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Journal

Family Practice, 37(3)

ISSN

0263-2136

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Publication Date

2020-07-23

DOI

10.1093/fampra/cmz078

Peer reviewed

Family Practice, 2020, 321–324
doi:10.1093/fampra/cmz078
Advance Access publication 21 January 2020

Epidemiology

Faecal immunochemical test-based colorectal cancer screening in Mexico: an initial experience

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Abstract

Background: In middle-income countries, the burden of colorectal cancer (CRC) is increasing in parallel with resources for diagnosis and treatment. There is a potential benefit of CRC screening programs in Mexico.
Objective: Since there are no organized screening programs in the country, we explored the willingness of individuals to complete a faecal immunochemical testing (FIT) based CRC screening program and its potential benefit in Mexico.
Methods: We conducted a CRC screening program pilot in Veracruz, Mexico, during 2015–16 using FIT. Individuals with FIT results >100 ng of haemoglobin/ml buffer were referred for diagnostic colonoscopy.
Results: Of 473 FIT kits distributed to adults aged 50–75, 85.8% (406) were completed by participants and analysed in the laboratory. Of these, 5.9% (24/406) of test results showed >100 ng haemoglobin/ml. Twenty-one participants completed colonoscopy. The positive predictive value of FIT >100 ng haemoglobin/ml for premalignant lesions was 33%.
Conclusion: These results provide preliminary evidence of the willingness of individuals to complete FIT-based CRC screening program in Mexico. However, further evaluation of health systems resources will be needed prior to large-scale implementation of CRC screening programs.

Key Words: Biopsy, colonoscopy, colorectal neoplasms, early detection of cancer, Mexico, occult blood.

Background

Mass colorectal cancer (CRC) screening may not be justified in most low-resource settings where capabilities for diagnosis and treatment are limited, a circumstance which confronts many low- and middle-income countries (LMICs) (1). However, in some of these countries, the burden of CRC is increasing in parallel with resources for diagnosis and treatment, and the potential benefit of CRC screening programs has become more apparent. In Mexico, age-standardized CRC incidence is relatively low (11.2 per 100 000) (2). However, the burden of CRC has rapidly increased in the last two decades,

Key Messages

- 85.8% of delivered faecal immunochemical tests (FIT) were available for analysis.
- 5.9% of participants had an abnormal FIT result.
- Positive predictive value of FIT for premalignant lesions was 33%.

particularly in urban regions (3,4). Starting in 2015, major publicly funded insurance plans covering 85% of the population (111 million people) began including full treatment coverage for CRC after diagnosis. However, as of now, there are no organized national or regional CRC screening programs in Mexico. We hereby describe the results of a pilot CRC screening program in Veracruz, Mexico.

Methods

The study was conducted between 15 May 2015 and 15 January 2016. During the initial 3-month period of the study, participants were recruited *via* weekly advertisements in two local newspapers. Volunteers were excluded if they were under the age of 50 or if they had symptoms of bleeding or a personal history of CRC or other diseases conferring an increased risk of CRC. Excluded individuals were asked to return for screening at the appropriate age or to visit their health care provider for further evaluation and treatment as indicated. All eligible volunteers signed an informed consent form prior to research participation. Eligible participants were interviewed to collect information on demographic characteristics, family history of CRC, current tobacco use, current alcohol consumption, chronic analgesic use, hypertension and diabetes. Family history of CRC was defined as history of CRC in first- or second-degree relatives and was registered as a dichotomous variable (yes/no). Current tobacco use and alcohol consumption, as well as chronic analgesic use, were reported as dichotomous variables (yes/no). Additional follow-up questions, such as number of cigarettes per day and standard drinks per week, were recorded. Chronic analgesic use was defined as the use of non-steroidal anti-inflammatory drugs (NSAIDs) for more than 2 months. We also measured body mass index (BMI) in kg/m^2. Participants received a FIT (OC FIT-CHEK®, Polymedco, Cortlandt Manor, NY) with printed instructions for home sample collection. We asked participants to return the completed test within 3 days. No incentives or rewards were given for their participation. All samples were processed by a central laboratory (Endomedica, Mexico City, Mexico) using an automated test method as defined by the manufacturer (Eiken Chemical, Tokyo, Japan). We used a cut-off point of >100 ng of haemoglobin/ml buffer (= 20 μg of haemoglobin/g faeces) as the threshold to define an abnormal FIT result and for referral to colonoscopy (5). Individuals with abnormal FIT results were contacted to schedule a colonoscopy. Colonoscopies were performed by an experienced and certified endoscopist with biopsies performed when indicated (AM-D). Biopsy specimens were reviewed by a gastrointestinal pathologist (PG-P). All participants completing FIT and/or colonoscopy were given their test results and recommendations for follow-up. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). This study was approved by the research, ethics and biosecurity Committees of the Universidad Veracruzana.

