Current Gastroenterology Reports (2019) 21: 36
https://doi.org/10.1007/s11894-019-0703-8

GI ONCOLOGY (R BRESALIER, SECTION EDITOR)

The Rise of Colorectal Cancer in Asia: Epidemiology, Screening, and Management

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Published online: 10 July 2019

Abstract

Purpose of Review Colorectal cancer (CRC) remains the third most commonly diagnosed cancer globally, and its incidence and mortality rates have been on the rise in Asia. In this paper, we summarize the recent trends and screening challenges of CRC in this region.

Recent Findings In 2018, Asia had the highest proportions of both incident (51.8%) and mortality (52.4%) CRC cases (all genders and ages) per 100,000 population in the world. In addition, there has been a rising trend of this disease across Asia with some regional geographic variations. This rise in CRC can be attributed to westernized dietary lifestyle, increasing population aging, smoking, physical inactivity, and other risk factors. In curbing the rising trend, Japan, South Korea, Singapore, and Taiwan have launched nationwide population-based screening programs. CRC screening across this region has been found to be effective and cost-effective compared with no screening at all. The emergence of new therapies has caused a reduction in case fatality; however, these new options have had a limited impact on cure rates and long-term survival due to the great disparity in treatment capacity/resources and screening infrastructures among Asian countries with different degrees of economic development.

Summary CRC is still rising in Asia, and implementation of screening is necessary for moderate- to high-incidence countries and construction of treatment capacity is the priority task in low-incidence and low-income countries. Unless countries in Asia implement CRC screening, the incidence and mortality rates of this disease will continue to rise especially with the rapidly rising population growth, economic development, westernized lifestyle, and increasing aging.

Keywords Colorectal cancer · Asia · Epidemiology · Population · Screening · Colonoscopy

Introduction

Globally, colorectal cancer (CRC) ranks third (1,849,518 new cases, 10.2% of total) as the most commonly diagnosed cancer after lung and breast cancer, with it being second in women and third in men in 2018 [1••]. It is also the second oncological cause of death worldwide, although with some global geographic differences in both incidence and mortality rates, with Asia contributing the highest, 957,896 (51.8%) of incident cases and 461,422 (52.4%) of deaths (all genders and ages) in the world [2]. However, screening of CRC has been found to be the most important aspect in reducing the incidence and mortality of this disease, and just a smaller proportion of people worldwide are offered this strategy [3••]. Today, in addition to the increasing cost of chemotherapy for advanced CRC, screening strategies for this disease have become cost-saving [4]. In Asia, a considerable number of countries including Japan, South Korea, Singapore, and Taiwan where CRC is highly prevalent, have developed population-based screening programs [3••]. During the period of 2004–2008, South Korea had the highest CRC incidence worldwide with an age-standardized incidence rate (ASRi) of 45 per 100,000, and currently, Hungary has the highest rate in the world (ASRi 51.2 per 100,000) [1, 5]. Change in the national healthcare

This article is part of the Topical Collection on *GI Oncology*

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policy toward efficient resource allocation and active screening with fecal immunochemical test (FIT) can significantly reduce the huge burden of CRC on the population as found in the case of Taiwan [6••].

Generally, the number of cancer patients has been on the rise globally, with the incidence and mortality of CRC being higher in countries with more development [7]. The trend of this disease, however, has been on the rise in Asia as well, especially in China, Japan, South Korea, Singapore, and Taiwan with a two- to four-fold increase in incidence during the last few decades, with South Korea having the highest incidence [3••, 5, 8]. Notwithstanding, in the recent 2 years, Taiwan has experienced a decline in the number of CRC incident and mortality cases [9].

The aim of this review is to present the various aspects of the changing trends of CRC and its screening challenges in Asia.

Methods

For this review, we collected information on CRC epidemiology, screening, and management within Asia from published literature within the last 20 years. We conducted a literature search using databases and relevant websites including PubMed and Google Scholar and retrieved information from the GLOBOCAN 2018 project website.

