Curr Gastroenterol Rep (2017) 19: 47
DOI 10.1007/s11894-017-0587-4

GI ONCOLOGY (R BRESALIER, SECTION EDITOR)

Colorectal Cancer Screening in Asia

Han-Mo Chiu[1] · Wen-Feng Hsu[2] · Li-Chun Chang[1] · Ming-Hsiang Wu[1]

Published online: 10 August 2017

Abstract

Purpose of Review Colorectal cancer (CRC) is increasing in Asia, especially in regions with higher levels of economic development. Several Asian countries have launched population CRC screening programs to combat this devastating disease because previous studies have demonstrated that either fecal occult blood test or lower gastrointestinal endoscopy can effectively reduce CRC mortality.

Recent Findings Screening includes engaging the population, testing, administering a confirmation examination, and treating screening-detected neoplasms; thus, monitoring the whole process using measurable indicators over time is of utmost importance. Only when the quality of every step is secured can the effectiveness of CRC screening be maximized. Screening and verification examination rates remain low in Asian countries, and important infrastructure, including cancer or death registry systems, colonoscopy capacity, and reasonable subsidization for screening, is lacking or insufficient.

Summary Future research should identify potential local barriers to screening. Good communication and dialog among screening organizers, clinicians, professional societies, and public health workers are indispensible for successful screening programs.

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

✉ Han-Mo Chiu
hanmochiu@ntu.edu.tw

[1] Department of Internal Medicine, National Taiwan University Hospital, Taipei City, Taiwan

[2] Department of Internal Medicine, National Taiwan University Hospital Hsin-Chu Branch, Hsinchu City, Taiwan

Keywords Colorectal cancer · Screening · Asia · Colonoscopy · Population screening · Fecal immunochemical test

Introduction

According to data from the World Health Organization, colorectal cancer (CRC) is currently the fourth leading cause of cancer death worldwide and is prevalent in Asia, where > 40% of the world's cases of CRCs are found [1]. CRC is nowadays not only an important problem in clinical practice but also is a critical challenge for public health. Screening is one of the most efficient ways to prevent CRC death, and previous randomized trials (RCT) with a guaiac fecal occult blood test (gFOBT) have proven effective in reducing death from CRC [2, 3]. Nevertheless, the epidemiology of CRC, in terms of CRC incidence and mortality, differs remarkably across Asian countries because of ethnic diversity, dietary habits, lifestyles, and the level of economic development [4•]. It is generally accepted that when the age-standardized CRC incidence rate exceeds 30 per 100,000, then implementation of population screening is justified [5•]. In Asian countries where CRC incidence and mortality is high, including Japan, Korea, Singapore, and Taiwan, population-based screening programs have been launched to combat this devastating disease [6]. Other regions in Asia are also encountering increasing rates of CRC, especially in economically developing urban areas, and the demand for screening is increasing. Screening, however, is not a single test or examination; rather, it involves a process of population engagement, diagnostic examinations, treatment of detected neoplasms, and periodic surveillance. Moreover, screening programs with measurable indicators are indispensible for ensuring its quality and maximizing the effectiveness of the entire program. In this review, we update the current status of CRC screening activity in Asia and also discuss its future prospects and challenges.

Epidemiology of CRC in Asia

Ethnic group and status of economic development are risk factors associated with CRC. In Asia, Chinese, Japanese, and Korean ethnic groups present higher risks of CRC, whereas Indians and Malays have a lower risk [1]. Even within an ethnic group, those who live in coastal cities have higher rates of CRC mortality and incidence compared with residents of inland cities in China, and Chinese people living in Singapore, Hong Kong, or Taiwan have even higher rates that are associated with their higher level of economic development and their longer duration of exposure to Western lifestyles [7].

