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Colorectal Cancer Screening Program Results in Iran

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Abstract

Background: Colorectal cancer (CRC) accounts for a large proportion of the global burden of cancer and is the fourth leading cause of cancer-related mortality worldwide. Fecal Immunochemical Testing (FIT) can be used for CRC screening programs due to its high accuracy and compliance. The present study reports the preliminary results of the CRC screening program in Iran among all people aged 50 to 69 years.

Methods: This cross-sectional study was carried out on 2,669,625 participants referred to health centers in Iran for CRC screening programs in 2018 and 2019. The data required for this study was taken from the CRC screening program. Relevant information for all individuals aged 50 to 69 referred to the health system that was called for colorectal cancer screening was extracted from the Integrated Electronic Health Records (SIB) database. Finally, the standards indices were calculated for all provinces. Gender, history of inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), history of colon cancer or adenoma in a first-degree family (father, mother, siblings or children), history of colon cancer in a second-degree family if occurred under the age of fifty (aunt, uncle, grandparents), lower gastrointestinal bleeding in a prior month, constipation in the prior month (with or without diarrhea, abdominal pain and feeling of fullness in the colon after defecation), more than ten percent weight loss in the last six months and FIT were assessed.

Results: Among a total number of over 2.6 million, 56.3% were female, and the number of people evaluated by health care providers for CRC screening programs in 2018 and 2019 were 1,365,248 (14.23%) and 1,304,377 (12.89%), respectively. The number of people with positive FIT evaluated for the CRC screening program in 2018 and 2019 was 33,299 (3.09%) and 33,583 (2.57%), respectively. Bushehr province (0.59%) and Isfahan province (7.35%) had the lowest and highest positive FIT rate in 2018, respectively. Also, the correlation between the above-mentioned variables and the number of people with a positive FIT across gender was statistically significant (p<0.05). The study of the relationship between the number of positive FIT cases and the variables examined by Behvarz and community health worker showed that the number of people with a family history of colon cancer in second-degree relatives under the age of 50 and also the number of people with an individual history of inflammatory bowel disease had a significant association with the number of positive FIT cases (p<0.05) (β=-0.718, 95% CI; -2.557-14.992, β=0.388, 95% CI; 0.322-16.737, respectively). The relationship between the number of positive FIT cases and effective variables was not statistically significant (p>0.05).

Conclusion: Positive cases should be referred for further evaluation and colonoscopy. Before performing a screening program, the conditions for performing colonoscopy for these people must be assessed and prepared. The FIT for CRC screening program can be easily promoted in Iran.

Keywords: Colorectal Cancer, Health System, Screening, FIT

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↑What is "already known" in this topic:
The present study reported the preliminary results of the colorectal cancer screening program of the Ministry of Health of Iran among all people aged 50 to 69 years in 2018 and 2019 to evaluate the CRC screening program and find out the potential risk factors for developing CRC.

→What this article adds:
Before performing a screening program, the conditions for performing colonoscopy for these people must be assessed and prepared. The FIT for CRC screening program can be easily promoted in Iran.

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Introduction

Colon cancer is the third leading cause of cancer deaths in men and women (1). According to statistics, 52,980 people will be dying due to colon cancer in the United States by 2021 (1). Colon cancer is most comm only diagnosed in people aged 65 to 74 years (2). It is estimated that 10.5% of new cases of colon cancer occur in people less than 50 years of age (3). The prevalence of colorectal cancer (especially adenocarcinoma) in adults aged 40 to 49 years increased by almost 15% from 2000-2002 to 2014-2016 (4). In 2016, 25.6% of eligible adults in the United States had never been screened for colon cancer, and in 2018, 31.2% were not up to date with screening (5-7).

In 2016, 25.6% of eligible adults in the US had never been screened for colorectal cancer and in 2018, 31.2% were not up to date with screening (7). It is also estimated that the incidence and mortality rate of colorectal cancer will increase by 77% and 80% until 2030, respectively (8). CRC is more common in developed countries than in the rest of the world (9). For example, CRC is the second most commonly diagnosed malignancy that results in death from cancer in the United States (10), and it is the second leading cause of cancer death in men and the third leading cause of cancer in women (11). It is also the second leading cause of mortality in Canada (12). The incidence of CRC in developing countries is also steadily increasing (13). CRC is also the third leading cause of death in Iran (14), and the incidence of CRC in Iran has been growing over the past 25 years and has been rising in developed countries affecting the younger population (15). Survival rates have been reported up to 5 years after diagnosis. There are six risk factors for colorectal cancer including those older than 50 years of age, familial history, diet, obesity, inactivity, and cigarette smoking. However, the main cause of it is not known accurately (13).

Secondary prevention is related to the stage before the onset of clinical symptoms and refers to the timely discovery and early treatment and other screening (16, 17). It should be noted that colorectal cancer is a good disease for screening due to an important health problem and it is possible to diagnose the disease early in the treatment process (18). Regular screening is one of the best and most valuable early detection methods for the disease (16, 19). There are several options for CRC screening programs, but FOBT or fecal occult blood test and colonoscopy are the most commonly used tests for colorectal cancer screening. It should be noted that Fecal Immunochemical Testing (FIT) is a viable version of FOBT (20).

Most cases of CRC can be prevented through the detection and removal of familial adenomatous polyps. It is better to survive the patients with colorectal cancer who are identified as early stages of the disease (21). Clinical trials and systematic reviews have shown that the 2-year screening program reduces dying from colorectal cancer by up to 16% through occult blood tests in the stool and follow-up of people with colonoscopy (21, 22). Recently it has been suggested that FIT can be used for population-based screening due to its high degree of accuracy and compliance (12, 20, 23). Based on health guidelines, the FIT screening test is provided free of charge for the entire population aged 50 to 75 years in health centers. The CRC screening program in Iran started in 2016 as a pilot in 4 cities (Naqadeh, Maragheh, Shahreza, and Baft). This program aimed to identify and register participants suspected of or suffering from colon disease and then provide appropriate services at different levels of the health care network and organize treatment and care of the participants. The present study reported the preliminary results of the colorectal cancer screening program of the Ministry of Health of Iran among all people aged 50 to 69 years in 2018 and 2019 to evaluate the CRC screening program and find out potential risk factors for developing CRC.

