Introduction

Delivering health care services to remote populations is a challenge to public health systems worldwide. Data from Australia show that people living in remote and rural areas tend to have lower life expectancies, higher rates of injuries and diseases, poorer access to health care services, and lower rates of bowel screening [1]. Regarding participation in colorectal screening programs, disparities between rural and urban zones as well as indigenous and non-indigenous populations are observed in...
many countries [2–7]. Cancer outcomes are worse for rural patients, and more advanced cancer stages at diagnosis may explain this difference [8]. It is difficult to measure the impact of remoteness itself, as there are other health determinants underpinning this scenario such as lower socioeconomic status and medical data underreporting in these locations.

In an attempt to overcome this issue, the Belterra Project (BP) was set up as a pilot initiative for gastrointestinal cancer screening in an Amazon rainforest village. It addressed population awareness of colorectal cancer screening, healthcare assistance, and medical capacity expansion for gastrointestinal cancer screening.

The objective of this study was to describe the implementation and present the results of the BP, which was created to provide gastrointestinal cancer screening for a small population in the Amazon rainforest.

Patients and methods

Study design and ethical concerns

This descriptive study was conducted at the Hospital Sírio-Libanês. The description of the BP was approved by the Local Research Ethical Committee (register number 1.273.137) on October 9, 2015.

Setting

Belterra is a small town in the Amazon rainforest, on the banks of the Tapajos River. It was founded in 1934 by Henry Ford as a center for the extraction and sale of latex for the American automobile industry. The municipality area is 2,640.699km², with over 80 % of forest preservation area. Its population was estimated at 18,000 inhabitants in 2014, most of whom lived in rural areas. Of this, the subpopulation aged 50 to 70 years has been estimated at 2,359 people. The main economic activities include subsistence agriculture and fishing. The town’s health infrastructure is poor, consisting of only six small health units with five nurses and 40 community health agents. There is only one hospital where six doctors work, and there are no endoscopic or surgical units. The nearest secondary health facility is located 34 km from Belterra.

Data collection

Data were collected using standard forms filled out by doctors and medical students enrolled in the program. Data included general and demographic information on each patient, endoscopic exam results, and anatomopathological results. All data were then entered into the REDCap (Research Electronic Data Capture) platform [9] and available to researchers only. Only clinical information specifically concerning an individual participant was sent to local health providers.

BP description and implementation

As previously stated, the BP encompasses three key goals: address population awareness of colorectal cancer screening, medical capacity expansion, and healthcare assistance. The first step was to raise awareness of the importance of screening for gastrointestinal cancer among the population and healthcare agents. To this end, marketing material was developed, and was strategically placed in different regional locations and delivered to the residents.

The second step was to increase the theoretical knowledge and improve the technical skills of local health professionals. Medical students, residents, and endoscopists from neighboring cities were invited to participate in training under the supervision of experienced endoscopists.

The third step consisted of offering gastrointestinal cancer screening to every individual between 50 and 70 years of age based on their medical history (risk factor, lifestyle, social determinants), physical examination, endoscopic examinations (including Helicobacter pylori testing), and stool tests. From October 2014 to December 2017, 19 expeditions to Belterra took place. Each expedition lasted four days, during which endoscopies (EGD) and colonoscopies were performed, and fecal samples were analyzed within 1 week from collection for fecal occult blood, using a Biopix qualitative fecal immunochemical test (FIT) and parasitological tests. Whenever a lesion was diagnosed, an endoscopic treatment with polypectomy or endoscopic mucosal resection was attempted if possible. In case of advanced lesion biopsies were taken and sent to histopathological exam. Bowel preparation regimen was constituted of clear liquid diet on the day before the exam and 500 milliliters of 20 % mannitol solution orally 6 hours previous to the expected time of the exam. A standard video endoscope (EG530 WR, Fujifilm Corporation, Tokyo, Japan) was used for upper gastrointestinal endoscopies (EGD) and adult video colonoscope (EC 530 WL, Fujifilm Corporation, Tokyo, Japan) for colonoscopy using an imaging processor FUJIFILM – EPX 2500.

In every expedition, three experienced endoscopists, one endoscopy resident, two medical students, two nurses, one nurse technician, and four or five other support members from different regions of the country comprised the team responsible for delivering screening to the target population.

