

The Performance of Colorectal Cancer Screening in Brazil: The First Two Years of the Implementation Program in Barretos Cancer Hospital



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ABSTRACT

Colorectal cancer is the second most common cancer in Brazil. Yet, a nationally organized colorectal screening program is not implemented. Barretos Cancer Hospital (BCH) is one of the largest Brazilian institution that cares for underserved patients. BCH developed a fecal immunochemical test (FIT)-based organized colorectal cancer screening program to improve colorectal cancer outcomes.

This study aims to present the quality/performance measures of the first 2 years of the FIT-based colorectal cancer screening program and its impact on the colorectal cancer disease stage. Between 2015 and 2017, a total of 6,737 individuals attending the Outpatient Department of Prevention or the Mobile Unit of BCH, which visits 18 cities of Barretos county, ages 50 to 65 years, were personally invited by a health agent/nurse practitioner. Exclusion criteria were personal history of colorectal cancer, adenomatous polyps,

inflammatory bowel disease, and colonoscopy, or flexible sigmoidoscopy performed in the past 5 years. European Union (EU) guidelines for colorectal cancer screening programs were evaluated. Overall, 92.8% returned the FIT, with an inadequate examination rate of 1.5%. Among the 6,253 adequately tested, 12.5% had a positive result. The colonoscopy compliance and completion rates were 84.6 and 98.2%, respectively. The PPVs were 60.0%, 16.5%, and 5.6% for adenoma, advanced adenoma, and cancer, respectively. Stage distribution of screen-detected cancers shows earlier stages than clinically diagnosed colorectal cancer cancers reported at BCH and Brazilian cancer registries. Our colorectal cancer screening program achieved desirable quality metrics, aligned with the EU guidelines. The observed shift toward earlier colorectal cancer stages suggests an exciting opportunity to improve colorectal cancer-related cancers in Brazil.

Introduction

Colorectal cancer is a significant health problem. Colorectal cancer ranks the third most common cancer and the second most lethal cancer worldwide, with over 1.8 million new cases

and 881,000 deaths estimated to occur in 2018 (1, 2). According to the incidence estimates of the Brazilian National Cancer Institute, colorectal cancer is the second most common type of cancer among men and women in Brazil in 2020 (3). Although the incidence of colorectal cancer is lower in Brazil than in very high human development index (HDI) countries, such as the United States, Germany, and the Netherlands, colorectal cancer mortality rates are similar (4, 5). This phenomenon reflects a disparity in the mortality-incidence ratio in Brazil, which may partially be attributable to the frequency of late-stage presentation (1, 4, 6).

Incidence rates vary significantly between countries with different HDI levels (1, 7). In the last decade, an increase in both incidence and mortality has been reported in medium and high HDI countries (rapidly transitioning countries), including China and Brazil (8). In contrast, a reduction in both colorectal cancer incidence and mortality has been reported in very high HDI countries such as the United States, Japan, and France (9). Several potential explanations have been proposed for these changes in colorectal cancer incidence. Best practices in colorectal cancer treatment and the impact of colorectal cancer

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Cancer Prev Res 2021;14:241-52

doi: 10.1158/1940-6207.CAPR-20-0179

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screening by fecal tests or colonoscopy followed by colonoscopic polypectomy in those with adenomas have been implicated in the United States (9). In rapidly transitioning countries, such as many in Latin America, rapid changes in risk factors associated with “life-style westernization,” inadequate access to the early detection with delays in diagnosis, and inadequate access to high-quality treatment may explain the increases in colorectal cancer incidence and mortality (9).

A long period of progression from a precursor lesion (adenoma) to cancer, about 7 to 10 years, and the evidence that colonoscopy polypectomy resulted in a lower incidence of colorectal cancer make colorectal cancer very suitable for screening (10). Screening for colorectal cancer can reduce mortality through the detection of cancer in the early stages and can prevent its occurrence via the removal of precursor lesions (11). The consequent reduction in the disparity in the mortality–incidence ratio justifies the development of screening and follow-up policies for colorectal cancer in countries where an increase in incidence and mortality has been observed, including Brazil (8). Further, increasing evidence suggests that colorectal cancer mortality is decreasing in countries following the implementation of organized national colorectal cancer screening programs (1, 9). Therefore, international guidelines have recommended colorectal cancer screening as an evidence-based strategy to reduce cancer-associated mortality for populations in which it is prevalent. As a result, many countries have implemented colorectal cancer screening, using fecal tests or colonoscopy (7).

In Brazil, colorectal cancer is frequently diagnosed in its advanced stages, and according to estimates, the number of deaths due to colorectal cancer will increase by 75% among men and 67.5% among women over the next 20 years (8). Similar trends have been observed at the Barretos Cancer Hospital (BCH; ref. 6). A study that examined data from the BCH registry between 2000 and 2009 reported 23.5% of colorectal cancer patients with metastatic disease at initial presentation over this period (6). Latest update reported 32.6% of stage IV disease in the diagnosis (<https://infogram.com/infograficos-do-cancer-2017-1hkv2nv3qqz6x3>). Despite that, colorectal cancer screening in Brazil is offered only through isolated and sporadic efforts, and there is still no nationally organized colorectal screening program.

To address this situation, an organized pilot colorectal cancer screening program was launched in July 2015 at the BCH, one of the largest Brazilian cancer hospitals, which is located in the city of Barretos, interior of São Paulo state (6, 12). BCH cares for the predominantly underserved healthcare population referred to the Brazilian Health Public System (SUS) and free of cost (13–17). Most of the patients arrived with advanced cancer. Indeed, more than 60% of our colorectal cancer patients presented with stage 3 or 4 disease. Given that outcomes are strongly related to presenting stage of colorectal cancer, we developed a fecal immunochemical test (FIT)-based organized colorectal cancer screening program as one part of our efforts to improve colorectal cancer outcomes.