Methods

This cross-sectional study was performed on participants referred to health centers covered by the Ministry of

Table 1. Indices and how to calculate indices

Calculation	Index
Number of screened people /target population	Percentage of evaluated people
Number of people tested with FIT / Number of people screened	Number of people tested with FIT
Number of people with positive FIT/Number of people tested with FIT	Percentage of people with a positive FIT
Number of people with a family history of CRC in a second-degree relative under the age of 50/number of people screened	Percentage of people with a family history of CRC in second-degree relative under the age of 50
Number of people with a family history of CRC or adenoma in first-degree relative/number of people screened	Percentage of people with a family history of CRC or adenoma in the first-degree relative
Number of people with an individual history of colon adenoma/ Number of screened people	Percentage of people with an individual history of colon adenoma
Number of people with an individual history of inflammatory bowel disease/ Number of screened people	Percentage of people with an individual history of inflammatory bowel disease
Number of people with symptoms of lower gastrointestinal bleeding in the last month/ Number of screened people	Percentage of people with an individual history of lower gastrointestinal bleeding
Number of people with symptoms of weight loss>10 % in the last six months/ Number of screened people	Percentage of people with weight loss>10%
Number of people with constipation in the last month/ Number of screened people	Percentage of people with constipation
Number of referred people with positive FIT/ Number of people with positive FIT	Percentage of people with positive FIT test referred to health centers

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Health of Iran for colorectal cancer (CRC) screening programs in 2018 and 2019. The data for all individuals aged 50 to 69 years referred to the health system that was called for colorectal cancer was extracted from the Integrated Electronic Health Records (SIB) database. To avoid missing data and duplicate cases, double-check was applied. Gender, history of inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), history of colon cancer or adenoma in a first-degree family (father, mother, brother, sister or children), history of colon cancer in a second-degree family who occurred under the age of fifty (aunt, uncle, grandparents), lower gastrointestinal bleeding in a recent month, constipation in a recent month (with or without diarrhea in a recent month, abdominal pain and feeling of fullness in the colon after defecation), more than ten percent weight loss in the last six months and FIT were assessed by Behvarz and community health worker.

Inclusion criteria were people between the ages of 50 and 69 years who have been called in for a colorectal cancer screening program and also people referred due to digestive problems in any age (age< 50 or > 69 years). If the participant was positive for any of the symptoms, his/her file was checked, and the positive FIT was considered a positive case in screening.

The participant aged 50-69 years is registered in the initial evaluation form by Behvarz and a community health worker and if the participant is under 50 or over 69 years old or at any age but in the intervals between routine examinations referred due to gastrointestinal problems, his/her details are also recorded and checked according to the instructions. Variables in the initial assessment form were gender, history of inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), history of CRC or adenoma in a first-degree relative (father, mother, brother, sister or children), history of CRC in the second-degree relative that has occurred under the age of fifty (aunt, uncle, grandmother and grandfather), gastrointestinal bleeding in a recent month, constipation in a recent month (with or without diarrhea over the past month, abdominal pain and a feeling of fullness in the anus after defecation, weight loss>10% in the last six months and FIT. Linear regression was used to predict positive FIT cases for 2-year-merged aggregate data. Indices and how to calculate indices are presented in Table 1. Figure 1 shows the colo-

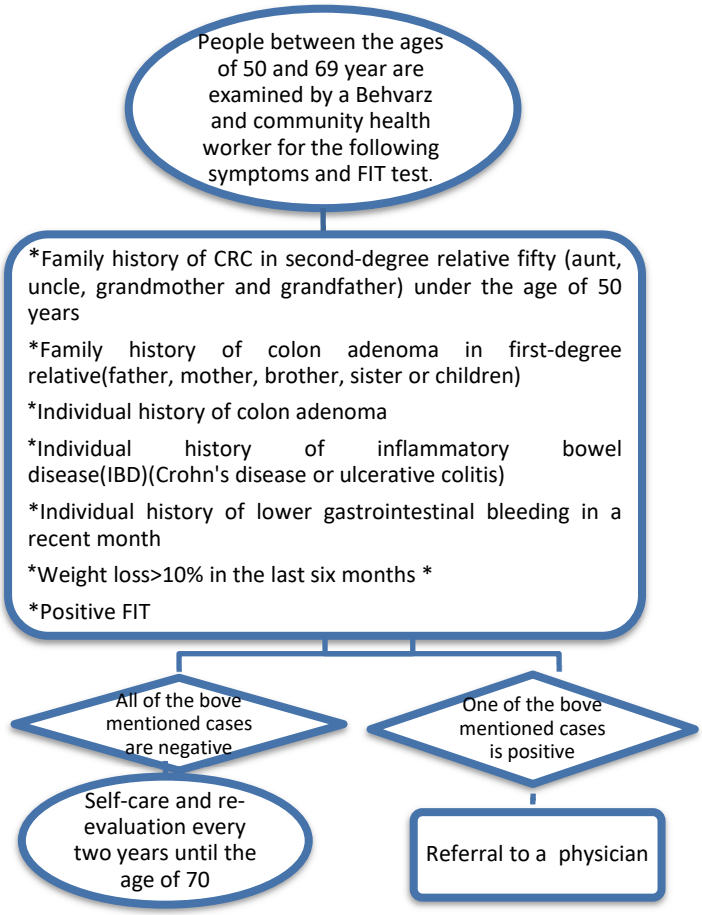

Fig. 1. Colorectal cancer screening flowchart

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rectal cancer screening flowchart.