Results

Of 502 individuals initially recruited, 29 were excluded from the study: 19 for being younger than age 50 and 10 for previous history of diseases (Fig. 1). Excluded individuals were asked to return at the appropriate age or referred to their health care provider for further evaluation or treatment as indicated. Of the 473 participants who received a FIT kit, 56 (11.8%) did not return it and 11 participants (2.3%) did not sample their stool correctly. No additional kits were available for repeating the test in these individuals. For the remaining 406 participants (85.8%), the mean age (SD) was 61.3 (±7.6) years and the age range was 50–90 years, with 17 participants (4%) over age 75. Close to one-third were men (n = 129) and close to 20% (n = 76) reported a family history of CRC (Table 1). FIT results showed a median concentration of 3 ng haemoglobin/ml (interquartile range, 0–14). The distribution of results is displayed in Figure 2.

We found that 24 participants (5.9%) had abnormal FIT results (>100 ng haemoglobin/ml). An additional nine participants had results between 76 and 100 ng haemoglobin/ml and 13 had results between 51 and 75 ng haemoglobin/ml. Among those with abnormal FIT results (>100 ng haemoglobin/ml), 18 participants had haemoglobin concentrations of >150 ng haemoglobin/ml and 14 had a haemoglobin concentration above 200 ng/ml. Three of the 24 participants with an abnormal FIT declined a follow-up colonoscopy because of fear of the procedure. Among the remaining 21 participants who completed colonoscopy, we found premalignant lesions (tubular and serrated adenomas) in 7 of them, non-malignant lesions (diverticulosis, haemorrhoidal disease, hyperplastic polyps, ulcerative or non-specific colitis and angiodysplasia) in 16 and no lesions in 4. Thus, the positive predictive value of FIT >100 ng haemoglobin/ml for premalignant lesions in this population was 33%. We performed a sensitivity analysis excluding participants with family history of CRC. Among participants without family history of CRC, 22 (6.7%) had abnormal FIT results (>100 ng haemoglobin/ml) and 20 participants completed colonoscopy. In six of them, we found premalignant lesions and the positive predictive value of FIT >100 ng haemoglobin/ml for premalignant lesions in this population was 30%.

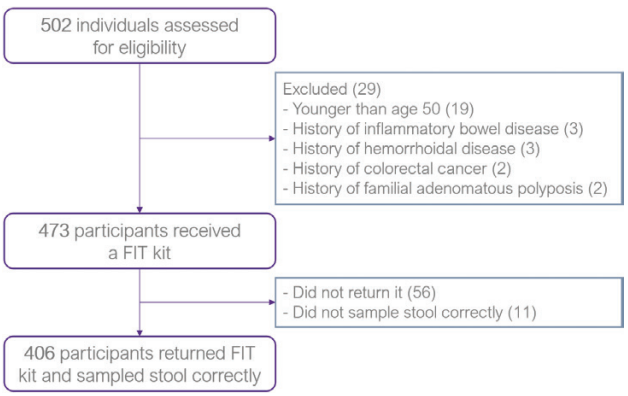

Figure 1. Diagram showing the flow of participants through stages of an initial experience in men and women in Veracruz, Mexico (2015–16).

Conclusions

In this initial experience in Veracruz, we found that FIT-based CRC screening for adults over 50 years using >100 ng of haemoglobin/ml as a cut point for further diagnostic evaluation resulted in a rate of colonoscopy referral and premalignant lesion detection similar to what has been observed in high-income countries (6–8). Our positivity rate was lower than observations in Uruguay (11.1%) (9), Brazil (9.7%) (10) and Thailand (8.7%) (11). According to GLOBOCAN, CRC incidence is almost three times higher in Uruguay (35 per 100 000) relative to Mexico, while incidence in Thailand is estimated to be 15.5 per 100 000 (12). Based on populations from high-income countries (13), using a lower cut-off point for referral may provide a better trade-off between sensitivity and specificity in settings with sufficient resources (5). Lowering the cut-off would result in a higher positivity rate (and higher sensitivity and lower specificity) and a larger number of individuals referred to colonoscopy. In middle-income countries, such as Mexico, where endoscopy capacity is limited, it is unlikely that adopting a lower FIT result threshold for colonoscopy referral would be beneficial. At the positivity rate observed in this study (5.9%), we could expect a sensitivity >65% and a specificity of >95% for CRC with each round of screening (14). The 100 ng/ml threshold has been commonly used in both large screening programs and clinical trials (15,16). The positive predictive value for premalignant lesions in our study was comparable to Uruguay (28.2% for both premalignant and malignant lesions) and high-income countries.

Table 1. Characteristics of 406 men and women that returned their FIT in an initial experience in Veracruz, Mexico (2015–16)

	n = 406
Mean age (±SD), years	61.3 ± 7.6
Male	31.7
Family history of colorectal cancer	18.7
Mean BMI (±SD), kg/m^2	27.6 ± 5.0
Overweight (25.0–29.9)	39.7
Obese (≥30.0)	26.3
Current tobacco smoking	7.1
Current alcohol intake	19.2
Diabetes	18.7
Hypertension	34.9
Chronic analgesic use	19.2

Data are presented as percentages unless otherwise specified.