Community health care agents were responsible for explaining the procedures, providing drugs for bowel preparation, and providing general information to the population. Any patient with conditions discovered during the examinations that could not be managed endoscopically was referred to a secondary hospital located in Santarem city, 34 km away from Belterra.

Barriers and facilitators for implementation.

Public-private partnerships were established in order to secure not only financial funding, but also to guarantee adequate treatment to patients whose lesions could not be managed endoscopically, to collect and analyze data, and to provide medical material and expertise.

Due to the demographic characteristics of the region, the project utilized not only the local hospital but also a boat (▶ Fig. 1), where two endoscopy units were built (▶ Fig. 2) in order to deliver screening to the riverside and hard-to-reach populations. Both facilities had very limited resources, and therefore all medical materials including image processors, screens, gastroscope and colonoscopes, anesthetics, syringes, needles, sharps disposals, endoscopic tweezers, electrosurgery equipment, oxygen tanks, emergency carts, endoscopes cleaning...
products, and other basic items needed for the procedures had to be transported to these health units.

Further, the BP relied on backup support from the Hospital Regional do Baixo Amazonas, which was the local secondary hospital that received referred patients who needed further treatment in the event of unexpected complications. This hospital was located 45 kilometers away from Belterra. Patients with adenocarcinoma were referred to this hospital which was then held responsible for staging and treatment of these patients. Patients diagnosed with adenomatous polyps and those with positive *H. pylori* tests were then referred to the Hospital Municipal de Belterra to receive adequate treatment and follow-up. ▶ Fig. 3 is a flowchart of the algorithm use for this project.

**Results**

**Screening results**

During the 19 expeditions to Belterra, 2,022 individuals were enrolled in the program and a mean of 80.9 patients were screened per campaign. The characteristics of the participants are shown on ▶ Table 1. Among the 1,903 participants whose...
Fecal occult blood test (FOBT) was available, 64 patients (3.4%) had a positive result. Of these 64 positive results, one patient (1.6%) was diagnosed with colorectal adenocarcinoma and 13 had at least one polyp diagnosed and removed. A total of 31 polyps were removed from these patients as a few had more than one polyp removed. Low-grade dysplasia was diagnosed in nine patients, another two patients had adenomas with high-grade dysplasia, and two had synchronous polyps with low- and high-grade dysplasia. From the remaining patients with negative FOBT, 38.2% had at least one abnormal finding, with polyps accounting for 65.4% of the cases. From the 459 patients with negative FOBT, but with polyps diagnosed on colonoscopy, 41 had high-risk adenomas and four had adenocarcinomas. Other abnormal findings were diverticulum (50.4%), flat lesion (3.8%), colitis (3.3%) and arterial-venous malformation (1.6%). Regarding the upper endoscopy findings within patients with negative FOBT, four patients had gastric cancer diagnosed and one had duodenal cancer. Other abnormal findings were esophagitis (7.7%) and gastric (26.7%) and duodenal (25.6%) peptic ulcers.

Overall, 1,952 (96.5%) participants underwent colonoscopy, the remaining patients either did not show up on the scheduled day (n=64) or did not have adequate bowel preparation (n=8). The colonoscopy was considered complete in 98.1% when the scope reached the cecum. The main reasons for an incomplete exam were bad quality of bowel preparation (n=31) and anatomical difficulties (n=6). This study had 514 patients with colonoscopic findings. Of the 471 polyps found, the majority were adenomas and were subdivided into high-risk (defined as a lesion with any of the following characteristics: size larger than 10 mm, more than 50% of villous component or high-grade dysplasia) and low-risk adenomas. High-risk adenomas represented 14.0% of the total number of adenomas. The adenoma detection rate (ADR) was 16.5%. The main findings from this test are summarized in Table 2.