Results

The Changing Epidemiology of Colorectal Cancer in Asia

More than three decades ago, CRC was said to be rare in Asia while it was most common in North America and Europe. Since then, there has been a steady but rapid increase in the incidence, prevalence, and mortality of CRC in Asia [8, 10, 11, 12••, 13]. It is becoming an important and growing concern for most Asian countries, and there has been an increase in incidence and mortality rates across the region (Table 1), with some countries experiencing declining rates recently [1••]. Additionally, there has been an observed increased risk among younger people with some gender, ethnic, and regional or geographic variations [3••, 8, 11, 14–16]. Lifestyle risk factors such as high alcohol consumption, obesity, diabetes, cigarette smoking, and high intake of red and processed meat have been associated with this changing trend [11, 14, 17]. In Asia, particularly in Japan, there has been a difference between men and women in the incidence of CRC over the last few decades with a rapid and increasing trend in women than in men, of about 10% in the proportion of proximal colon cancer. However, the increasing incidence of rectal cancer for both sexes is also noticed from a population-based study though at a slower rate for women than for men [18]. Ethnicity has been found to be an important etiological factor for CRC in Asia [19]. Some ethnic groups such as Chinese, Korean, and Japanese have higher CRC incidence. In certain countries with multi-ethnic populations such as Singapore and Malaysia, the Chinese population, in particular, have a substantially greater incidence of CRC compared to Malays and Indians though living in the same environment with similar lifestyle and dietary habits [8, 19, 20••]. Even among the same ethnic groups, for example in China, higher incidence and mortality rates have been shown in those living in coastal areas compared with those in the hinterlands [20••, 21]. Status of economic development in addition to ethnic group variation is also a significant risk in developing CRC. According to the International Agency for Research on Cancer (IARC) as of November 2018, South Korea still has the highest ASRi (44.5 per 100,000 population) in Asia (Table 1) [1••]. The estimated ASRi and ASRm for this region are represented on these figures (Figs. 1 and 2), respectively. Nevertheless, there is some geographic variation of the ASRi and ASRm across the region.

Screening Modalities and Activities of CRC in Asia

Screening of CRC remains the most important and cost-effective strategy in reducing the incidence and mortality of this disease, though with a lesser contribution from both risk factor reductions and improved therapies [22]. In Asia however, most countries still lack any form of CRC screening activities while only a few of them actually have organized, pilot or practice opportunistic screening (Tables 1, 2) [3••, 41]. Organized CRC screening has been recommended by the Asia Pacific Colorectal Cancer Working Group in regions with an age-standardized incidence rate (ASRi) above 30 per 100,000 population, targeting average-risk persons and those aged 50–75 years with quantitative FIT [40•]. The Asia Pacific Colorectal Cancer Working Group also recommends quality control measures to be included in CRC screening programs. Generally, early diagnosis and removal of cancerous or precancerous lesions can significantly cut down CRC incidence and mortality. Moreover, early detection gives room for less invasive procedures, lower morbidity, and less therapeutic cost. CRC screening in Asia as well as in other countries has been shown to be cost-effective or even cost-saving compared with no screening at all [42, 43••].

Generally, the screening modalities of CRC include the non-invasive fecal occult blood tests targeting either heme (guaiac fecal occult blood test (gFOBT)) or human hemoglobin (FIT) and the invasive endoscopy-based investigations (flexible sigmoidoscopy and total colonoscopy) for making a diagnosis [44–46]. FIT screening has been found to be generally associated with much higher participation and usually offers higher sensitivity for detecting advanced adenomas and CRCs compared with gFOBT

Table 1 Changing trends in incidence and mortality rates for select countries in Asia (updated November 2018)

Country	ASRi		ASRm		Screening program type [3]
	2015	2018	2015	2018	
South Korea	45	44.5	12	8.7	Organized full
Japan	32.2	38.9	11.9	12	Organized full
Singapore	33.7	36.8	11.8	17.3	Organized full
Brunei	25	35	12	13.9	Opportunistic
China	14.2	23.7	7.4	10.9	Regional pilot
Hong Kong	38.4	40.5*	14.1	14.0*	Phase II of territory-wide full‡
Taiwan	45.3	41.3*	14.9	14.6**	Organized full
Malaysia	18.3	19.9	9.4	11.2	No organized
Thailand	12.4	15.5	7.3	8.4	Regional pilot
Philippines	13.10	18.9	7.8	11.0	Opportunistic

ASRi age-standardized incidence rate per 100,000 population

ASRm age-standardized mortality rate per 100,000 population

*2016, **2017, ‡ only for residents aged 56 to 75 years

[47–49]. Moreover, previous studies have demonstrated that the Asian population prefers the stool test over endoscopy screening [35, 50]. Colonoscopy, on the other hand, is usually considered the gold standard method for detecting CRC and precancerous neoplasms and proven effective in reducing CRC incidence and mortality. Its invasiveness, high cost, and manpower demanding characteristics hinder its use as a primary screening tool in most organized screening settings [44, 46, 51–53].