Ethical consideration

This study was approved by the ethics committee of the Iran University of Medical Sciences. After obtaining the necessary permissions and the code of ethics (IR.IUMS.REC.1398.689), the researcher began to get the aggregate data from the authorities. Due to the nature of the obtained data (aggregated data), the identities of the participants are unknown and anonymous.

Statistical analysis

The data were entered into SPSS software and presented as frequency and percentage. Also, Spearman correlation test was performed between continuous variables evaluated, and the number of people with positive FIT and the correlation of the variables evaluated was calculated with the number of people with a positive FIT. To predict the outcomes of interest, a linear regression model was used. A P value less than 0.05 was considered significant.

Results

This study was performed on 2,669,625 people who were referred to health centers covered by the Ministry of Health of Iran, in which 56.33% of the participants (n=1,566,442) were female and 43.67% of the participants (n=1,214,599) were male. The number of people evaluated by Behvarz and community health workers for the CRC program in 2018 and 2019 were 1,365,248 (14.23%) and 1,304,377 (12.89%), respectively.

The lowest rate of evaluated people in 2018 was related to Qom province (2.35%), and the highest screening coverage was related to Fars province (24.19%). The lowest rate of evaluated people in 2019 was related to Qom province (1.34%) and the highest coverage was related to Fars province (27.83%). The evaluated indices in 2018 and 2019 at the country level across gender were reported in Table 2.

The lowest rate of people with a family history of CRC in the second-degree relative under the age of 50 in 2019 was related to Sistan and Baluchestan provinces (0.06%) and the highest rate was related to Yazd province (0.74%). Also, the lowest rate in 2019 was related to the Bushehr province (0.03%) and the highest rate was related to Yazd province (0.67%). The lowest rate of people with a family history of CRC or adenoma in the first-degree relative in 2018 was related to Sistan and Baluchestan provinces (0.19%) and the highest rate was related to Yazd province (1.89%). The lowest rate in 2019 was related to Sistan and Baluchestan provinces (0.14%) and the highest rate was related to Yazd province (1.84%).

According to the results, the lowest number of people with a family history of CRC or adenoma in 2018 belonged to Sistan and Baluchestan (0.02%), Hormozgan (0.02%), and Hamedan (0.02%) provinces, and the highest rate belonged to Yazd province (0.16%). The lowest rate in 2019 was related to Khuzestan (0.02%) and Semnan (0.02%) provinces and the highest rate was related to Qom province (0.13%). The lowest rate of individuals with a history of inflammatory bowel disease in 2018 was related to Sistan and Baluchestan provinces (0.03%) and the highest rate was related to Qazvin (0.27%) and Isfahan (0.27%) provinces. The lowest rate in 2019 was related to Sistan and Baluchestan provinces (0.05%) and the highest rate was related to Qazvin province (0.44%). The lowest rate of people with lower gastrointestinal bleeding in the last month of 2018 was related to Bushehr province (0.12%) and the highest rate was related to Isfahan province (0.92%). The lowest rate in 2019 was related to Bushehr province (0.06%) and the highest rate was related to

Table 2. Indices evaluated in 2018 and 2019 at the country level across gender

Index	2018			2019		
	Total (%)	Female (%)	Male (%)	Total (%)	Female (%)	Male (%)
Percentage of people evaluated	1,304,377 (12.89)	719,244 (14.08)	585,133 (11.66)	1,365,248 (14.23)	783,935 (16.12)	581,313 (12.28)
Number of people tested with FIT	1,304,351 (99.99)	719,230 (99.99)	585,121 (99.99)	1,078,967 (79.03)	618,194 (78.85)	460,773 (79.26)
Percentage of people with a family history of CRC in second-degree relative under the age of 50	3,024 (0.23)	2,003 (0.27)	1,021 (0.17)	3,675 (0.27)	2,501 (0.43)	1147 (0.20)
Percentage of people with a family history of CRC or adenoma in the first-degree relative	8,777 (0.67)	3,318 (0.46)	5,459 (0.93)	10,632 (0.78)	6,842 (0.87)	3,790 (0.65)
Percentage of people with history of colon adenoma	704 (0.05)	359 (0.05)	345 (0.06)	661 (0.05)	370 (0.04)	291 (0.05)
Percentage of people with history of inflammatory bowel disease	1,917 (0.15)	1,028 (0.14)	899 (0.15)	1,991 (0.15)	1,146 (0.15)	845 (0.14)
Percentage of people with a history of lower gastrointestinal bleeding	4,330 (0.33)	2,651 (0.36)	1,679 (0.28)	5,172 (0.38)	3,262 (0.41)	1,910 (0.32)
Percentage of people with weight loss>10%	1,871 (0.14)	871 (0.12)	1,000 (0.17)	2,226 (0.16)	1117 (0.14)	1,109 (0.19)
Percentage of people with constipation	19,593 (1.50)	13,026 (1.81)	6567 (1.12)	24,145 (1.77)	16,705 (1.13)	7,440 (1.28)
Percentage of people with positive FIT test referred to health centers	27,731 (82.57)	15,761 (83.47)	11,970 (81.41)	30,335 (91.10)	18,189 (91.24)	12,149 (90.90)

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Isfahan province (0.93%). The lowest rate of people with lower gastrointestinal bleeding in the last month of 2018 was in Kohgiluyeh and Boyer-Ahmad provinces (0.08%) and the highest rate was related to Yazd province (0.34%). The lowest rate in 2019 was related to Ardabil province (0.06). %) and the highest rate was related to Qom province (0.49%).

The lowest rate of people with constipation in the last month of 2018 was related to Sistan and Baluchestan provinces (0.61%) and the highest rate was related to Yazd province (4.49%). The lowest rate of people with constipation in 2019 was related to Sistan and Baluchestan provinces (0.4%) and the highest rate was related to Qom province (5.05%). The lowest rate of people with positive FIT referred to health centers in 2018 was related to Sistan and Baluchestan provinces (61.4%) and the highest rate was related to Qom province (95.45%). The lowest rate in 2019 was related to Bushehr province (22.22%) and the highest rate was related to Qom province (97.95%). Relevant tables for the above-mentioned statistics are presented in Appendix.