The qualitative FIT Hemosure was used as the primary test, followed by diagnostic colonoscopy for FIT-positive screens. The implementation of this program and the choice of FIT were based on several factors; for instance, FIT is a noninvasive and low-cost test that is acceptable to the Brazilian general population. However, the implementation of a successful screening program requires careful and continuous attention to quality and monitoring of outcomes to achieve its aims. Here, we present the quality/performance measures of the first 2 years (2015–2017) of the FIT-based colorectal cancer screening program implemented at the BCH and its impact on the colorectal cancer disease stage. We wished to determine whether colorectal cancers detected at the BCH screening program are diagnosed at earlier stages than colorectal cancer reported in the BCH cancer and Brazilian national registries.

Materials and Methods

This study was an exploratory cross-sectional observational study, approved by the BCH Institutional Review Board (no. 1138/2016).

The Barretos Cancer Hospital colorectal cancer screening program settings

The colorectal cancer screening program at BCH was initiated in July 2015. The participants were enrolled in this trial as a convenience sample. The target population in this implementation phase included consecutive individuals ages 50 to 65 years from the general population attending the Outpatient Department of Prevention of the BCH (Fixed Recruitment Unit), located in Barretos, in the southeast region of Brazil, with limited access to medical care from across the country, or the BCH Mobile Unit, which visits 18 cities of the Barretos county. The target population was personally invited and received six interview questions to determine whether they were eligible for the screening program (**Table 1**). The following individuals were considered ineligible if they had: (i) a previous colonoscopy or flexible sigmoidoscopy in the past 5 years; (ii) a personal history of colorectal cancer or adenoma; and (iii) documented inflammatory bowel disease. Symptomatic invitees were recommended not to participate in the colorectal cancer screening but to directly consult their general practitioner.

An eligible individual was personally invited by a health agent or nurse practitioner to participate in the screening program. If they agreed to participate, they signed an informed consent. The nurse practitioner dispensed a program-branded FIT kit and taught each participant how to collect the required fecal samples. The FIT used was Hemosure one-step immunologic fecal occult blood test. Hemosure is a qualitative FIT, which detects human hemoglobin as low as 50 µg Hb/g feces. The cutoff of hemoglobin concentration for a positive test (0.05 µg Hb/mL) is dictated by the manufacturer and the assay is read as positive or negative (18). All participants could collect the fecal sample at home and send it to BCH via the BCH

Table 1. Six interview questions used to determine participant eligibility for the BCH screening program.

Six interview questions used to determine participant eligibility
Are you under 50 years old?
Are you over 65 years old?
Have you had bowel cancer in the past?
Have you had colon polyps in the past?
Have you had a colonoscopy or flexible sigmoidoscopy within past 5 years?
Do you have a bowel inflammatory disease?

specimen laboratory transportation service or by bringing it to the clinic personally. Participants with the negative FIT result are contacted and invited to repeat the screening test (FIT) in 1 year. If the FIT result was positive, the nurse practitioner contacted the participant by phone to schedule a precolonoscopy interview at the endoscopic service of the BCH Prevention Center. If a cancer was diagnosed, the participant was referred to treatment at the BCH. If an adenoma was diagnosed, subsequent surveillance colonoscopy was scheduled based on recommendations of the US Multi-Society Task Force on Colorectal Cancer (19).

Colonoscopy procedure and lesions

The diagnostic colonoscopy procedure was performed by senior endoscopists serving in the endoscopic service of the Prevention Center. This endoscopic service was explicitly built for screening upper and lower gastrointestinal endoscopies and is separated from routine therapeutic endoscopy.

All colonoscopies were performed under carbon dioxide insufflation with a high-definition colonoscope (Olympus GIF 180). In each colonoscopy, a dye spraying of the entire colon with 0.4% indigo carmine solution was used to enhance mucosal detection of flat adenomas and serrated lesions (20). Bowel preparation was graded by an endoscopist according to the Boston bowel preparation scale (BBPS; ref. 21). The definition of complete colonoscopy indicates that the colonoscope has reached the cecum or terminal ileum.

All detected lesions were removed if possible or underwent biopsy. Histologic analysis was performed by experienced pathologists using the latest WHO criteria (22). Criteria of advanced adenoma included an adenoma with any of the following characteristics: (i) at least 10 mm in diameter, (ii) at least 25% of villous architecture, (iii) high-grade dysplasia, or (iv) early invasive cancer. The pathologic stage of each case was classified according to the AJCC (American Joint Committee on Cancer) 7th edition TNM staging system (23).

Data collection and outcomes analysis

Data collected on the study cohort included state of origin, age, gender, participation status rate, FIT test result, colonoscopy findings, and pathology results. These variables were collected prospectively and entered into a Microsoft Office Excel spreadsheet database. The performance indicators were

evaluated following the European quality assurance guidelines on cancer screening (11).

The participation rate reflected the participants who returned FIT and was calculated as the number of persons who have been FIT tested divided by the number of persons invited to participate in the program. Inadequate FIT test rate was defined as the number of people who returned inadequate FIT test divided by the number of persons FIT returned test. The positive FIT test rate was defined as the number of people with a positive FIT test result divided by the persons adequately FIT tested. Follow-up colonoscopy compliance rate was defined as the number of persons who attended a colonoscopy examination following a positive FIT test result.

The completion follow-up colonoscopy rate was defined as the proportion of complete colonoscopy during the study time frame. Follow-up colonoscopy detection rates comprised negative colonoscopy defined as no identified lesions or adenomas or cancer, the presence of any adenoma, any nonadvanced adenoma, any advanced adenoma, and any cancer.

