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 (IHR) 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.
Introduction

Colorectal 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 commonly 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 Immunochromatographic 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 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.

Table 1. Indices and how to calculate indices

| Calculation | Index |
|-------------|-------|
| Number of screened people / target population | Number of evaluated people |
| Number of people tested with FIT / Number of people screened | Number of people tested with 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 six months / Number of screened people | Percentage of people with a positive FIT |
| Number of people with weight loss > 10% in the last six months / Number of screened people | Percentage of people with weight loss > 10% |
| Number of referred people with positive FIT / Number of people with positive FIT | Percentage of evaluated people |
| 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 colorectal cancer screening flowchart.
Participations are unknown and anonymous.

**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 referred 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 Hamedan (0.02%) provinces, and the highest rate was related to Yazd province (0.16%). 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%).

**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 (79.03)              | 585,133 (61.66)               | 1,365,248 (14.23)             | 783,935 (79.26)              | 581,313 (60.47)              |
| Number of people tested with FIT                                    | 1,304,351 (99.99)             | 719,230 (99.99)              | 585,121 (99.99)               | 1,078,867 (99.99)             | 618,194 (99.99)              | 460,773 (99.99)              |
| 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 (0.37)                 | 1,477 (0.27)                 |
| 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 (0.73)                  | 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)                  | 1,117 (0.14)                 | 1,099 (0.19)                 |
| Percentage of people with constipation                              | 19,593 (1.50)                 | 13,026 (1.01)                | 6567 (1.12)                   | 24,145 (1.77)                 | 16,705 (1.23)                | 7,440 (0.87)                 |
| 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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The number of people with positive FIT evaluated for CRC screening programs in 2018 and 2019 by provinces and gender.

### Table 3

| Province                      | Male (%) | Female (%) | Total (%) | Male (%) | Female (%) | Total (%) |
|-------------------------------|----------|------------|-----------|----------|------------|-----------|
| 2018                          | 2019     | 2018       | 2019      | 2018     | 2019       | 2019      |
| East Azerbaijan               | 756(2.56)| 1274(3.14)| 2030(3.90)| 321(1.16)| 404(1.23)  | 725(1.19) |
| West Azerbaijan               | 363(2.27)| 518(2.49)| 881(3.29)| 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)| 755(4.92)| 1117(7.56)| 593(4.22)| 890(4.34)  | 1491(4.29)|
| Isfahan                       | 4473(7.41)| 5783(7.31)| 10256(7.35)| 4183(6.90)| 7495(6.65)| 8978(6.65)|
| Ilam                          | 611(1.30)| 866(1.47)| 1477(3.17)| 82(1.14)| 105(1.33)  | 187(1.24) |
| Bushehr                       | 70(0.37)| 160(0.79)| 230(1.09)| 80(0.49)| 105(0.54)  | 185(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(0.88)| 138(1.28)| 222(2.09)| 235(1.55)| 313(1.82)  | 548(1.70) |
| South Khorasan                | 301(3.98)| 461(4.06)| 762(4.03)| 456(4.28)| 661(5.14)  | 1171(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(3.65) |
| Semnan                        | 164(6.42)| 210(6.72)| 374(5.9)| 130(4.0)| 169(4.90)  | 300(4.67) |
| Sistan and Baluchestan        | 125(1.13)| 204(1.41)| 329(1.29)| 342(1.77)| 390(1.78)  | 714(1.78) |
| Fars                          | 379(0.65)| 482(0.72)| 861(0.68)| 818(0.79)| 850(0.75)  | 1668(0.76)|
| Qazvin                        | 573(2.6)| 823(3.40)| 1397(3.4)| 115(1.0)| 150(0.8)  | 266(0.67) |
| Qom                           | 605(6.66)| 726(3.60)| 1321(5.99)| 594(4.94)| 870(3.33)  | 1466(5.52)|
| 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(2.92)| 96(0.70)| 107(0.67)  | 203(0.68)|
| Lorestan                      | 860(7.4)| 119(0.72)| 2007(7.77)| 157(0.77)| 1880(7.67)| 3450(7.71)|
| Mazandaran                    | 547(1.56)| 758(1.74)| 1305(1.66)| 774(1.89)| 1930(2.12)| 3802(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)| 2071(1.10)| 80(0.64)| 97(0.65)  | 177(0.64)|
| Hamadan                       | 476(3.65)| 740(3.66)| 1216(3.66)| 531(3.25)| 750(3.51)  | 1281(3.39)|
| Yazd                          | 160(0.77)| 23(1.11)| 183(0.94)| 138(2.85)| 112(2.42)  | 250(2.64)|

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 Bushhehr 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 and gender.

Table 4.

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).