Accordingly, FIT remains the most widely and frequently used primary screening modality in population-based screening programs in Asia and also in many European countries [3••, 37•]. Colonoscopy is also used as a primary screening modality in opportunistic screening especially in countries like Japan, Korea, and Taiwan while the use of flexible sigmoidoscopy is less common in this region [3••, 8, 20••, 37•]. For CRC screening programs in Asia to be effective, there is a need to consider several factors including actively engaging the public in allaying their fears and negative perceptions of screening and the use of colonoscopy exam after a positive FIT test [54]. Some other issues that need to be addressed include constructing necessary infrastructure such as healthcare system to treat screening-detected lesions and cancers, nation- and territory-wide

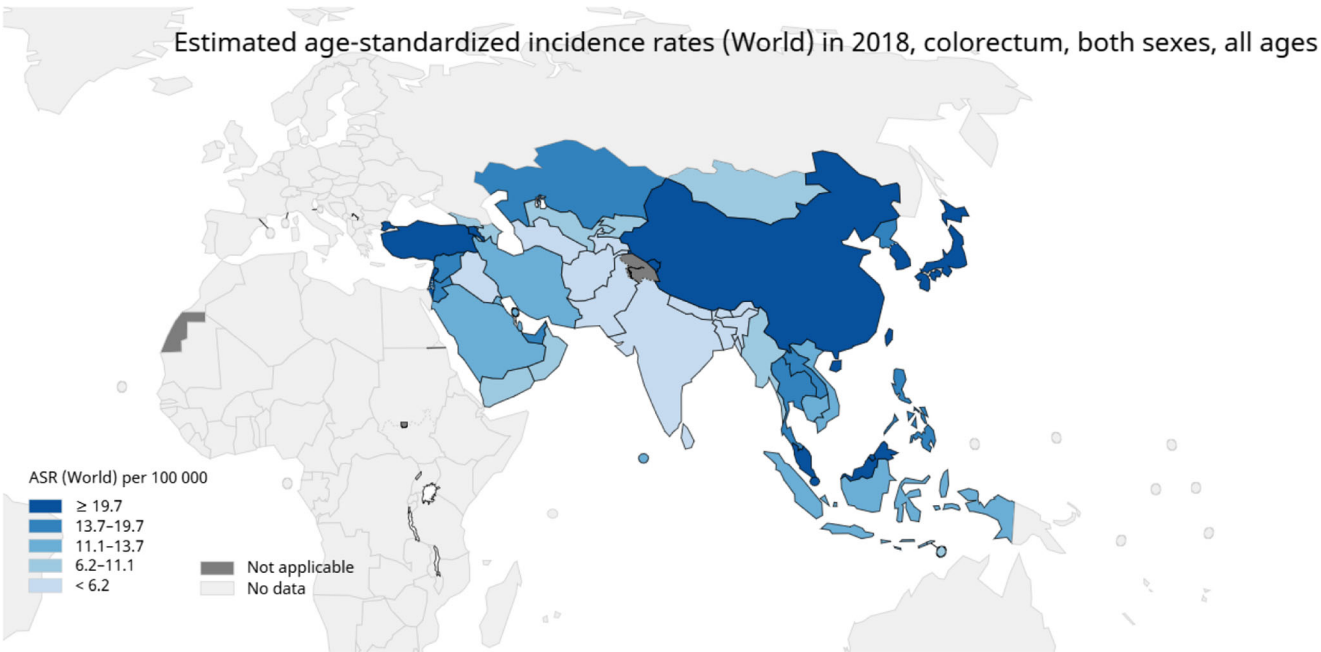

Fig. 1 Estimated CRC age-standardized incidence rates in Asia (both sexes and all ages). Source: GLOBOCAN 2018. (Permission from IARC granted to use content for non-commercial research/educational purposes)