Data regarding the colorectal cancer stage distribution for São Paulo State and Brazil, which are publicly available at Fundação Oncocentro de São Paulo (FOSP; <http://200.144.1.68/cgi-bin/dh?rhc/rhc-geral.def>) and Brazilian National Cancer Institute (INCA; https://irhc.inca.gov.br/RHCNet/selecionaTabulador.action?initial=1&local=todosho_sp&unidFed=) were collected by incidence date (2015 and 2017) and age (50–65 years; refs. 24, 25).

Statistical analysis

Statistical analyses were performed in the SPSS program for Windows, using version 21.0, from data collected in a Microsoft Office Excel spreadsheet during the study period. The sociodemographic characteristics of the study cohort were described according to the mean, standard deviation, minimum, maximum, and quartiles for the quantitative variables and frequency tables for the qualitative variables. If more than one lesion was present, the patient was classified by the most advanced lesion, in the descending order of severity: adenocarcinoma, advanced adenoma, nonadvanced adenoma, and serrated sessile lesion. In all statistical analyses, patients with diverticula, hemorrhoids, or hyperplastic polyps were classified as having normal (nonneoplastic) findings. Estimates of the indicators of interest were calculated, by gender, as pooled proportions with 95% CIs. Associations between variables were assessed by the chi-square test or the Fisher exact test, and *P* value < 0.05 was considered as statistically significant.

Results

Participation and positivity rates

Between July 2015 and July 2017, a total of 6,737 persons meeting the eligibility criteria agreed to participate in the BCH colorectal screening program and signed the consent inform. Out of these, 4,956 (73.6%) were women and 1,781 (26.4%)

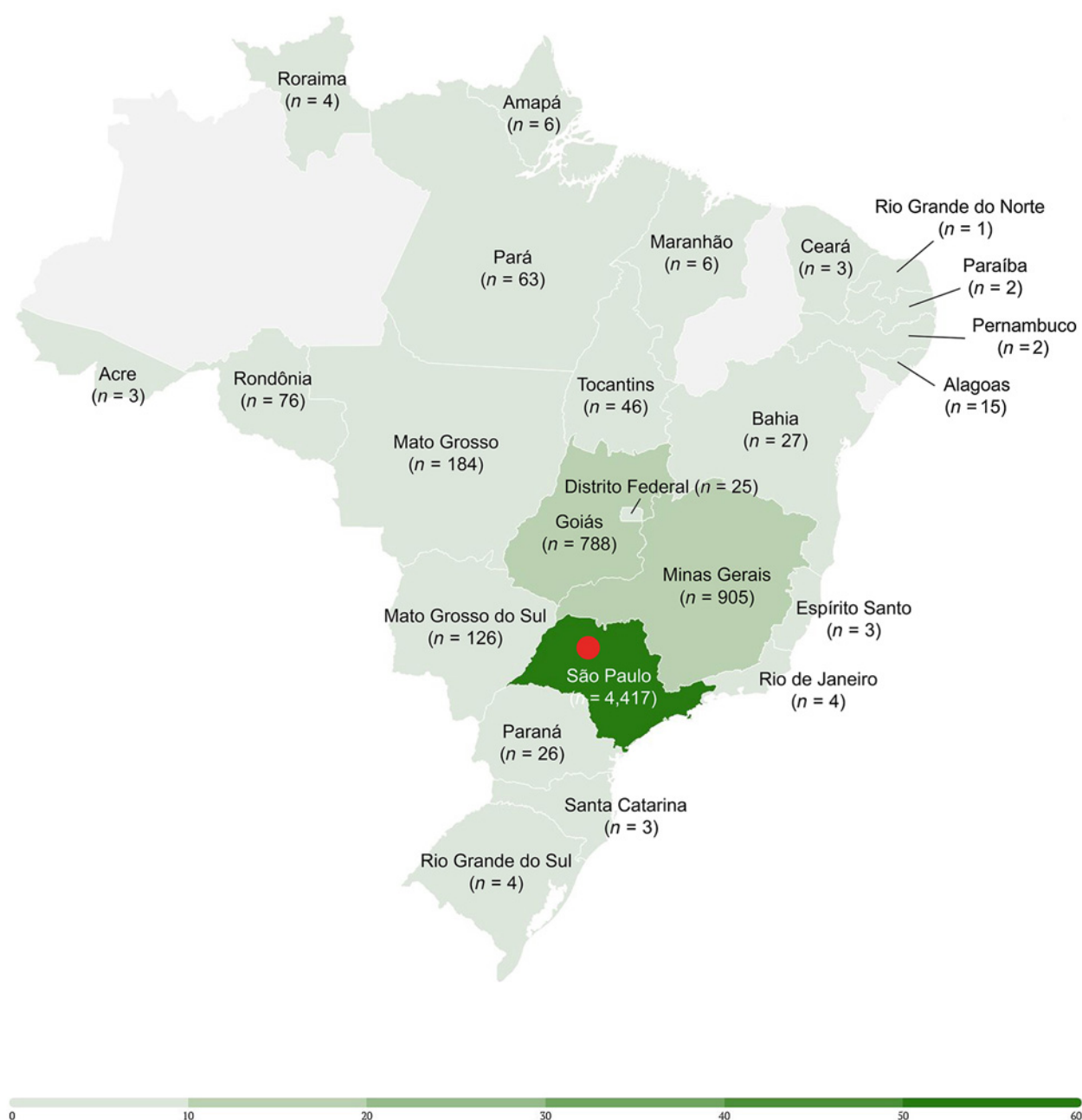


Figure 1.

