Editorial



# Usefulness of the mass screening program for colorectal cancer in China: further long-term validation is needed to confirm its value

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## Colorectal cancer screening rationale in China

According to worldwide cancer statistics, in 2018, colorectal cancer (CRC) was the second and third most common cancer in women and men, respectively, accounting for approximately one-tenth of all cancer cases and cancer-related deaths.

Developed countries and regions such as North America, Europe, Australia/New Zealand, and East Asia (Japan, Korea, Singapore) have the highest incidence rates (1). However, over the last two decades, the incidence of CRC and associated deaths have significantly increased in Asian countries (2). Rapid rise in the incidence of CRC is one of the major public health issues in China (3).

Most CRCs arise from adenomatous colon polyps that progress from small (<8 mm) to large (≥8 mm) polyps and undergo dysplastic changes and subsequent malignant transformation. Adenomatous polyps occur in about 30% of men and up to 20% of women. Progression from adenoma to carcinoma is believed to occur over at least 10 years.

Screening tests for CRC can improve the disease prognosis by identifying early-stage CRC that is easier to treat and has a lower mortality rate than that detected after development of symptoms. In addition, screening can prevent CRC by enabling the detection and removal of premalignant polyps before they progress to CRC.

## Selection of screening tools and risk assessment for CRC

CRC screening is currently recommended in many countries worldwide (4). Colon imaging by colonoscopy and/or colonography is the main screening methods in the United States and some European countries including Germany. However, in many other countries, non-invasive stool testing including fecal occult blood test (FOBT) is preferred as the primary screening test (5). The fecal immunochemical test (FIT) has rapidly replaced guaiac-based FOBT due to higher sensitivity for advanced adenomas and malignancies, the quantitative outcome yields, the ease of handling, and high participation rates (6).

There are no optimal tests or programs because of international differences in CRC screening. Across the multiple tests that are recommended for screening by major guidelines, the number of averted CRC-related deaths appear to be relatively similar, although the sensitivity and specificity for detection of polyps and CRC vary. The sensitivity and specificity per lesion for CRC detection in asymptomatic screened patients were 84.0% and 88.0% respectively for CT colonography, 95.0% and 87.0% respectively for sigmoidoscopy, and 95.0% and 86.0% respectively for colonoscopy. Furthermore, the sensitivity and specificity per person for CRC detection were 92.3%

and 89.8% respectively for FIT-DNA, 73.8% and 96.4% respectively for FIT, and 70.0% and 92.5% respectively for FOBT (7,8).

Sensitivity and specificity, evidence of effectiveness, convenience, safety, availability, and cost provide an insight into the effectiveness of the screening program (9-11).

In view of this, "*An early report of a screening program for colorectal cancer in Guangzhou, China*", a recent publication by Fang and colleagues (12), is very notable. In this article, they reported the effectiveness of a screening questionnaire and the early results of the program. This screening program for CRC consisted of a questionnaire and two consecutive FITs used as the primary screening method. Subjects with positive results on one or more of the two tests were referred for further testing with colonoscopy. A screening test was conducted with a questionnaire provided to a total of 6,971 inhabitants in Yuexiu District, Dadong Street, of which 5,343 received at least one FIT. A total of 1,219 colonoscopy subjects were identified by questionnaire or FIT. Among them, 647 (53.1%) underwent colonoscopy. As of the time the article was published, 623 colonoscopy results were obtained, among which 270 (43.3%) had positive findings. The authors concluded that this screening program was effective for identifying patients with colon neoplasms at an early stage and precluding the progression of the malignant disease.

A very important initial indicator in a group-based screening program is compliance, which is closely related to the motivation of the participants (13). In a meta-analysis by Deng *et al*. (14), the authors concluded that common reasons for low attendance rates were cost, lack of understanding, fear of complications of the screening test, and lack of communication or awareness of symptoms (14). Previous studies have shown that the highest compliance rates in North America and Europe for FOBT or FIT were between 40% and 70% (15). The study by Fang *et al.* (12) showed relatively high attendance rates for one FIT (76.6%), two FITs (65.5%), and colonoscopy (51.3%). This attendance rate can be explained as being the result of free colonoscopy tests and raising of public awareness regarding the benefits and safety of colonoscopy through a questionnaire, a self-evaluation tool.

However, the article by Fang *et al.* (12) has certain weaknesses. Because of the early report of a screening program, the long-term outcomes (the change of overall survival or cancer-specific survival, the number of subjects identified to have progressive malignancies per 1,000 persons examined or invited, etc.) of the screened subjects remain unknown. Therefore, readers should be careful in interpreting the results of this paper. Second, the sensitivity and specificity of FIT, 0.475 and 0.673, respectively, in the study were relatively low compared to the 0.8 and 0.9 in previous studies (16). The authors explain this difference due to the variation between the brand of FIT and the method of sample collection, however, it is difficult to determine if it is sufficient. Lastly, they did not recommend an age and interval for screening in the Guangzhou region. Nevertheless, the strength of this paper lies in it being able to provide practical assistance to areas with limited resources by describing the potential of a questionnaire as a useful tool in the screening program for colorectal cancer.

## Harms associated with CRC screening

Most of the harms associated with CRC screening are related to the risks from colonoscopy, including perforation. Any abnormal results on the initial noninvasive screening tests (stool tests or virtual colonoscopy) necessitate colonoscopy to evaluate the abnormality. Thus, all screening modalities are associated with the potential for colonoscopy-associated complications. Further, sigmoidoscopy and colonoscopy have the disadvantages of being relatively invasive, expensive, and requiring a high level of expertise. Therefore, these may not be appropriate as a primary screening test for CRC in resource-poor areas. In the study by Fang *et al.* (12), it is important to note that the addition of the questionnaire has led to a sharp decline in specificity from 0.673 to 0.088, indicating that many of the healthy individuals who completed the questionnaire might have undergone unnecessary colonoscopies. Therefore, we believe that to improve specificity, the usefulness of the questionnaire should be augmented through continuous additional validation.

## Conclusions

The CRC screening program in Guangzhou, China was able to provide practical assistance to the area with limited resources using questionnaire and FITs for identifying patients with colon neoplasms at an early stage, precluding the progression of the malignant disease. Further long-term validation of this program might provide an important policy model for regions that have just begun or are planning CRC screening.

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.03.33). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work and in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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