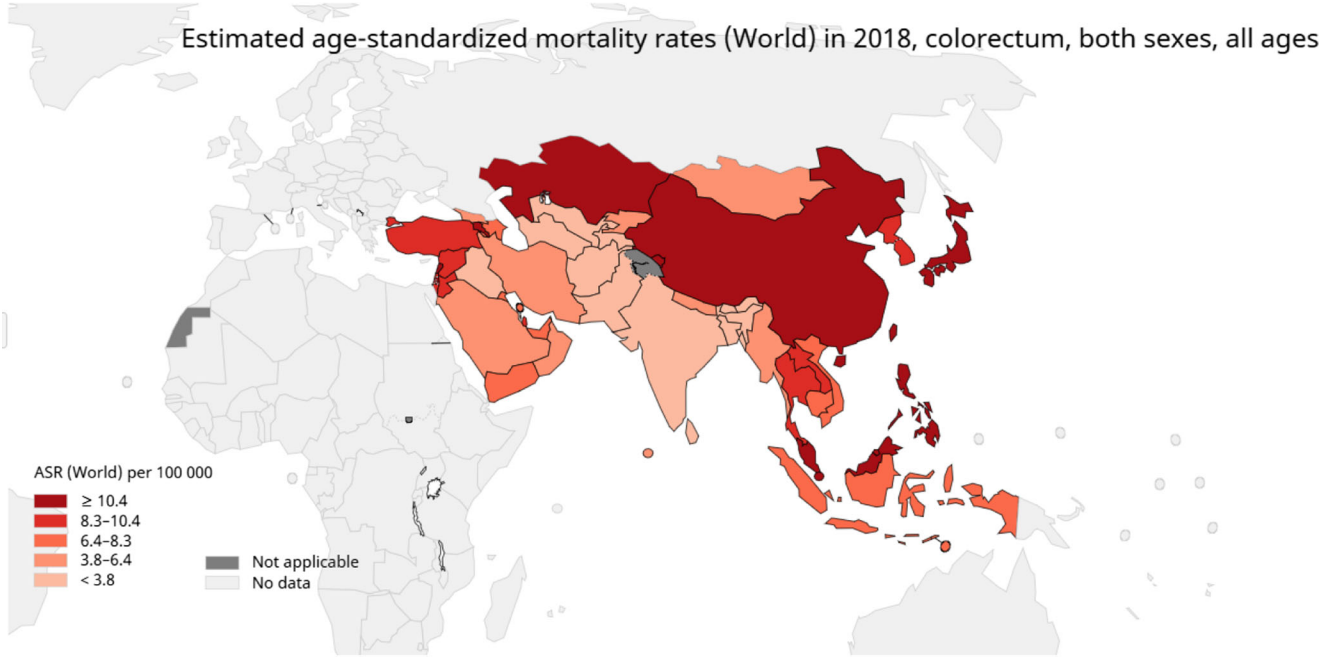

Fig. 2 Estimated CRC age-standardized mortality rates in Asia (both sexes and all ages). Source: GLOBOCAN 2018. (Permission from IARC granted to use content for non-commercial research/educational purposes)

cancer/death registry system, and FIT laboratories, securing sufficient manpower pertaining to screening such as endoscopists and public health workers, and obtaining consensus of different aspects/parties.

The pathway of CRC screening programs (organized and opportunistic) commonly carried out in Asia includes activities from inviting an eligible population, collection of stool samples, clinical verification/diagnosis, therapies, and follow-up as represented by Fig. 3 [55]. In organized screening, compared with opportunistic screening, there is usually regular monitoring of screening activity, quality (including positivity rate, detection rate, and colonoscopy rate), and linkage to national or regional cancer/death registries thereby monitoring the quality and effectiveness of the program. Some subjects with negative colonoscopy findings may proceed to surveillance colonoscopy rather than going back to the general screening pool, as shown in Fig. 3.

Treatment Offered Following CRC Screening in Asia

Screening has been found to be an effective strategy in reducing CRC incidence and mortality; however, other strategies including treatment are indispensable for improving the effectiveness of screening and quality of life. Treatment is usually targeted and categorized according to the nature of the lesion (precancerous or invasive cancer) and stage of cancer, that is, local disease, local and metastatic disease, and metastatic disease [56]. Colonoscopy has been reported to be associated with a 56% reduction in incidence and a 68% reduction in mortality of CRC [57]. Resection of screening-detected non-invasive neoplasms (adenoma and carcinoma in situ) and surgical resection of invasive cancers are important for the effectiveness of screening as well.