The number of people with positive FIT evaluated for CRC screening programs in 2018 and 2019 by provinces were 33,299 (3.09%), 33,583 (2.57%), and 1,290 (1.16%), respectively. The lowest positive FIT rate in 2018 was related to Bushehr province (0.59%) and the highest positive FIT rate was related to Isfahan province (7.35%). The lowest positive FIT rate in 2019 was related to Bushehr province (0.52%) and the highest rate was related to Qazvin province (9.67%). Table 3 shows the number of people with positive FIT evaluated for the CRC screening program in 2018 and 2019 by provinces by province and gender.

The lowest rate of people with a family history of CRC in the second-degree relative under the age of 50 in 2019 was related to Sistan and Baluchestan provinces (0.06%) and the highest rate was related to Yazd province (0.74%). Also, the lowest rate in 2019 was related to the Bushehr province (0.03%) and the highest rate was related to Yazd province (0.67%), the lowest rate was related to Bushehr (0.00%), Ardabil (0.00%), Khuzestan (0.00%), Zanjan (0.00%), Qom (0.00%) and Hormozgan (0.00%) provinces and the highest rate was related to Qazvin province (2.86%). Table 3 shows the percentage of people with a family history of CRC in second-degree relatives under the age of 50 years evaluated in 2018 and 2019 by provinces.

The correlation between the variables examined by Behvarz and the number of people with positive FIT across gender was examined. The results showed that all evaluated variables were directly correlated with the number of people with the positive FIT across gender (p<0.05) (Table 4).

The study of the relationship between the number of positive FIT cases and the variables examined by Behvarz and community health worker showed that the number of people with a family history of colon cancer in second-degree relatives under the age of 50 and also the number of people with an individual history of inflammatory bowel disease had a significant correlation with the number of positive FIT cases (p<0.05) (β=-0.718, 95% CI; -2.557-14.992, β=0.388, 95% CI; 0.322-16.737, respectively).

Table 3. Number and percentage of people with positive FIT evaluated for CRC screening program in 2018 and 2019 by provinces and gender

Province	2018			2019		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
East Azerbaijan	756(2.56)	1274(3.14)	2030(2.90)	321(1.16)	404(1.23)	725(1.19)
West Azerbaijan	363(2.27)	518(2.49)	881(2.39)	404(2.26)	493(2.22)	897(2.24)
Ardabil	250(2.19)	469(3.04)	719(2.68)	150(1.61)	238(1.91)	388(1.78)
Alborz	364(3.96)	753(4.92)	1117(4.56)	593(4.22)	898(4.34)	1491(4.29)
Isfahan	4473(7.41)	5783(7.31)	10256(7.35)	4183(6.90)	4795(6.45)	8978(6.65)
Ilam	61(1.30)	86(1.47)	147(1.40)	82(1.14)	105(1.33)	187(1.24)
Bushehr	7(0.37)	16(0.79)	23(0.59)	8(0.49)	10(0.54)	18(0.52)
Tehran	1359(4.69)	2623(5.16)	3982(4.99)	1438(3.73)	2443(4.31)	3881(4.07)
Chaharmahal and Bakhtiari	84(1.08)	138(1.28)	222(1.20)	235(1.55)	313(1.82)	548(1.70)
South Khorasan	301(3.98)	461(4.06)	762(4.03)	456(4.82)	661(5.14)	1117(5.00)
Razavi Khorasan	482(4.37)	816(5.30)	1298(4.91)	354(3.26)	580(4.01)	934(3.69)
North Khorasan	240(4.42)	372(4.54)	612(4.49)	89(1.83)	115(1.64)	204(1.72)
Khuzestan	242(1.55)	357(1.76)	599(1.67)	185(1.34)	230(1.38)	415(1.36)
Zanjan	176(2.51)	222(2.50)	398(2.51)	192(4.65)	215(4.12)	407(4.36)
Senman	164(6.42)	219(6.72)	383(6.59)	131(4.40)	169(4.90)	300(4.67)
Sistan and Baluchestan	125(1.13)	204(1.41)	329(1.29)	324(1.77)	390(1.78)	714(1.78)
Fars	379(0.65)	482(0.72)	861(0.68)	818(0.79)	850(0.73)	1668(0.76)
Qazvin	57(3.26)	82(3.40)	139(3.34)	115(10.00)	151(9.44)	266(9.67)
Qom	60(5.66)	72(6.30)	132(5.99)	59(4.94)	87(8.33)	146(6.52)
Kurdistan	164(1.15)	228(1.31)	392(1.24)	144(0.87)	190(0.98)	334(0.93)
Kerman	536(1.89)	755(2.03)	1291(1.97)	485(1.37)	560(1.33)	1045(1.35)
Kermanshah	780(3.17)	1156(3.36)	1936(3.28)	1655(4.58)	2069(4.77)	3724(4.68)
Kohgiluyeh and Boyer-Ahmad	70(1.64)	81(1.45)	151(1.53)	78(1.22)	100(1.23)	178(1.23)
Gilan	235(2.09)	349(2.46)	584(2.29)	96(0.70)	107(0.67)	203(0.68)
Lorestan	86(0.74)	118(0.72)	204(0.73)	157(0.77)	188(0.67)	345(0.71)
Mazandaran	547(1.56)	758(1.74)	1305(1.66)	774(1.89)	1030(2.12)	1804(2.01)
Markazi	428(2.60)	656(2.85)	1084(2.74)	428(2.17)	530(2.08)	958(2.12)
Hormozgan	84(1.02)	123(1.16)	207(1.10)	80(0.64)	97(0.65)	177(0.64)
Hamdan	476(3.65)	740(3.66)	1216(3.66)	531(3.25)	750(3.51)	1281(3.39)
Yazd	16(0.77)	23(1.11)	39(0.94)	138(2.85)	112(2.42)	250(2.64)