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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 2020 were 3.09%, 2.57% and 1.6%, respectively. In a study performed in New Zealand (7.1%), the United...
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 polyposis (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 ammobiacetate 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         | 79069  | 46070  |
| West Azerbaijan         | 47717  | 40048  |
| Ardabil                 | 2911   | 21755  |
| Alborz                  | 33320  | 34743  |
| Isfahan                 | 14801  | 134998 |
| Ilam                    | 1399   | 15101  |
| Bushehr                 | 57146  | 3491  |
| Tehran                  | 98060  | 95299  |
| Chaharmahal and Bakhhtiari | 22737  | 23280  |
| South Khorasan          | 20561  | 22240  |
| Razavi Khorasan         | 35439  | 25325  |
| North Khorasan          | 17609  | 11877  |
| Khuzestan               | 52825  | 30506  |
| Zanjan                  | 19517  | 9344   |
| Semnan                  | 7165   | 6429   |
| Sistan and Baluchestan  | 32419  | 40160  |
| Fars                    | 18130  | 22080  |
| Qazvin                  | 6340   | 2750   |
| Qom                     | 37002  | 22381  |
| Kurdistan               | 46765  | 35808  |
| Kerman                  | 78022  | 77416  |
| Kermanshah              | 63422  | 79539  |
| Kohgiluyeh and Boyer-Ahmad | 15350  | 14503  |
| Gilan                   | 37488  | 29671  |
| Lorestan                | 41549  | 48361  |
| Mazandaran              | 108059 | 89652  |
| Markazi                 | 44515  | 45196  |
| Hormozgan               | 29546  | 27471  |
| Hamadan                 | 37757  | 37741  |
| Yazd                    | 78845  | 94656  |

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         | 1356  | 1101  |
| West Azerbaijan         | 8008  | 5550  |
| Ardabil                 | 6802  | 2901  |
| Alborz                  | 15145 | 11132 |
| Isfahan                 | 68904 | 5848  |
| Ilam                    | 21015 | 260   |
| Bushehr                 | 5009  | 103   |
| Tehran                  | 37601 | 2527  |
| Chaharmahal and Bakhhtiari | 5102  | 6520  |
| South Khorasan          | 4120  | 4219  |
| Razavi Khorasan         | 89025 | 600   |
| North Khorasan          | 36020 | 2219  |
| Khuzestan               | 6312  | 517   |
| Zanjan                  | 31016 | 1011  |
| Semnan                  | 33046 | 2103  |
| Sistan and Baluchestan  | 18006 | 2907  |
| Fars                    | 54400 | 534   |
| Qazvin                  | 14022 | 6022  |
| Qom                     | 21057 | 5022  |
| Kerman                  | 11224 | 650   |
| Kermanshah              | 11710 | 920   |
| Kohgiluyeh and Boyer-Ahmad | 2135  | 1309  |
| Gilan                   | 11531 | 812   |
| Lorestan                | 11703 | 11624 |
| Mazandaran              | 31329 | 264   |
| Markazi                 | 13129 | 880   |
| Hormozgan               | 48016 | 320   |
| Hamadan                 | 82022 | 620   |
| Yazd                    | 58074 | 630   |

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         | 5222  | 374   |
| West Azerbaijan         | 2122  | 1800  |
| Ardabil                 | 2470  | 119   |
| Alborz                  | 3951  | 344   |
| Isfahan                 | 1934  | 1730  |
| Ilam                    | 590   | 670   |
| Bushehr                 | 250   | 13    |
| Tehran                  | 1131  | 788   |
| Chaharmahal and Bakhhtiari | 134  | 166   |
| South Khorasan          | 133   | 165   |
| Razavi Khorasan         | 265   | 193   |
| North Khorasan          | 128   | 84    |
| Khuzestan               | 244   | 82    |
| Zanjan                  | 123   | 51    |
| Semnan                  | 108   | 69    |
| Sistan and Baluchestan  | 610   | 56    |
| Fars                    | 1258  | 1227  |
| Qazvin                  | 500   | 351   |
| Qom                     | 531   | 21    |
| Kerman                  | 255   | 423   |
| Kermanshah              | 355   | 234   |
| Kohgiluyeh and Boyer-Ahmad | 650   | 480   |
| Gilan                   | 355   | 234   |
| Lorestan                | 268   | 273   |
| Mazandaran              | 984   | 761   |
| Markazi                 | 428   | 339   |
| Hormozgan               | 144   | 87    |
| Hamadan                 | 266   | 254   |
| Yazd                    | 149   | 179   |