In some of these Asian regions, there is still inadequate clinical capacity in terms of infrastructures (endoscopy units, cancer registries, etc.), oncologists, gastroenterologists, and surgeons (especially females in some Muslim countries) to manage screening-detected lesions [58–63].

CRC Survival Rates and Prognosis in Asia

With the rapidly rising trend of CRC in Asia, survival rates from this disease are mostly dependent on the stage of the disease at the point of diagnosis ranging from a 90% 5-year survival rate for cancers detected at the localized stage and 70% for regional to 10% for people diagnosed with distant metastatic cancer, and this is influenced by the adequate treatment at each stage [14, 64]. However, with recent advances in treatment, mortality rates remain high despite an increase in survival time [64]. A recent study conducted in Malaysia revealed survival rates also depend on ethnicity, with the Chinese patients having the lowest 5-year survival compared with Malay and Indian patients and with male having a lower survival rate [65]. The rates from this Malaysian study were comparable with those found in some Asian countries though still lower than those of more developed

Table 2 Current important issues (clinical or public health) of CRC in Asia

	Challenges	Possible solutions	References
	Screening barriers		
1	Negative attitudes and beliefs including religious or cultural beliefs, aversion, and fatalism Confidence in traditional medicines Embarrassment	- Increase public awareness toward CRC and CRC screening - Targeted public education - Public and physician education - Increase information dissemination - Propaganda, mass media, social networking, NGO	[23–26]
2	Lack of public awareness and poor knowledge (CRC risk factors, symptoms, screening tests, benefits, etc.) Inadequate population engagement	- Increase public awareness toward CRC and CRC screening - Targeted public education - Increase the role of mass media, social networking, and NGO in information dissemination	[27–31]
3	Language barrier	- Information should be disseminated in other languages	[27, 32]
4	Lack of insurance/funding to the program	- Government should provide subsidy - Involvement of NGO - Improvement in the government insurance system	[20, 25, 33, 34]
	Treatment barriers		
5	Low participation in colonoscopy	- CRC screening promotion from physicians - Increase public awareness regarding the very high CRC risk in FIT-positive population - Increase manpower - More detailed explanations needed from physicians to make an informed choice of procedure - Physician's recommendation and improve CRC awareness - Government should provide subsidy for colonoscopy and/or sedation costs	[23, 33, 35, 36]
6	Poverty and the high cost of chemotherapy/target therapy	- Insurance - Unavailability of therapeutic agents (drug lag)	[26, 35]
7	Lack of infrastructure (surgical and endoscopy capacity, equipment) Lack of cancer registry systems Lack of mortality registry system	- Increase funding for the construction of facilities - Infrastructure development - Professional training (involvement of professional societies)	[20, 33, 37]
8	Lack of accessibility (limited service)	- Increase accessibility - Provision of health insurance - Medical resource allocation (minimize inequity) - Reaching out to communities of lower socioeconomic background	[23–26]
9	Lack of adherence (non-compliance) to colonoscopy Low acceptance of colonoscopy The high cost of colonoscopy in some regions/countries	- Using sedated-assisted colonoscopy - The targeted population for colonoscopy after a positive FIT - Insurance - Professional training	[35, 37–39]
10	Lack of the willingness to pay (out-of-pocket)	- Insurance - Financial support	[20, 37, 38]
11	Lack of surveillance guidelines and auditing system	- National programs should develop guidelines using the regional recommendations	[20, 36, 37, 40]

countries [65, 66]. In India, survival rates were lower compared with those in other Asian nations, and this was attributed to inadequate treatment delivery at various stages of the disease at diagnosis [66].