Distribution of screening participants across the geographical Brazilian regions. BCH is localized in the state of São Paulo (red dot).

men, with a mean age (\pm SD) of 57 ± 4.45 years. The majority of the population invited to participate in the program came from the state of São Paulo (4,417, 65.6%), followed by the state of Minas Gerais (905, 13.4%), and then of Goiás (788, 11.7%; **Fig. 1**).

Among the 6,737 invited participants, 6,253 (92.8%) returned the stool sample for analysis (**Fig. 2**). The FIT test return participation rate varied among the participants invited from the different regions of Brazil. The FIT test return

participation rate ranged from 97% to 100% in the North, Northeast, Midwest, and South compared with 91.6% in the Southeast ($P < 0.001$; **Table 2**). The FIT test return participation rate was higher among participants ages 50 to 54 years than among ages 55 to 65 years ($P = 0.017$) but does not differ between genders (**Table 3**).

Among the returned tests for analysis, 96 (1.5%) were inadequate. Overall, among 6,157 participants with an adequate test, 779 (12.7%) had a positive result (**Fig. 2**).

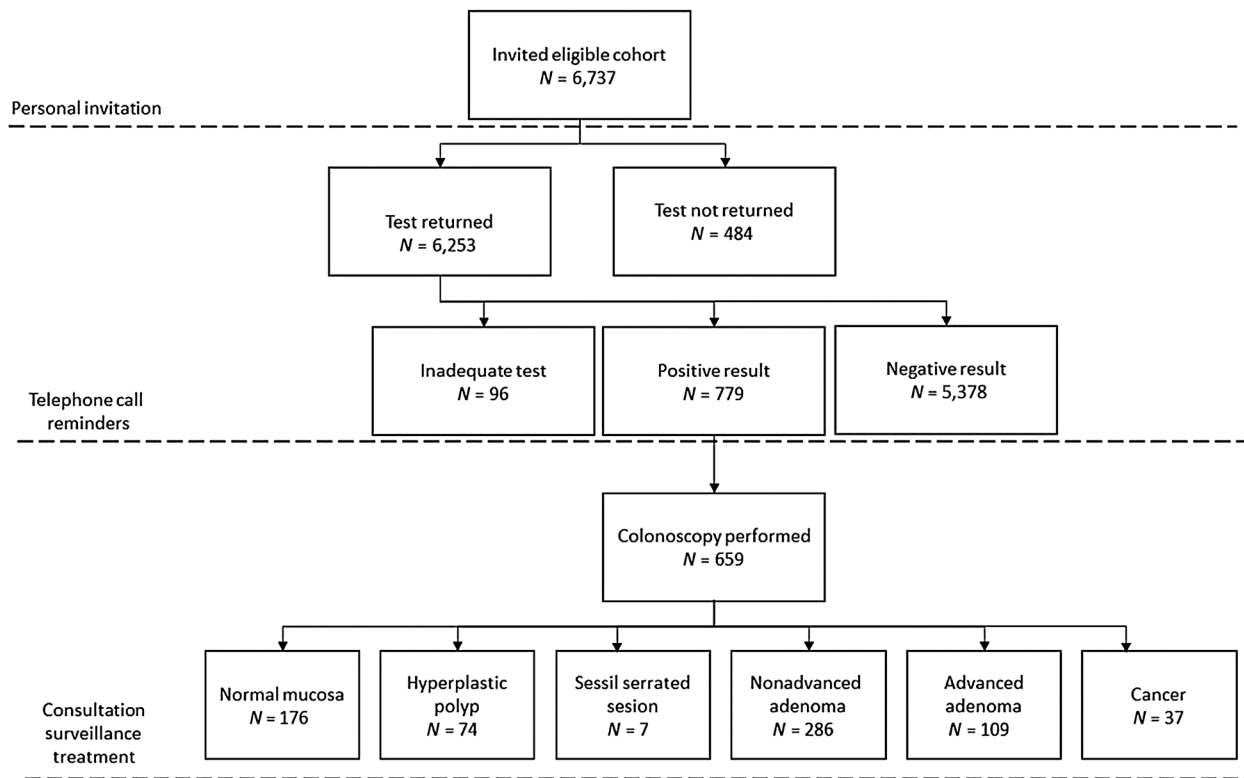


Figure 2.

Flow chart of the screening colorectal cancer program: invitation, participation, and early outcomes (considering the worst prognostic lesion detected in the colonoscopy).

Follow-up colonoscopy rates and outcome

Out of the 779 participants with FIT positive, 659 (84.6%) performed a diagnostic colonoscopy (Fig. 2). All but one patient did colonoscopy at BCH. This patient received a diagnostic colonoscopy in another hospital and following their receipt of a cancer diagnosis was referred to BCH for treatment. Colonoscopy and pathology reports from this patient were not available. The mean time interval between the FIT test result and the diagnostic colonoscopy was 50.3 ± 77.8 days. Among the participants who underwent colonoscopy, 313 (47.6%) did it within 31 days following the result of the FIT test.

Cecum intubation was achieved in 653 out of 658 (99.2%) patients. The reasons for incomplete colonoscopy in 5 patients

were obstructing tumor in two and loop formation of the colon in three. In 643 colonoscopies, the bowel preparation quality could be evaluated by using the BBPS. The mean BBPS total score was 8.82 ± 0.56 , ranging from 5 to 9. In 641 (96.7%) colonoscopies, the BBPS total score was ≥ 6 . The withdrawal mean time was of 17 ± 7 minutes (range, 5–54 minutes).