Colonoscopy findings were diagnosed in 472 patients. The majority of the patients presented with adenomas (n=284), of which 267 (92.4%) had tubular adenomas, while 22 had tubulovillous adenomas (7.6%). Regarding the histologic grade, 276 (95.5%) had a total of 370 low-grade dysplasia, while 13 (4.5%) had high-grade dysplasia. Another 27 patients had sessile serrated lesions (SSL), of which two had high-grade dysplasia and 20 had low-grade dysplasia. Data were not available for five patients with SSL. The distribution of the polyps was 637 (57.5%) located in the right colon (cecum, ascending and transverse colon) and 440 (40.1%) in the left colon (descending colon, sigmoid, and rectum). There were 21 polyps with unknown localization. The characteristics and location of the colorectal polyps are shown in Table 2. The average size of polyps removed was 5 mm (range 1 to 40 mm; median 4 mm).

Among the five patients diagnosed with colorectal adenocarcinoma, one had a positive FOBT result. Moreover, of 45 patients with high-risk adenoma, 41 tested negative for fecal occult blood.

Overall, 1,958 participants underwent upper endoscopy (96.83%) and the remainder did not show up on the scheduled day (64 patients). The main findings are detailed in Table 2.

No adverse events requiring medical intervention were observed during the program.

### Table 2

<table>
<thead>
<tr>
<th>Colonoscopic findings</th>
<th>Number (%)</th>
<th>Histopathological finding</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyps</td>
<td>471 (24.12)</td>
<td>Low-risk adenoma</td>
<td>277 (14.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-risk adenoma</td>
<td>45 (2.31)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperplastic polyp</td>
<td>149 (7.63)</td>
</tr>
<tr>
<td>Tumors</td>
<td>7 (0.61)</td>
<td>Adenocarcinoma</td>
<td>5 (0.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neuroendocrine tumor</td>
<td>2 (0.10)</td>
</tr>
<tr>
<td>Flat lesions</td>
<td>31 (1.59)</td>
<td>Low-risk adenoma</td>
<td>31 (1.59)</td>
</tr>
</tbody>
</table>
To the best of our knowledge, this is the first report of a colorectal cancer screening program within an Amazonian population and the findings are key to future interventions in this region.

Providing gastrointestinal screening to remote and underserved populations has proved to be a challenge. Notwithstanding the geographical, cultural, and financial barriers, we suggest that through the participation of volunteers and the establishment of partnerships with the public and private sector, the implementation of a cancer screening program for remote Brazilian populations is feasible. Of the several barriers that have been identified, we highlighted difficulties in transporting all medical material and professionals to an unequipped hospital, which was required to reach riverside populations that are not accessible by roads. We also highlighted difficulties in providing adequate training to health professionals who are not familiar with population-based screening.

In addition, we presented main results from the project, which included diagnosis of lesions in 26% of participants undergoing colonoscopy, and nine patients diagnosed with malignancies undergoing upper gastrointestinal endoscopy.

We observed over 95% adherence to the screening project, which is considered very high. Other studies from different countries have shown much lower adherence rates, such as 10.5% and 45.4% [10–12]. This surprisingly high adherence is likely due to a conjunction of factor, such as the investment in marketing and promotion of the screening program through outdoor posters, flyers, and the work of community health care agents who promoted the campaign for population awareness. Further, the implementation of such a program in a small and restricted population facilitates the spread of the information among all inhabitants.

Moreover, in this study, the ADR was 16.5%, below that recommended by the American Society for Gastrointestinal Endoscopy, which considers the target ADR of 20% to be a quality indicator [13]. The low ADR observed in this study may be explained by the characteristics of the population screened within this study, or by the lack of imaging magnification modes or high-resolution endoscopic devices used, which may have compromised our ability to diagnose small lesions [14–18].

Five patients (0.26%) were diagnosed with colorectal adenocarcinoma. The adenocarcinoma detection rate varies widely in the literature, from 0.2% to 3.1% [19–22]. Therefore, our results fall within the variability described in other studies.