Challenges of CRC Screening and Management in Asia

Usually, screening of CRC in Asia poses a lot of challenges to nationwide screening programs especially in terms of the screening logistics and engaging the population to participate in the initial and subsequent screenings. Low participation and verification rates, lack of public awareness, unawareness of the usefulness of screening by some governments, lack of government willingness to spend on constructing relevant infrastructures, and inadequate manpower remain the major challenges for CRC screening programs in this region [35, 37••]. For the people to participate fully, there is a need for them to have some knowledge of the disease and understanding of the benefits for screening [23•, 67]. It has been observed that negative perception of CRC screening especially among high-risk groups in Malaysia and other Asian communities has been a great challenge within the population [23•, 24–26, 32, 68]. Additionally, researchers need to determine barriers to screening and to look for means to mitigate them thereby creating an environment of

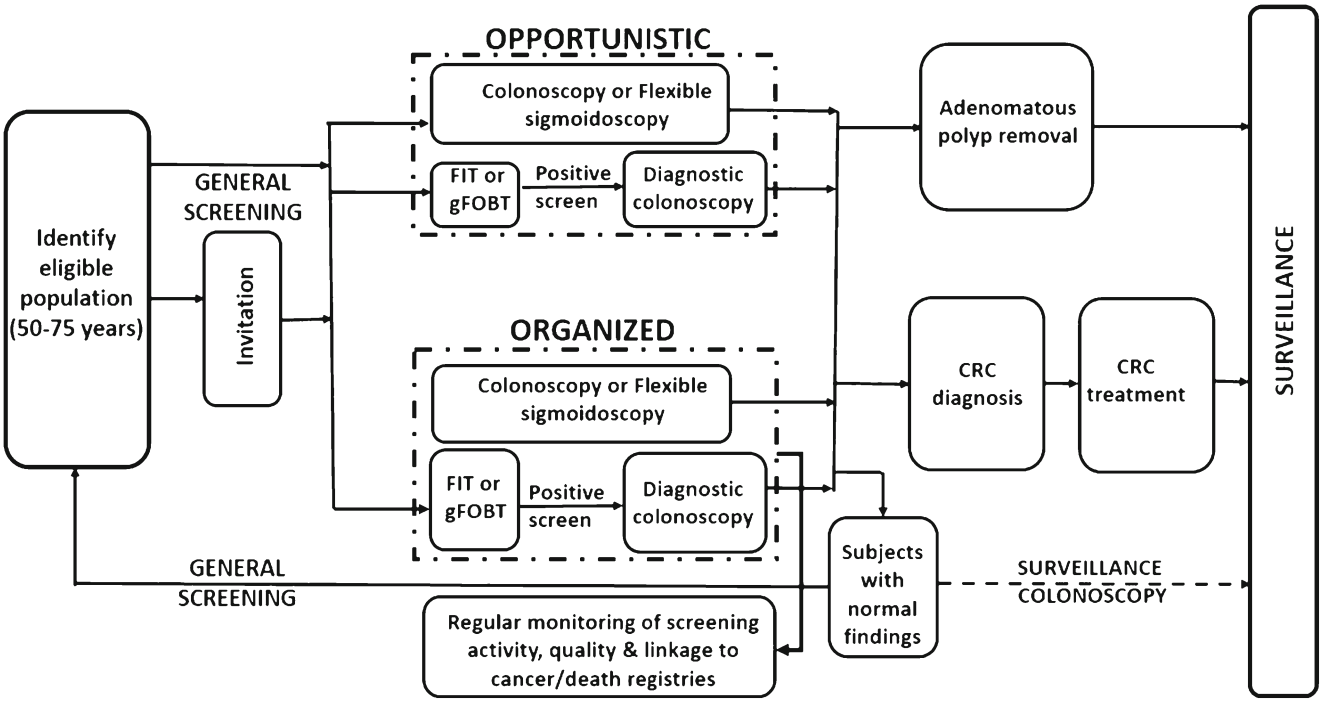

Fig. 3 Common colorectal cancer screening algorithm. Note: generally screening age range is 50 to 75 years, but in Asia, some countries start screening at an earlier age (e.g., Japan, from 40 years) and some have no upper age limit (e.g., Japan and South Korea)

public acceptance. A language barrier has also been found to be a challenge for CRC screening [27, 32, 68]. A lack of health insurance appropriate for CRC screening has been observed as a barrier [20, 25, 33, 69, 70]. Another important barrier to CRC screening is the issue of ethnicity, as in the case of multi-ethnic countries like Malaysia, where the risk of CRC is quite distinct among Chinese, Malay, and Indian [71–73], with the incidence per 100,000 population being highest in Chinese and lowest among Indians [71]. Therefore, it is difficult to obtain a consensus on running a nationwide screening program in such regions [34, 40•].