On colonoscopy, 176/659 (22.2%) participants had normal mucosa. Hyperplastic polyp was detected in 231 participants, sessile serrated lesion in 29, early adenoma in 391, advanced adenoma in 118, and cancer in 37 participants. Considering the worst prognostic lesion detected in the colonoscopy, hyperplastic polyp was the worst lesion in 74 participants, sessile serrated lesion in 7, early adenoma in 286, advanced adenoma in 109, and cancer in 37 participants (Fig. 2). The detection rate of any clinically significant lesion (i.e., early adenoma, advanced adenoma or cancer) was 70.1 per 1,000 participants tested. The detection rates for any adenoma, advanced adenoma, and cancer were 64.1‰, 17.7‰, and 6.0‰, respectively. The positive predictive value (PPV) for the adenoma was 60.0% (395/659), for advanced adenoma was 16.5% (109/659), and for the cancer was 5.6% (37/659). The PPV for adenoma was 61.1% (118/193) in men and 59.4% (277/466) in women. There is no statistically significant difference in PPV for nonadvanced adenoma, advanced adenoma, or cancer between genders (Table 3).

Table 2. Distribution of number of FIT tested and returning cards among the regions of Brazil.

Regions of Brazil	FIT tests distributed	FIT test return participation rate, <i>n</i> (%)
North	198	196 (99.0%)
Northeast	54	54 (100.0%)
Midwest	1,123	1,089 (97.0%)
Southeast	5,329	4,882 (91.6%)
South	33	32 (99.1%)

Table 3. Performance indicators of the colorectal cancer screening program of BCH.

	Participation N (%)	P	FIT Positivity N (%)	P	PPV NA N (%)	P	PPV AA N (%)	P	PPV CA N (%)	P
All	6,253 (92.8)		779 (12.7)		395 (60.0)		109 (16.5)		37 (5.6)	
Gender										
Male	1,669 (93.7)	0.097	226 (13.8)	0.109	86 (44.8)	0.730	32 (16.6)	0.999	15 (7.8)	0.137
Female	4,584 (92.5)		553 (12.2)		200 (42.9)		77 (16.5)		22 (4.7)	
Age										
50–54	2,208 (97.1)	0.017	259 (11.9)	0.045	99 (45.2)	0.671	33 (15.1)	0.058	10 (4.6)	0.612
55–59	2,101 (93.8)		248 (12.0)		89 (44.1)		26 (12.9)		11 (5.4)	
60–65	1,944 (93.1)		272 (14.2)		98 (41.2)		50 (21.0)		16 (6.7)	

Abbreviations: PPV NA, positive predictive value for nonadvanced adenomas; PPV AA, positive predictive value for advanced adenomas; PPV CA, positive predictive value for colorectal cancers.

Older individuals with age ranging from 60 to 65 years had a higher test positivity rate, PPV for advanced adenoma, and cancer than younger (50–59) individuals. However, only the FIT test positivity rate was statistically significant (Table 3).

Among the study's 37 cancer patients, histologic examinations of colonoscopic biopsies confirmed adenocarcinoma in 34 patients. In the three other colorectal cancer patients, histologic examination showed rectal neuroendocrine tumor grade 2 and grade 1 in two cases, and leiomyosarcoma of the anal canal in one. Out of the 34 cancer patients, 3 could not be effectively staged. In the 31 adenocarcinomas, 7 (22.6%) were stage 0, 5 (16.1%) stage I, 9 (29.0%) stage IIA, 7 (22.6%) stage IIIB, 1 (3.2%) stage IIIC, and 2 (6.5%) were metastatic cancer at diagnosis. Stage distribution of screen-detected cancers shows earlier stages than among clinically diagnosed colorectal cancer cancers at BCH and those reported at Brazilian national and São Paulo State cancer registries during the same period and age group ($P < 0.001$; Fig. 3A). There was a similar pattern after stratifying populations by sex. The frequency of cancer stages, in males (Fig. 3B) and females (Fig. 3C), respectively, was as follows—stage 0: 9.1% and 30.0%; stage I: 27.3% and 10.0%; stage II: 18.2% and 35.0%; stage III: 36.4% and 20.0%; stage IV: 9.1% and 5.0%. Regardless of sex, earlier stages were seen in the screen-detected cancer population than in BCH- and Brazilian population-based registries during the same period and the 50–65 age range ($P < 0.001$; Fig. 3B and C).

Discussion

In 1968, Wilson and Junger defined a set of principles for organized screening programs that have been extended and further elaborated for the implementation of the national screening programs in the Netherlands (26–28). Together, they judged several issues that should be carefully considered before the implementation of a screening program. Among other variables, they cited the relevance of the disease as a health problem, the availability of a simple and effective screening test, the presence of facilities for diagnosis and treatment, and quality assurance and control. Most of the countries that have implemented systematic colorectal screening programs have considered all these points as crucial issues before initiation of

their programs (29, 30). Indeed, colorectal screening programs are resource intensive and should be carefully considered and planned. Therefore, for low- and middle-income countries, colorectal cancer screening programs should be implemented with attention to clear goals and quality performance measures in order to maximize benefits, minimize risks, and avoid inappropriate costs.

Despite the demonstration of a reduction in colorectal cancer incidence and mortality by screening programs with different tests, some studies show that the majority of colorectal cancer deaths in this population are due to some failure during the screening stages (31). Doubeni and colleagues reported that being up to date with screening tests for bowel cancer can decrease the risk of colorectal cancer death by up to 62% compared with patients who do not perform the tests correctly or who are not up to date with their tests (31). Therefore, to achieve the potential benefit of colorectal cancer screening, quality must be optimized in each step of the process (11), including target population participation, the performance of the test used, and follow-up diagnostic colonoscopy, treatment, and follow-up. The outcome and quality of the screening program depend on the greater participation of the population in each of the stages. To get the best results of a screening program, a series of parameters called “quality indicators” should be monitored. This allows improvement of the screening program as it is implemented to ensure its efficacy and efficiency. Acceptable and desirable levels have been recommended by the European Union (EU) guidelines for quality assurance in colorectal cancer screening (11).