Unlike many colorectal screening projects [11–12,23–28], this study provided every participant with both FOBT and colonoscopy, making it possible to analyze the efficacy of these examinations under the circumstances of remote populations. The positivity of FOBTs observed in this study was similar to that in other studies, with a positivity rate of 2.4% to 7.7% [25–28]. We found a surprisingly low sensitivity of FIT for adenocarcinoma in our study, among the five patients diagnosed with adenocarcinoma, only one (20%) had a positive FOBT. Other studies that have also performed colonoscopy and FOBTs in all patients have found positive FOBT results in patients diagnosed with colorectal adenocarcinoma at higher rates than those observed in this study [19,20]. The low sensitivity of the

| Table 3 | Polyps characteristics and location. |
|------------------|------------------|------------------|------------------|
| Characteristic or location | Number of patients | Percentage of patients with polyps (%) | Number of polyps | Percentage of polyps (%) |
| Sessile | 429 | 86.3 | 672 | 84.3 |
| Pedunculated | 57 | 11.5 | 113 | 14.2 |
| No data available | 10 | 2.1 | 11 | 1.4 |
| Transverse colon | 137 | 23.1 | 271 | 24.7 |
| Sigmoid | 130 | 22.0 | 216 | 19.7 |
| Ascending colon | 128 | 21.6 | 259 | 23.6 |
| Descending colon | 77 | 13.0 | 136 | 12.4 |
| Cecum | 52 | 8.8 | 107 | 9.2 |
| Rectum | 52 | 8.8 | 88 | 8.0 |
| No data available | 16 | 2.7 | 21 | 1.9 |

| Table 4 | Main upper endoscopic and histopathological findings (n = 1,958). |
|------------------|------------------|------------------|------------------|
| Endoscopic findings | Number (%) | Histopathological finding | Number (%) |
| Suspected gastroduodenal lesions | 9 (0.46) | Adenocarcinoma | 6 (0.31) |
| | | Lymphoma | 1 (0.05) |
| | | Neuroendocrine tumor | 1 (0.05) |
| | | High-grade dysplasia adenoma | 1 (0.05) |
FOBT in this study raises concerns about its use in remote regions, where the storage and transportation of stool samples is not optimal and may lead to decreased efficacy.

There are controversies regarding gastric cancer screening efficacy, and recommendations are based on its incidence in each country or region. Countries with high gastric cancer incidence, such as Japan, South Korea, Venezuela, and Chile, have implemented screening, each of them with their own protocol regarding time interval and modality of screening [29–31].

Nevertheless, our project had a series of limitations that must be pointed out. First, given the voluntary nature of this work and the multiple sources of funding, an accurate measurement of the actual costs is underestimated and out of the scope of this paper. However, this factor plays a major role when considering the possibility of reproducing this model on a nationwide scale. Further, data are lacking regarding colon preparation and scope withdrawal time, which are considered important aspects when analyzing the colonoscopy quality. Finally, we did not follow up the patients with adenomatous polyps and invasive carcinomas; therefore, we lack information about their clinical stages and further treatments.

Clinical studies comparing the benefits and risks of these interventions and further cost-effectiveness analyses addressing this topic are needed. Another remaining question concerns the feasibility of adapting this model for larger populations, within the context of national public health systems.

Conclusions

Despite the geographical, cultural, and financial barriers, this study suggests that through volunteer participation and the establishment of partnerships with the public and private sector, the implementation of a gastrointestinal cancer screening program for remote Brazilian populations is feasible. Our results showed that nearly 26 % of Belterra inhabitants who underwent colonoscopy screening had some type of colonic lesion.

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Competing interests

Dr. Marcelo Averbach is a board member for Boston Scientific, Inc. Dr. Ferrari is a medical consultant for Boston Scientific, Inc. and Olympus.

Funding

To make the project feasible, several partnerships were established with both public and private sectors. The municipal health department of Belterra provided the Municipal Hospital facilities and allowed the team of nurses and community health care agents to collaborate on the project. Fujinon Corporation provided endoscopic equipment, such as endoscopes, image processors, and screens, for every expedition. Hospital Sírio-Libanés, through its teaching and research institute, provided the software and expertise for data collection and analysis and performed histopathological tests of the sample specimens. Boston Scientific Corporation was responsible for all costs related to transport and accommodation of the team, and also provided facilities for endoscopic procedures. Moreover, the company also provided a team of two nurses who were sent to Belterra before every expedition in order to set up the working space for the rest of the team. Further, the project was supported by the Hospital Regional do Baixo Amazonas, a local secondary hospital that received patients who needed additional treatment in case of unexpected complications. The sources of funding had no role in the design, conduct, data analysis, and reporting of this study.

References


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