunochemical test: should faecal haemoglobin cut-offs differ by age and sex? BMC Cancer 2017;17(1):577. doi:10.1186/s12885-017-3555-3, PMID:28851318.

[8] Carethers JM. Stool-Based Screening Tests for Colorectal Cancer. JAMA 2023;329(10):839–840. doi:10.1001/jama.2023.0547, PMID:36800187.

[9] Bujanda L, Sarasqueta C, Castells A, Pellisé M, Cubiella J, Gil I, *et al*. Colorectal cancer in a second round after a negative faecal immunochemical test. Eur J Gastroenterol Hepatol 2015;27(7):813–818. doi:10.1097/MEG.0000000000000366, PMID:25856688.

[10] Von Karsa L, Patnick J, Segnan N, Atkin W, Halloran S, Lansdorp-Vogelaar I, *et al*. European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. Endoscopy 2013;45(1):51–59. doi:10.1055/s-0032-1325997, PMID:23212726.

[11] Idigoras I, Arrospide A, Portillo I, Arana-Arri E, Martínez-Indart L, Mar J, *et al*. Evaluation of the colorectal cancer screening Programme in the Basque Country (Spain) and its effectiveness based on the Miscan-colon model. BMC Public Health 2017;18(1):78. doi:10.1186/s12889-017-4639-3, PMID:28764731.

[12] Unanue-Arza S, Idigoras-Rubio I, Fernández-Landa MJ, Bilbao-Iturribarria I, Bujanda L, Portillo I. Analysis of Post-Colonoscopy Colorectal Cancer and Its Subtypes in a Screening Programme. Cancers (Basel) 2021;13(20):5105. doi:10.3390/cancers13205105, PMID:34680254.

[13] Arrospide A, Idigoras I, Mar J, de Koning H, van der Meulen M, Soto-Gordoa M, *et al*. Cost-effectiveness and budget impact analyses of a colorectal cancer screening programme in a high adenoma prevalence scenario using MISCAN-Colon microsimulation model. BMC Cancer 2018;18(1):464. doi:10.1186/s12885-018-4362-1, PMID:29695234.

[14] Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010;17(6):1471–1474. doi:10.1245/s10434-010-0985-4, PMID:20180029.

[15] Solís-Ibinagagoitia M, Unanue-Arza S, Díaz-Seoane M, Martínez-Indart L, Lebeña-Maluf A, Idigoras I, *et al*. Factors Related to Non-participation in the Basque Country Colorectal Cancer Screening Programme. Front Public Health 2020;8:604385. doi:10.3389/fpubh.2020.604385, PMID:33363095.

[16] Mosquera I, Mendizabal N, Martín U, Bacigalupe A, Aldasoro E, Portillo I, *et al*. Inequalities in participation in colorectal cancer

screening programmes: a systematic review. Eur J Public Health 2020;30(3):416–425. doi:10.1093/eurpub/ckz236, PMID:32361732.
[17] Molina-Barceló A, Salas JM, Peiró-Pérez R, Arroyo G, Cabanell JI, Espí MV, *et al*. Inequalities in access to cancer screening programs in Spain and how to reduce them: data from 2013 and 2020. Rev Esp Salud Pública 2021;95:e202101017.
[18] Unanue-Arza S, Solís-Ibinagagoitia M, Díaz-Seoane M, Mosquera-Metcalfe I, Idigoras I, Bilbao I, *et al*. Inequalities and risk factors related to non-participation in colorectal cancer screening programmes: a systematic review. Eur J Public Health 2021;31(2):346–355. doi:10.1093/eurpub/ckaa203, PMID:33313657.
[19] Toes-Zoutendijk E, Portillo I, Hoeck S, de Brabander I, Perrin P, Dubois C, *et al*. Participation in faecal immunochemical testing-based colorectal cancer screening programmes in the northwest of Europe. J Med Screen 2020;27(2):68–76. doi:10.1177/0969141319879712, PMID:31645173.