In the past, colorectal cancer was considered to be a problem almost exclusively limited to very-high-income countries. Progressively, this cancer appears as a serious problem and a leading cause of cancer-associated death also in low- and middle-income countries (32). It is well recognized that the burden of colorectal cancer in Brazil is increasing and represents a significant cause of cancer-related death and disability. However, the complexity of implementing a colorectal cancer screening program makes it a challenge in Brazil.

Brazil is divided into five geographical regions: north, northeast, midwest, southeast, and south, each of which differs significantly in demographic, economic, social, cultural, and

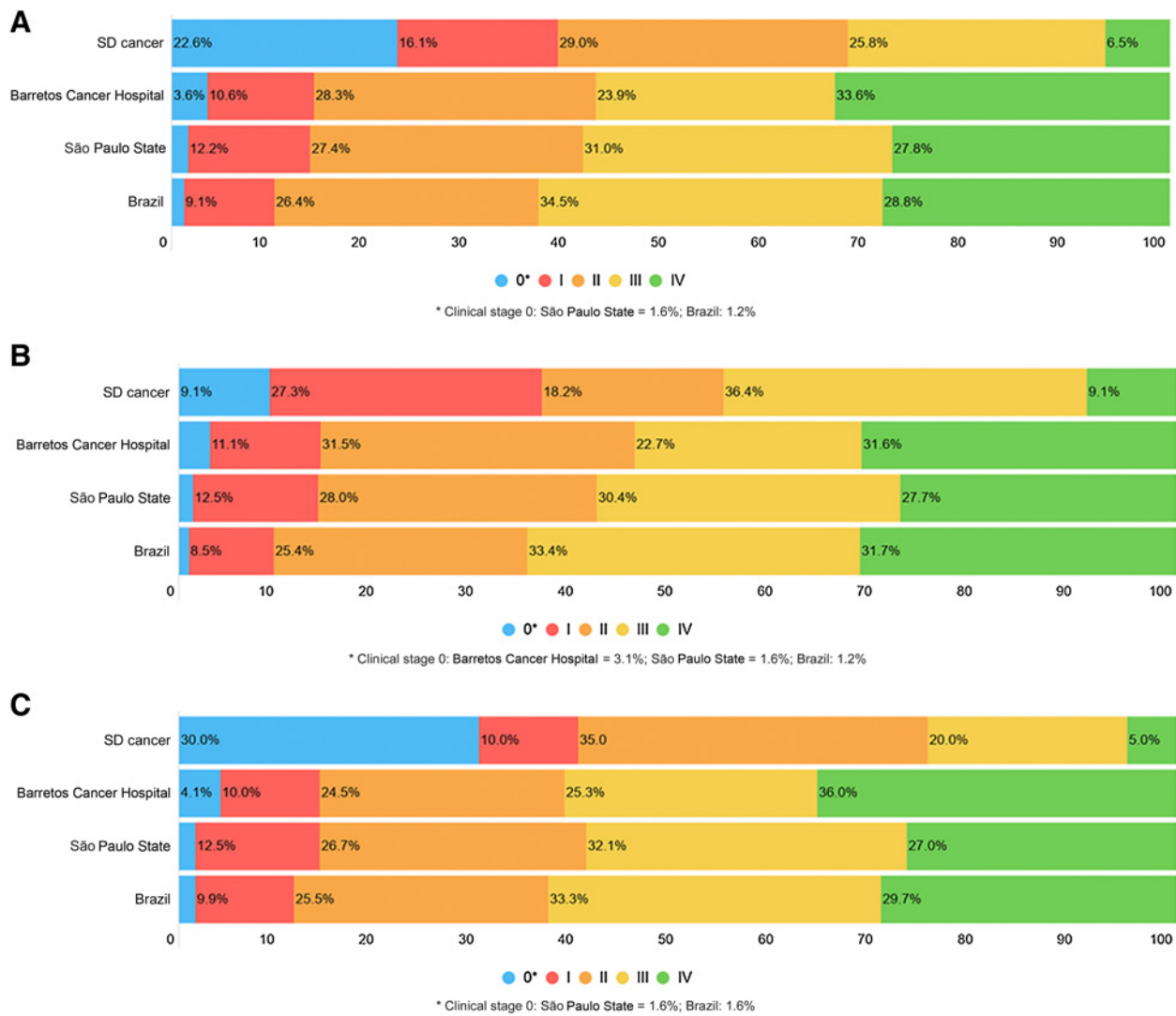


Figure 3. Cancer stage distribution: screening detected cancer at BCH screening program (SD cancer); BCH cancer registry (Barretos Cancer Hospital); São Paulo State cancer registry (Source: Fundação Oncocentro de São Paulo—FOSP (<http://200.144.1.68/cgi-bin/dh?rhc/rhc-geral.def>; São Paulo State), and from Brazil cancer registry (Source: Instituto Nacional do Câncer Integrador RHC; https://irhc.inca.gov.br/RHCNet/selecionaTabulador.action?initial=1&local=todosho_sp&unidFed=) (Brazil). **A**, All cases; **B**, Male; **C**, Female.