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Table 4. Correlation of variables evaluated with the number of people with positive FIT across gender

Variable		Number of people with positive FIT evaluated by Behvarz and community health worker	
		Male	Female
Number of people with a family history of colon cancer in second-degree relatives under the age of 50	Pearson correlation	0.708	0.821
	P Value	<0.001	<0.001
Number of people with a family history of colorectal cancer or adenoma in a first-degree relative	Pearson correlation	0.783	0.880
	P Value	<0.001	<0.001
Number of people with an individual history of colon adenoma	Pearson correlation	0.728	0.694
	P Value	<0.001	<0.001
Number of people with an individual history of inflammatory bowel disease	Pearson correlation	0.844	0.905
	P Value	<0.001	<0.001
Number of people with symptoms of lower gastrointestinal bleeding in the last month	Pearson correlation	0.964	0.971
	P Value	<0.001	<0.001
Number of people with symptoms of weight loss>10% in the last six months	Pearson correlation	0.856	0.848
	P Value	<0.001	<0.001
Number of people with constipation in the last month	Pearson correlation	0.974	0.976
	P Value	<0.001	<0.001

Table 5. Linear regression to predict the number of positive FIT cases using the variables examined by Behvarz and community health worker

Variable	Standardized Coefficients	t	95.0% Confidence Interval for B		*P*-Value
	Beta		Lower Bound	Upper Bound	
Number of people with a family history of colon cancer in second-degree relatives under the age of 50	-0.718	-2.927	-14.992	-2.557	0.008
Number of people with a family history of colorectal cancer or adenoma in a first-degree relative	0.408	1.548	-0.623	4.297	0.136
Number of people with an individual history of colon adenoma	-0.243	-1.108	-46.263	14.052	0.280
Number of people with an individual history of inflammatory bowel disease	0.388	2.155	0.322	16.737	0.042
Number of people with symptoms of lower gastrointestinal bleeding in the last month	0.384	1.456	-1.223	6.981	0.160
Number of people with symptoms of weight loss>10% in the last six months	0.171	1.166	-3.433	12.258	0.256
Number of people with constipation in the last month	0.533	1.693	-0.215	2.128	0.104

The relationship between the number of positive FIT cases and other variables was not statistically significant (p>0.05). Table 5 shows the results of linear regression to predict the relationship between the number of positive FIT cases and the variables examined by Behvarz and the community health workers.

Discussion

This study examined the population covered by the colorectal cancer screening program of the Ministry of Health of Iran, and the initial assessment included the variables examined by Behvarz and community health workers. The results of the present study showed that the percentage of people participating in the screening program at the beginning of the colorectal cancer screening program of the Ministry of Health of Iran in 2018 and 2019 were 14.23%, 12.89% and 1.08%, respectively. In a report by Klabunde et al., 15 screening programs in 12 countries revealed that the coverage rate of the screening program ranged from 30% to 100%, and that of individuals participating in the screening program ranged from 7% to 67.7% (24). Monteiro et al. reported 29% of the participants in the screening program, which was higher than the present study (25). Besides, selection bias can be arisen due to a lack of invitation. A direct invitation strategy can be considered as one of the most effective methods. All European countries eventually adopted such an intervention, which also simplifies data concentration and timely use of limited resources (25).

The fact that adherence in the primary phase was only about 13% should not discourage the health care system. Adherence to any screening intervention grows in the medium to long term, which requires public loyalty and trust in the screening program. Other innovative methods to promote adherence to colonoscopy screening should be considered in the future, as full coverage of the program is achieved and the reasons for non-participation can be explored.

This study is the first report for the FIT for CRC screening program in Iran. In some middle-income countries, the growing availability of screening tests, as well as increased access to assessment and diagnostic treatment, provide an opportunity to reduce the burden of CRC (26). This initial experience showed that FIT for screening might be an appropriate screening strategy in Iran. However, the effectiveness of this strategy requires the continuation of the screening program in the covered population. Also, to ensure widespread acceptance of screening by the general public, other strategies are needed to attract participants in order to reach the minimum adherence rate recommended by EU experts of 45% (27).

The results of this study showed that the percentage of people with positive FIT evaluated by Behvarz and community health workers in 2018, 2019 and the first quarter of 020 were 3.09%, 2.57% and 1.6%, respectively. In a study performed in New Zealand (7.1%), the United

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States (5.9%), Uruguay (11.1%), Brazil (9.7%) and Thailand (8.7%), the statistics for positive FIT were close (26, 28-31).

The United States and European CRC screening program recommendations are useful guidelines for middle-income countries such as Iran, where CRC mortality is increasing along with disease diagnosis and treatment capacity. However, defining effective CRC screening program policies in Iran requires strong and well-designed local strategies that are tailored to national priorities and resources. Iran, like other middle-income countries, should invest in clinical and epidemiological research studies to better understand the feasibility of the CRC screening programs by evaluating FIT performance, appropriate incision, and patient admission. In addition, local information should be generated to define the most appropriate screening population and geographic locations for the screening program according to CRC risk and health care capacity (26).

One of the risk factors that should be considered for the CRC screening program is family history. Although advances have been made in the hereditary predisposition to colorectal cancer (32), the nature of hereditary predisposition and the specific gene or genes responsible for hereditary predisposition to cancer are not fully understood. In the present study, about one percent of screened participants had a family history of colorectal cancer. De Rosa et al. reported that up to 30% of CRC patients have a family history of neoplasms and those with first-degree relatives are 2 to 4 times more likely to be at risk. The increased risk also extends beyond first-degree relatives (33). People with a family history of colorectal cancer are relatively common and may experience complications and mortality from colorectal cancer at a younger age than people without a family history. Families should be familiar with factors facilitating their patients' survival (34-36).