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         | 3004   | 369   |
| West Azerbaijan         | 130   | 17    |
| Ardabil                 | 140   | 12    |
| Alborz                  | 100   | 16    |
| Isfahan                 | 109   | 10    |
| Ilam                    | 60    | 7     |
| Bushehr                 | 20    | 2     |
| Tehran                  | 60    | 46    |
| Chaharmahal and Bakhhtiari | 140   | 11    |
| South Khorasan          | 60    | 11    |
| Razavi Khorasan         | 180   | 25    |
| North Khorasan          | 50    | 70    |
| Khuzestan               | 180   | 7     |
| Zanjan                  | 60    | 30    |
| Semnan                  | 50    | 10    |
| Sistan and Baluchestan  | 70    | 17    |
| Fars                    | 91    | 118   |
| Qazvin                  | 40    | 36    |
| Qom                     | 10    | 10    |
| Kerman                  | 21    | 18    |
| Kermanshah              | 27    | 26    |
| Kohgiluyeh and Boyer-Ahmad | 70    | 11    |
| Gilan                   | 17    | 22    |
| Lorestan                | 21    | 25    |
| Mazandaran              | 82    | 74    |
| Markazi                 | 20    | 22    |
| Hormozgan               | 70    | 80    |
| Hamadan                 | 70    | 15    |
| Yazd                    | 13    | 11    |

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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 | 160(0.11) | 250(0.17) |
| Bushehr | 70(0.12) | 0(0.11) |
| Tehran | 189(0.19) | 137(0.14) |
| Chaharmahal and Bakhtiari | 230(0.10) | 44(0.14) |
| South Khorasan | 230(0.11) | 36(0.16) |
| Razavi Khorasan | 480(0.14) | 36(0.14) |
| North Khorasan | 170(0.15) | 159(0.17) |
| Khuzestan | 41(0.08) | 200(0.07) |
| Zanjan | 220(0.11) | 13(0.14) |
| Semnan | 150(0.21) | 170(0.26) |
| Sistan and Baluchestan | 180(0.03) | 200(0.05) |
| Fars | 186(0.10) | 224(0.10) |
| Qazvin | 170(0.27) | 120(0.44) |
| Qom | 20(0.05) | 3(0.13) |
| Kurdistan | 550(0.12) | 49(0.14) |
| Kerman | 660(0.08) | 560(0.09) |
| Kermanshah | 940(0.15) | 163(0.20) |
| Kohgiluyeh and Boyer-Ahmad | 160(0.10) | 180(0.12) |
| Gilan | 680(0.17) | 53(0.18) |
| Lorestan | 680(0.14) | 61(0.13) |
| Mazandaran | 230(0.21) | 180(0.21) |
| Markazi | 540(0.12) | 42(0.11) |
| Hormozgan | 230(0.08) | 20(0.07) |
| Hamadan | 380(0.10) | 310(0.09) |
| Yazd | 180(0.23) | 250(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) | 1280(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 | 420(0.30) | 30(0.20) |
| Bushehr | 70(0.12) | 2(0.06) |
| Tehran | 523(0.53) | 402(0.42) |
| Chaharmahal and Bakhtiari | 680(0.30) | 810(0.25) |
| South Khorasan | 930(0.45) | 337(0.61) |
| Razavi Khorasan | 1470(0.41) | 1040(0.41) |
| North Khorasan | 121(0.69) | 340(0.29) |
| Khuzestan | 780(0.15) | 39(0.13) |
| Zanjan | 530(0.27) | 360(0.39) |
| Semnan | 490(0.68) | 320(0.50) |
| Sistan and Baluchestan | 500(0.15) | 490(0.12) |
| Fars | 377(0.21) | 413(0.19) |
| Qazvin | 180(0.28) | 200(0.73) |
| Qom | 210(0.57) | 70(0.13) |
| 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 | 300(0.20) | 210(0.14) |
| Gilan | 930(0.25) | 350(0.12) |
| Lorestan | 980(0.24) | 970(0.20) |
| Mazandaran | 257(0.24) | 214(0.24) |
| Markazi | 178(0.40) | 155(0.34) |
| Hormozgan | 480(0.18) | 270(0.10) |
| Hamadan | 140(0.37) | 1360(0.36) |
| Yazd | 650(0.82) | 84(0.89) |
### 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                           | 648(90.26)  | 324(83.51)  |
| Alburz                            | 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                            | 362(91.34)  | 351(86.54)  |
| Senamane                          | 342(89.30)  | 219(73.00)  |
| Sistan and Baluchestan            | 202(61.40)  | 188(26.53)  |
| Fars                              | 689(80.02)  | 962(57.67)  |
| Qazvin                            | 132(94.96)  | 250(93.98)  |
| Qom                               | 126(95.45)  | 143(97.95)  |
| Kurdistan                         | 315(86.36)  | 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                        | 182(89.37)  | 103(55.19)  |
| Hamadan                          | 1108(91.12) | 1108(86.49) |
| Yazd                             | 36(92.31)   | 207(82.80)  |