health conditions; each region also has widespread internal inequalities. The Brazilian Constitution of 1988 guarantees access to primary, secondary, and tertiary healthcare free of cost to every Brazilian citizen through the national health system. In 1990, a complex health system (the Unified Health System; SUS) was implemented, aiming to provide universal preventive and curative care financed by the state at the federal, state, and municipal levels (33). However, the Brazilian SUS is often underfunded, which potentially compromises its ability to guarantee the quality of and access to care. Hence, SUS is a health system that is still struggling to enable universal and equitable coverage (34). Along with the SUS foundation, norms were drawn to regulate the cancer care network in Brazil. Since then, cancer treatment is performed in specialized centers and

units (CACON, UNACON, and hospital complexes), which are distributed among the health administration regions according to population criteria (35). However, there are significant disparities in the availability of high-complexity oncology services in Brazil (35). According to da Silva and colleagues, there are only 44 licensed CACONs (high-complexity oncology centers, which treat all cancers) in Brazil, and most of those (70.5%) are situated in the south and southeast regions (35). In addition, the Brazilian regulatory norm does not consider screening as a priority. Altogether, financial and organizing aspects can explain why no nationally organized colorectal screening program has been implemented in Brazil so far.

BCH has a long history of cancer prevention, including a prevention department with healthcare professionals and

facilities mainly directed to breast and cervical cancers (13–17). More recently, an endoscopic service for diagnostic colonoscopies following FIT-positive screens was built at the prevention department with all necessary levels for detection and removal of screen-detected lesions. Therefore, in July 2015, we initiated a pilot colorectal cancer screening program. Considering the remaining life expectancy, which is lower than in very-high-income countries, so far, the target population for this program was people ages 50 to 65 years and, the immunochemical fecal test (FIT) was the screening test chosen. There is compelling evidence that FIT reduces colorectal cancer mortality (36, 37). FIT was first used in 1980 for screening in Japan. Since then, a progressively large body of literature, including from our group, has been described the clinical benefit of FIT and its superiority to the guaiac fecal occult blood test (gFBOT) (38, 39). FIT is the choice of most countries with colorectal cancer population-based screening programs (40).

This study evaluated the performance and quality indicators of the first two years (first round) of this program. Here, the FIT return participation rate in the first 2 years of the BCH program was higher than the desirable level of the EU guidelines for quality assurance in colorectal cancer screening (>65%; refs. 11, 41). Indeed, the FIT return participation rate

in our program was higher among participants from more distant regions of Brazil than from the local region (i.e., the state of São Paulo). Our FIT return participation rate results may be explained by the efficient structure of the program and the fact that most of the participants over these 2 years were also participants in other BCH screening programs, such as those for breast or cervical cancer (13, 42). Previous studies have demonstrated that integrating colorectal cancer screening with the breast and cervical cancer screening can increase participation rates in remote areas, probably by removing barriers to access and offering a comprehensive screening approach inclusive of all evidence-based modalities at once (43). In contrast to European countries where the participation rates were higher among people older than 59 years as compared with people in younger age groups, in our program the FIT return participation rate was higher among people younger than 55 years.

Rates of colonoscopy compliance in our program (84.6%; 95% CI, 81.87%–87.06%) were close to the highest rates reported among EU countries (74.44%; 95% CI, 74.24%–74.64%), but still lower than the desirable level (>95%) defined in the EU guidelines for quality assurance in colorectal cancer screening (Table 4). Colonoscopy completion is an important

Table 4. Participation and outcome rates in BCH and European screening programs.

Participation and outcome rates	BCH program % (95 CI)	EU programs % (95 CI)	EU guidelines Desirable level %
Participation rates, all	92.8 (92.20–93.40)	—	>65%
Women	92.49 (91.73–93.21)	—	—
Men	93.71 (92.48–94.79)	—	—
Positive test rate, all	12.5 (11.70–13.30)	6.94 (6.91–6.96)	—
Women	12.46 (11.65–13.30)	5.67 (5.64–5.70)	—
Men	13.54 (11.93–15.28)	8.48 (8.44–8.52)	—
Follow-up colonoscopy compliance rate, all	84.6 (81.87–87.06)	74.44 (74.24–74.64)	>95
Women	84.27 (80.96–87.20)	77.5 (77.21–77.79)	—
Men	85.40 (80.11–89.73)	74.38 (74.10–74.65)	—
Wait time for colonoscopy <31 days, all	47.6 (43.73–51.49)	—	>95
Follow-up colonoscopy completion rate, all	99.1 (98.04–99.67)	94.5 (94.38–94.62)	>95
Women	99.57 (98.46–99.95)	93.96 (93.79–94.13)	—
Men	98.44 (95.50–99.68)	95.60 (95.45–95.75)	—
Adenoma detection rate, all	64.2% (58.2–70.6)	37.90% (37.7–38.10)	—
Women	61.30% (54.50–68.70)	24.50% (24.30–24.70)	—
Men	72.00% (59.90–85.50)	54.00% (53.60–54.30)	—
Advanced adenoma detection rate, all	17.7% (14.6–21.3)	14.0% (13.90–14.10)	—
Women	17.00% (13.50–21.30)	8.80% (8.70–8.90)	—
Men	19.50% (13.40–27.40)	20.30% (20.00–20.50)	—
Cancer detection rate, all	6.0% (4.20–8.30)	2.30% (2.30–2.40)	—
Women	4.90% (3.10–7.40)	1.90% (1.80–1.90)	—
Men	9.20% (5.10–15.10)	2.80 (2.80–2.90)	—
PPV adenoma, all	59.94 (56.08–63.70)	72.92 (72.70–73.13)	—
Women	60.75 (56.10–65.25)	58.19 (57.83–58.54)	—
Men	61.14 (53.88–68.06)	84.66 (84.42–84.89)	—
PPV advanced adenoma, all	16.54 (13.78–19.60)	26.96 (26.75–27.17)	—
Women	16.89 (13.56–20.65)	20.89 (20.59–21.18)	—
Men	16.58 (11.63–22.59)	31.80 (31.50–32.10)	—
PPV cancer, all	5.61 (3.98–7.66)	4.46 (4.36–4.56)	—
Women	4.82 (3.05–7.21)	4.45 (4.30–4.60)	—
Men	7.77 (4.41–12.49)	4.45 (4.32–4.59)	—

quality indicator for this procedure and is often considered a key indicator of colorectal cancer screening programs. Rates of colonoscopy completion were higher in our program (99.1%; 95% CI, 98.04%–99.67%) as compared with the rates reported in EU FIT-based programs (94.5%; 95% CI, 94.38%–94.62%) and above the desirable level (>95%) specified in the EU guidelines for quality assurance in colorectal cancer screening (Table 4; refs. 11, 41).