This study is the first report for FIT-based CRC screening in Mexico but was limited in sample size and our capacity to evaluate FIT performance. In some middle-income countries, the growing availability of screening tests, as well as the increasing access to diagnostic evaluation and treatment, offer an opportunity to lower CRC burden. This initial experience showed that most FIT kits were returned and the vast majority of individuals completed the screening process. Thus, FIT-based screening may be an appropriate screening strategy in Mexico. However, the effectiveness of this strategy would require repeating the test at least every 2 years in participants with normal test results (17,18), and it is unknown how easy it would be to facilitate repeat testing in the cohort that participated in this study. Participants were recruited through newspaper advertisements and most of the respondents were female. Since participants recruited through these strategies can be more health conscious and, therefore, have greater adherence to screening follow-up, it is not clear if participants in this study were representative of the general population. Other strategies of participant recruitment are needed to assure widespread adoption of screening by the general population.

US and European CRC screening recommendations provide useful guidance for middle-income countries like Mexico where CRC mortality is increasing along with capacity to diagnose and treat the disease. However, defining effective CRC screening policies in Mexico will require robust and locally designed strategies that are tailored to national priorities and resources. Mexico, like other middle-income countries, should invest in clinical and epidemiological research studies to better understand the feasibility of CRC screening by evaluating FIT performance, appropriate cut-off and patient acceptability. Additionally, local information should be generated to define the most appropriate screening population and geographic locations for a screening program according to CRC risk and health care capacity.

In 2015, CRC was added to the list of reimbursable conditions for Mexico's Popular Health Insurance (Seguro Popular), which

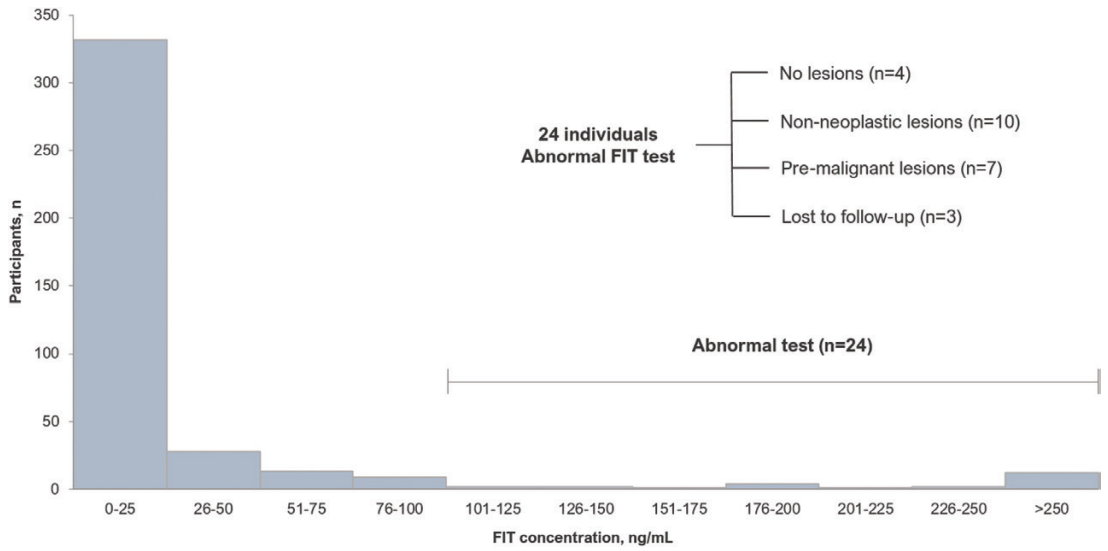

Figure 2. FIT haemoglobin distribution in an initial experience in 406 men and women in Veracruz, Mexico (2015–16).

insures 44% of the population of Mexico (19). Currently, all major publicly funded insurance schemes (covering 85% of the Mexican population) offer full treatment coverage for CRC. Understanding the cost structure of a screening program is necessary to inform decision makers of the long-term benefits of the implementation of an FIT-based program.

In conclusion, FIT-based CRC screening may be feasible in a middle-income country setting. However, there is a need to further evaluate test performance in this setting as well as individual and health system factors in Mexico that could influence the success of CRC screening completion.

Declaration

Funding: This research was partly funded by the National Cancer Institute (grant 1P20CA210286-01 and supported by the UCSF Open Access Publishing Fund.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional national research committee of the Universidad Veracruzana and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Declarations of interest: JMR-T received a donation of OC FIT-CHEK® kits for this project from Endomédica (Mexico City, Mexico). ML previously received a modest research grant from AstraZeneca. GH-G, PE-T, AM-D, PG-P, KVL and MBP have no conflicts of interest to disclose.

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