Nevertheless, this population with a family history may be more likely than the general population to make lifestyle changes to prevent cancer. A history of colorectal cancer in a first-degree relative (for example, parents or siblings) doubles the risk of developing colorectal cancer in a lifetime (37). Familial adenomatous polyps (FAP) and Gardner syndrome (GS) are rare inherited syndromes characterized by hundreds to thousands of colon adenomatous polyps. Colon cancer occurs at an early age in both diseases unless the colon is removed. Peutz-Jeghers syndrome (PJS) and familial polyposis of adolescents are definite factors for colorectal cancer (38). Inflammatory bowel disease (IBD) is widely accepted as an important risk factor for colorectal cancer. The modeling results in this study showed that IBD is associated with the number of positive FIT cases. IBD is the third disease with the highest risk for CRC, after FAP) and hereditary nonpolyposis colorectal cancer syndrome (HNPCC) (39). In a study by Tashiro et al., constipation was reported in 10.3% of men and 27.7% of women (40). In this study, constipation was reported in about one and a half percent of people screened. Several proposed mechanisms explain the association between CRC and constipation. One of them is the presence of fermented bile acids and ammonium acetate in feces. They are carcinogenic, especially when they have a longer contact time with the intestinal mucosa (41). In a study by Low et al., 0.4% weight loss was reported, which was less in the present study (42). Significant unwanted weight loss may be the first sign of gastrointestinal cancer and we have shown that not only in advanced stages, but it is also a strong prognosis for a weaker prognosis. It seems that prognostic weight loss may act as an indicator of disease severity (43).

Study Limitations

In the present study, the cross-sectional nature of the design was a potential limitation. The lack of complete data from all universities was another limitation. However, this was what it was. We used all available data for analysis and reporting colorectal cancer status in Iran. We did not examine the final status of participants after being positive for screening. Therefore, an exact conclusion cannot be obtained on the success rate of the screening program.

Conclusion

Finally, FIT for CRC screening program is possible in middle-income countries. However, there is a need to further evaluate the performance of the experiment in this environment, as well as individual factors and the health system in Iran, which can affect the success of completing CRC screening. It is also necessary to use other strategies to attract participants in order to achieve a minimum adherence rate recommended by EU experts of 45%.

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Conflict of Interests

The authors declare that they have no competing interests.

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Appendix

Table 1. Number and percentage of people evaluated by Behvarz for CRC screening program in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	79009(13.06)	60704(9.53)
West Azerbaijan	47737(10.68)	40040(8.47)
Ardabil	29111(15.30)	21755(10.82)
Alborz	33203(9.40)	34743(9.29)
Isfahan	148019(19.04)	134998(16.51)
Ilam	13983(18.42)	15101(18.66)
Bushehr	5714(4.40)	3491(2.54)
Tehran	98060(7.95)	95299(7.25)
Chaharmahal and Bakhtiari	22737(17.46)	32280(23.54)
South Khorasan	20561(19.49)	22340(20.20)
Razavi Khorasan	35439(14.97)	25325(10.15)
North Khorasan	17609(14.38)	11871(9.22)
Khuzestan	52825(9.90)	30508(5.38)
Zanjan	19517(13.02)	9344(5.94)
Senman	7165(10.46)	6429(8.91)
Sistan and Baluchestan	32419(14.13)	40166(16.49)
Fars	181830(24.19)	220080(27.83)
Qazvin	6340(3.72)	2750(1.52)
Qom	3700(2.35)	2238(1.34)
Kurdistan	46676(20.93)	35898(15.26)
Kerman	78023(21.36)	77416(20.11)
Kermanshah	63422(20.62)	79539(24.65)
Kohgiluyeh and Boyer-Ahmad	15350(19.41)	14503(17.16)
Gilan	37489(8.14)	29671(6.16)
Lorestan	41549(17.10)	48361(18.82)
Mazandaran	108059(18.37)	89652(14.63)
Markazi	44515(17.01)	45198(16.47)
Hormozgan	29546(16.46)	27471(14.48)
Hamdan	37757(14.12)	37741(13.45)
Yazd	7884(5.30)	9465(6.07)

Table 2. Number and percentage of people with a family history of CRC in second-degree elative under the age of 50 years evaluated by Behvarz in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	133(0.17)	110(0.18)
West Azerbaijan	80(0.17)	55(0.14)
Ardabil	68(0.23)	29(0.13)
Alborz	151(0.45)	111(0.32)
Isfahan	689(0.47)	584(0.43)
Ilam	21(0.15)	26(0.17)
Bushehr	5(0.09)	1(0.03)
Tehran	376(0.38)	253(0.27)
Chaharmahal and Bakhtiari	51(0.22)	65(0.20)
South Khorasan	41(0.20)	42(0.19)
Razavi Khorasan	89(0.25)	60(0.24)
North Khorasan	36(0.20)	22(0.19)
Khuzestan	63(0.12)	53(0.17)
Zanjan	31(0.16)	10(0.11)
Senman	33(0.46)	21(0.33)
Sistan and Baluchestan	18(0.06)	29(0.07)
Fars	544(0.30)	534(0.24)
Qazvin	14(0.22)	6(0.22)
Qom	21(0.57)	5(0.22)
Kurdistan	112(0.24)	65(0.18)
Kerman	117(0.15)	92(0.12)
Kermanshah	95(0.15)	132(0.17)
Kohgiluyeh and Boyer-Ahmad	23(0.15)	13(0.09)
Gilan	115(0.31)	81(0.27)
Lorestan	117(0.28)	116(0.24)
Mazandaran	313(0.29)	264(0.29)
Markazi	131(0.29)	88(0.19)
Hormozgan	48(0.16)	32(0.12)
Hamdan	82(0.22)	62(0.16)
Yazd	58(0.74)	63(0.67)