A wide variability in lesion detection rates was reported among different screening programs in the EU countries (11, 41). Nevertheless, detection rates in our program were higher for adenoma detection and cancer detection compared with the highest values of EU programs (Table 4; ref. 41). The PPV for adenoma was higher in men than in women, as demonstrated previously by the US Multi-Society Task Force on Colorectal Cancer (44). The higher cancer PPV than most of other FIT-based screening population programs suggests that an eventual presence of symptomatic individuals can occur in our program population. To prevent this situation, all symptomatic individuals are recommended not to participate and directly consult their general practitioners as other screening programs, which have also reported symptomatic individuals among FIT-positive participants (45, 46).

The present study exhibits some limitations. It lacks a systematical collection of data on symptoms for the first 2 years of our pilot program preventing this important evaluation. Moreover, it would be better to compare PPV results to those from our Brazilian population since the prevalence of colorectal adenomatous polyps varies widely from country to country, and it is related to colorectal cancer incidence in each country. However, the Brazilian prevalence has not been reported so far. The prevalence would affect the sensitivity and specificity of the FIT brand used here, which is a qualitative assay. A previous study performed a quality-study comparing colonoscopy with the Hemosure—the same FIT used in our program (47). The authors reported a sensitivity and specificity for colorectal cancer and advanced adenoma of 54 (95% CI, 32%–74%) and 89% (95% CI, 88%–90%) and 37% (95% CI, 30%–44%) and 91% (95% CI, 90%–91%), respectively (47). Despite these limitations, our results showed a clear shift to earlier stages in the colorectal cancer detected at our program compared with those colorectal cancer clinically diagnosed at BCH and those reported in the Brazilian national cancer registry. A significant increase in stage 0–I colorectal cancers from 10.2% in the Brazilian national cancer registry (BNCR) and 14.2% in the BCH cancer registry to 38.7% in the BCH screening program, and concomitant reduction in stage IV colorectal cancers from 28.8% in the BNCR to 6.5% in the BCH screening program. A shift to earlier stages has also been reported in the National Bowel Cancer Screening Program in England and the Scottish colorectal cancer screening program (48, 49).

For the next phases, a REDCap (Research Electronic Data Capture) database (50) was built to allow close monitoring of the program's performance, including data collection on

symptoms, allowing us to make rapid adjustments that could optimize the screening program's results. In addition, participants' blood and FIT tests will be stored in the BCH biobank to permit future biomarker studies (51–53).

Conclusion

Results of performance indicators of the first 2 years (first round) of the colorectal cancer screening program of BCH showed a successful implementation with a high test return participation rate, colonoscopy completion, and detection lesion rates. Further, colorectal cancers were detected at an earlier stage in participants invited for the screening program than those reported in the Brazilian national and BCH cancer registries, suggesting a very exciting opportunity to improve colorectal cancer–related cancers in Brazil if they hold up on further follow-up.

Authors' Disclosures

E.T. Hawk reports other from Boone Pickens Distinguished Chair for Early Prevention of Cancer (endowed chair award) and grants from NIH 5P30CA016672 during the conduct of the study. No disclosures were reported by the other authors.

Authors' Contributions

D.P. Guimarães: Conceptualization, resources, data curation, supervision, funding acquisition, investigation, methodology, writing—original draft, project administration, writing—review, and editing. **L.A. Mantuan:** Data curation and investigation. **M.A. de Oliveira:** Data curation, and formal analysis. **R.L. Junior:** Investigation. **A. Mafra da Costa:** Data curation and formal analysis. **S. Rossi:** Data curation and investigation. **G. Fava:** Data curation and investigation. **L.N. Taveira:** Data curation and investigation. **K.M. Giardina:** Data curation and investigation. **T. Talarico:** Data curation and formal analysis. **M. Costa:** Data curation and investigation. **C. Scapulatempo-Neto:** Investigation. **M.M. Matsushita:** Investigation. **C.A. Véio:** Investigation. **J.H.T. Fregnani:** Conceptualization, data curation, and investigation. **R.M. Reis:** Conceptualization, resources, funding acquisition, validation, investigation, writing—review, and editing. **E.T. Hawk:** Investigation, writing—review, and editing. **E.C. Mauad:** Conceptualization, investigation, writing—original draft, writing—review, and editing.

Acknowledgments

This study was funded by MCTI/FINEP/CT-INFRA (Centro de Estudos em Prevenção e Diagnóstico Precoce do Câncer), by the Public Ministry of Labor Campinas (Research, Prevention, and Education of Occupational Cancer), and by Barretos Cancer Hospital internal funds. A. Mafra da Costa is a recipient of a Post-Doc fellowship (FAPESP's Thematic Research Project, 2018/22097-0 and 2019/21722/0), and R.M. Reis is a recipient of CNPq Productivity Fellowship.

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Received May 1, 2020; revised August 1, 2020; accepted September 22, 2020; published first September 30, 2020.

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