Due to the large population of most countries in Asia, surgical capacity and manpower have been another challenge in the screening and management of CRC coupled with the fact that there are fewer gastroenterologists and surgeons to perform endoscopies [4, 20••, 33, 37••]. Socioeconomic factors and inequities such as poverty and lack of insurance, especially out-of-pocket expenses with the associated rising cost of chemotherapy, make it very difficult for those in need to access screening, care, and further management of CRC [4, 20••, 33, 37••, 70, 74•, 75].

In addition to other challenges, there is still a lack of national guidelines and auditing system for colorectal cancer screening across Asia except for Japan, Korea, and Taiwan [36, 37••, 40•, 76]. Despite the rising CRC incidence in some of these countries or regions in Asia, the CRC population screening program is still not in place. However, some pilot studies were recently initiated in order to combat this rising incidence of CRC in these regions, particularly in Hong Kong (September 2016) and Thailand (April 2011) [77, 78]. In August 2018, Hong Kong's pilot study finally graduated into a full territory-wide CRC screening program, now in the phase II stage, that started on January 1, 2019, covering asymptomatic residents aged 56 to 75 years, while that of Thailand is ongoing [33, 77, 78]. The CRC pilot study in Lampang, Thailand, is to assess the feasibility, acceptability, and safety of CRC screening in both urban and rural settings and to probably inform the authorities on how best to introduce an organized CRC screening program across the country making use of the existing public health facilities [78–80].

In regions where CRC screening programs are not in place, there is a need to consider using the Asia-Pacific Risk Score to stratify people in terms of CRC risk and guide them through for either FIT or direct colonoscopy. Several studies have demonstrated the usefulness of this strategy in Asia [81–84].

Colonoscopy Quality Assurance and Surveillance Guidelines

The quality assurance for any CRC screening will likely include quality assurance of colonoscopy, professional training, quality assurance of histopathology, management of detected lesions, colonoscopic surveillance after adenoma removal, and communications with subjects [40•]. Auditing of FIT laboratories has equally been shown to be very important in Asia from recent studies in Korea and Taiwan [85, 86]. Therefore, quality assurance is very relevant and a colonoscopy database is indispensable for any organized CRC screening to be effective and

reputable, with Japan and Taiwan taking the lead in Asia [87••, 88]. The Japanese Gastroenterological Endoscopy Society is currently constructing a big colonoscopy database known as the JED Project [88, 89]. The Taiwan screening colonoscopy database is under the framework of the national screening program which has demonstrated the importance of colonoscopy quality assurance [87••].

After screening and treatment of CRC, there is a need for post-screening periodic surveillance, which usually includes performing a post-colonoscopy and quality assurance. By offering surveillance colonoscopy, missed or newly developed neoplasm could be detected thereby providing additional protection against incident CRC. By tailoring the surveillance interval based on the subsequent risk for developing advanced neoplasm, we can also make the most efficient use of constrained colonoscopy resources. In Asia, some countries including Japan and Korea already have some surveillance guidelines following CRC screening [90, 91].

Conclusions

CRC incidence and mortality within Asia vary considerably among countries. This review highlights the changing trends of CRC incidence, mortality, screening modalities, screening challenges, and management approaches in Asia. Asia contributes to the highest CRC disease burden in the world, in terms of incidence and mortality proportions per 100,000 population. In most parts of Asia, the non-invasive stool-based tests (especially FIT) remain the commonly used tools for large-scale organized CRC population screening programs which have become an urgent task for this region. The screening barriers or challenges currently encountered by CRC screening programs in this region need to be dealt with as soon as possible to enable effective screening of the eligible population thereby reducing the CRC incidence and mortality rates.

Acknowledgments The authors thank the staff of the Breast, Oral, and Colorectal Cancer Screening Evaluation Center, College of Medicine, National Taiwan University, for their support.

Funding Source This study was supported by the Health Promotion Administration, Ministry of Health and Welfare of Taiwanese Government (A1011119, A1021227, A1031135, A1041122, A1051013, A1061224, and A1071016).

Compliance with Ethical Standards

Conflict of Interest Elias Onyoh, Wen-Feng Hsu, Li-Chun Chang, Yi-Chia Lee, Ming-Shiang Wu, and Han-Mo Chiu declare no conflict of interest.

Human and Animal Rights and Informed Consent This review does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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