Appendix. Continued

Table 3. Number and percentage of people with a family history of colon adenoma in first-degree relative evaluated by Behvarz in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	522(0.66)	374(0.62)
West Azerbaijan	212(0.44)	180(0.45)
Ardabil	247(0.85)	119(0.55)
Alborz	395(1.19)	344(0.99)
Isfahan	1934(1.31)	1730(1.28)
Ilam	59(0.42)	67(0.44)
Bushehr	25(0.44)	13(0.37)
Tehran	1131(1.15)	788(0.83)
Chaharmahal and Bakhtiari	134(0.59)	166(0.51)
South Khorasan	133(0.65)	165(0.74)
Razavi Khorasan	265(0.75)	193(0.76)
North Khorasan	128(0.73)	84(0.71)
Khuzestan	244(0.46)	82(0.27)
Zanjan	123(0.63)	51(0.55)
Senman	108(1.51)	69(1.07)
Sistan and Baluchestan	60(0.19)	55(0.14)
Fars	1258(0.69)	1227(0.56)
Qazvin	50(0.79)	35(1.27)
Qom	53(1.43)	21(0.94)
Kurdistan	260(0.56)	167(0.47)
Kerman	385(0.49)	263(0.34)
Kermanshah	255(0.40)	423(0.53)
Kohgiluyeh and Boyer-Ahmad	65(0.42)	48(0.33)
Gilan	355(0.95)	234(0.79)
Lorestan	268(0.65)	273(0.56)
Mazandaran	984(0.91)	761(0.85)
Markazi	420(0.94)	330(0.73)
Hormozgan	144(0.49)	87(0.32)
Hamdan	266(0.70)	254(0.67)
Yazd	149(1.89)	174(1.84)

Table 4. Number and percentage of people with an individual history of colon adenoma in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	30(0.04)	30(0.05)
West Azerbaijan	13(0.03)	17(0.04)
Ardabil	14(0.05)	12(0.06)
Alborz	10(0.03)	16(0.05)
Isfahan	109(0.07)	104(0.08)
Ilam	6(0.04)	7(0.05)
Bushehr	2(0.04)	2(0.06)
Tehran	61(0.06)	46(0.05)
Chaharmahal and Bakhtiari	14(0.06)	11(0.03)
South Khorasan	6(0.03)	11(0.05)
Razavi Khorasan	18(0.05)	25(0.10)
North Khorasan	5(0.03)	7(0.06)
Khuzestan	18(0.03)	7(0.02)
Zanjan	6(0.03)	3(0.03)
Senman	5(0.07)	1(0.02)
Sistan and Baluchestan	7(0.02)	17(0.04)
Fars	91(0.05)	118(0.05)
Qazvin	4(0.06)	3(0.11)
Qom	1(0.03)	3(0.13)
Kurdistan	21(0.04)	18(0.05)
Kerman	27(0.03)	26(0.03)
Kermanshah	17(0.03)	33(0.04)
Kohgiluyeh and Boyer-Ahmad	9(0.06)	11(0.08)
Gilan	17(0.05)	22(0.07)
Lorestan	21(0.05)	25(0.05)
Mazandaran	82(0.08)	74(0.08)
Markazi	20(0.04)	22(0.05)
Hormozgan	7(0.02)	8(0.03)
Hamdan	7(0.02)	15(0.04)
Yazd	13(0.16)	10(0.11)

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Appendix. Continued

Table 5. Number and percentage of people with an individual history of inflammatory bowel disease in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	106(0.13)	71(0.12)
West Azerbaijan	40(0.08)	51(0.13)
Ardabil	48(0.16)	21(0.10)
Alborz	68(0.20)	53(0.15)
Isfahan	394(0.27)	393(0.29)
Ilam	16(0.11)	25(0.17)
Bushehr	7(0.12)	4(0.11)
Tehran	189(0.19)	137(0.14)
Chaharmahal and Bakhtiari	23(0.10)	44(0.14)
South Khorasan	23(0.11)	36(0.16)
Razavi Khorasan	48(0.14)	36(0.14)
North Khorasan	17(0.10)	15(0.13)
Khuzestan	41(0.08)	20(0.07)
Zanjan	22()0.11	13()0.14
Senman	15(0.21)	17(0.26)
Sistan and Baluchestan	10(0.03)	20(0.05)
Fars	186(0.10)	224(0.10)
Qazvin	17(0.27)	12(0.44)
Qom	2(0.05)	3(0.13)
Kurdistan	55(0.12)	49(0.14)
Kerman	66(0.08)	66(0.09)
Kermanshah	94(0.15)	163(0.20)
Kohgiluyeh and Boyer-Ahmad	16(0.10)	18(0.12)
Gilan	65(0.17)	53(0.18)
Lorestan	60()0.14	61(0.13)
Mazandaran	230(0.21)	188(0.21)
Markazi	54(0.12)	48(0.11)
Hormozgan	23(0.08)	20()0.07
Hamdan	38(0.10)	31(0.08)
Yazd	18(0.23)	25(0.26)

Table 6. Number and percentage of people with an individual history of lower gastrointestinal bleeding in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	329(0.42)	128(0.21)
West Azerbaijan	102(0.21)	88(0.22)
Ardabil	128(0.44)	49(0.23)
Alborz	188(0.57)	162(0.47)
Isfahan	1356(0.92)	1258(0.93)
Ilam	42(0.30)	30(0.20)
Bushehr	7(0.12)	2(0.06)
Tehran	523(0.53)	402(0.42)
Chaharmahal and Bakhtiari	68(0.30)	81(0.25)
South Khorasan	93(0.45)	137(0.61)
Razavi Khorasan	147(0.41)	104(0.41)
North Khorasan	121(0.69)	34(0.29)
Khuzestan	78(0.15)	39(0.13)
Zanjan	53(0.27)	36(0.39)
Senman	49(0.68)	32(0.50)
Sistan and Baluchestan	50(0.15)	49(0.12)
Fars	377(0.21)	413(0.19)
Qazvin	18(0.28)	20(0.73)
Qom	21(0.57)	7(0.31)
Kurdistan	120(0.26)	92(0.26)
Kerman	214(0.27)	144(0.19)
Kermanshah	179(0.28)	254(0.32)
Kohgiluyeh and Boyer-Ahmad	30(0.20)	21(0.14)
Gilan	93(0.25)	35(0.12)
Lorestan	98(0.24)	97(0.20)
Mazandaran	257(0.24)	214(0.24)
Markazi	178(0.40)	155(0.34)
Hormozgan	48(0.16)	27(0.10)
Hamdan	140(0.37)	136(0.36)
Yazd	65(0.82)	84(0.89)

Appendix. Continued

Table 7. Number and percentage of people with weight loss>10% in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	131(0.17)	59(0.10)
West Azerbaijan	41(0.09)	58(0.14)
Ardabil	28(0.10)	12(0.06)
Alborz	83(0.25)	56(0.16)
Isfahan	376(0.25)	275(0.20)
Ilam	17(0.12)	29(0.19)
Bushehr	10(0.18)	4(0.11)
Tehran	191(0.19)	152(0.16)
Chaharmahal and Bakhtiari	28(0.12)	39(0.12)
South Khorasan	32(0.16)	44(0.20)
Razavi Khorasan	60(0.17)	64(0.25)
North Khorasan	58(0.33)	23(0.19)
Khuzestan	74(0.14)	34(0.11)
Zanjan	33(0.17)	14(0.15)
Senman	12(0.17)	9(0.14)
Sistan and Baluchestan	31(0.10)	43(0.11)
Fars	220(0.12)	253(0.11)
Qazvin	6(0.09)	5(0.18)
Qom	6(0.16)	11(0.49)
Kurdistan	61(0.13)	36(0.10)
Kerman	98(0.13)	75(0.10)
Kermanshah	103(0.16)	116(0.15)
Kohgiluyeh and Boyer-Ahmad	13(0.08)	21(0.14)
Gilan	68(0.18)	48(0.16)
Lorestan	88(0.21)	68(0.14)
Mazandaran	141(0.13)	121(0.13)
Markazi	58(0.13)	57(0.13)
Hormozgan	45(0.15)	32(0.12)
Hamdan	87(0.23)	80(0.21)
Yazd	27(0.34)	33(0.35)

Table 8. Number and percentage of people with constipation in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	1480(1.87)	584(0.96)
West Azerbaijan	568(1.19)	407(1.02)
Ardabil	737(2.53)	310(1.42)
Alborz	1061(3.20)	918(2.64)
Isfahan	5831(3.94)	5024(3.72)
Ilam	180(1.29)	139(0.92)
Bushehr	52(0.91)	15(0.43)
Tehran	2357(2.40)	1865(1.96)
Chaharmahal and Bakhtiari	286(1.26)	312(0.97)
South Khorasan	370(1.80)	540(2.42)
Razavi Khorasan	752(2.12)	496()1.96
North Khorasan	425(2.41)	193(1.63)
Khuzestan	480(0.91)	192(0.63)
Zanjan	378(1.94)	201(2.15)
Senman	237(3.31)	125(1.94)
Sistan and Baluchestan	197(0.61)	159(0.40)
Fars	1657()0.91	1692(0.77)
Qazvin	123(1.94)	138(5.02)
Qom	98(2.65)	113(5.05)
Kurdistan	650(1.39)	465(1.30)
Kerman	977(1.25)	567(0.73)
Kermanshah	1037(1.64)	1779(2.24)
Kohgiluyeh and Boyer-Ahmad	142 (0.93)	111(0.77)
Gilan	359(0.96)	188(0.63)
Lorestan	536(1.29)	467(0.97)
Mazandaran	917(0.85)	800(0.89)
Markazi	742(1.67)	479(1.06)
Hormozgan	433(1.47)	296(1.08)
Hamdan	729(1.93)	621(1.65)
Yazd	354(4.49)	397(4.19)

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Appendix. Continued

Table 9. Number and percentage of people with positive FIT test referred to health centers in 2018 and 2019 by provinces

Province	2018	2019
East Azerbaijan	1886(92.91)	480(66.21)
West Azerbaijan	772(87.63)	706(78.71)
Ardabil	649(90.26)	324(83.51)
Alborz	1059(94.81)	1355(90.88)
Isfahan	9696(94.54)	8234(91.71)
Ilam	120(81.63)	137(73.26)
Bushehr	15(65.22)	4(22.22)
Tehran	3637(91.34)	3435(88.51)
Chaharmahal and Bakhtiari	190(85.59)	407(74.27)
South Khorasan	695(91.21)	1040(93.11)
Razavi Khorasan	1221(94.07)	778(83.30)
North Khorasan	554(90.52)	159(77.94)
Khuzestan	526(87.81)	301(72.53)
Zanjan	352(88.44)	351(86.24)
Senman	342(89.30)	219(73.00)
Sistan and Baluchestan	202(61.40)	188(26.33)
Fars	689(80.02)	962(57.67)
Qazvin	132(94.96)	250(93.98)
Qom	126(95.45)	143(97.95)
Kurdistan	315(80.36)	252(75.45)
Kerman	1196(92.64)	833(79.71)
Kermanshah	1735(89.62)	3266(87.70)
Kohgiluyeh and Boyer-Ahmad	114(75.50)	76(42.70)
Gilan	517(88.53)	79(38.92)
Lorestan	137(67.16)	122(35.36)
Mazandaran	1197(91.72)	1546(85.70)
Markazi	932(85.98)	666(69.52)
Hormozgan	185(89.37)	103(58.19)
Hamdan	1108(91.12)	1108(86.49)
Yazd	36(92.31)	207(82.80)

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