According to the data from IARC (GLOBOCAN 2012) and regional health statistics, the age-adjusted incidence (per 100,000) of CRC is 48.1 (male) and 30.7 (female) in Hong Kong, 42.1(male) and 23.5 (female) in Japan, 58.7 (male) and 33.3 (female) in South Korea, 40.1(male) and 28.0 (female) in Singapore, and 53.7 (male) and 37.3 (female) in Taiwan, and most of these rates exceed those in North America or Western Europe [1, 8, 9]. A recent research in China showed a significant increase in CRC incidence (12.8 per 100,000 in 2003 and 16.8 per 100,000 in 2011) and mortality (5.9 to 7.8 per 100,000 during the same period) during the past decade and also showed a discrepancy among regions with different levels of urbanization; the highest rates were found in the eastern coastal provinces [7]. The CRC disease burden is expected to increase in Asia, especially in urbanized regions where screening programs are not in place or have only low levels of screening rate. In addition, the high smoking rates and increasing prevalence of obesity—both of which are significant risk factors associated with CRC—in Asian countries are also of concern [10, 11]. Further action for both primary and secondary prevention of CRC is urgently needed.

Selection of Screening Modality

Both the effectiveness and also the cost-effectiveness are equally important when public health officials select an optimal screening modality for organized screening because public health resource allocation is important.

The effectiveness of sigmoidoscopy in reducing both incidence of and mortality from CRC has been proved by previous RCTs, but its protective effect was confined to the distal colon and rectum because of limitations in the extent to which this examination can reach [12]. Colonoscopy has the advantages of higher performance in detecting colorectal neoplasms (> 95% for invasive cancers and 90% for advanced adenoma) and also of being able to resect noninvasive neoplasms [13]. Although RCTs are lacking, several cohort studies have reported the effectiveness of colonoscopy for reducing CRC incidence and mortality. The results from the US National Polyp Study demonstrated that colonoscopy could reduce CRC incidence of 76–90% and mortality of 53% [14, 15]. Nishihara et al. also reported that colonoscopy was associated with a 56% lower incidence of CRC (after negative colonoscopy) and 68% lower mortality [16]. Despite colonoscopy's greater effectiveness in reducing CRC mortality and incidence, its high cost and invasiveness, staffing and facilities requirements, lower screening uptake levels, and questionable public acceptance, especially among Asian populations, have limited its use as a primary screening modality in this region [17, 18].

Screening with a gFOBT has proven effective in reducing CRC mortality of 15% according to a pooled analysis of previous RCTs [2]. Avoiding the need for dietary restriction with a more user-friendly stool collection device, the fecal immunochemical test (FIT) has demonstrated a better ability than gFOBT to detect early CRC and advanced adenoma, and its effectiveness in reducing CRC mortality has recently also been demonstrated in Taiwanese programs [19, 20•, 21••]. FIT is currently the most widely used primary screening test in population screening programs in Asia [22••, 23]. Approaches to screening intervals and the number of stool samples required for FIT screening, however, vary among programs and should be further investigated and standardized (Table 1).

Postcolonoscopy Surveillance in Asia

Surveillance colonoscopy provides additional protection against CRC after previous colonoscopy by detecting missed or incident neoplasms. Current evidence from Asian countries shows that the risk of advanced neoplasm after baseline colonoscopy in opportunistic colonoscopy screening population is similar compared with that in Western populations [24, 25]. Japan and Korea have national surveillance guidelines, whereas other countries typically follow major US or European guidelines [26]. Although we lack empirical data regarding the use of surveillance colonoscopy in Asian countries, the formulation of surveillance guidelines is of utmost importance to ensure the most efficient use of resources for colonoscopy. The diagnostic yield of early surveillance colonoscopy (surveillance much earlier than the recommended interval) is, however, usually lower than that in the colonoscopy performed for prevalent screening. In addition, early surveillance colonoscopy may consume large portions of existing endoscopy capacity, place additional stress on already overstretched staff, and further prolong the waiting time for colonoscopy following positive FITs. Taken together, these factors may compromise the effectiveness of the screening program [27]. On the other hand, delayed surveillance or noncompliance with recommendations following surveillance colonoscopy may also lead to an increased risk of incident CRC [28].

Table 1 Organized population colorectal cancer screening program in Asia

Country	Age range	Primary screening modality	Screening interval (year)	Verification exam	Subsidization	Start year
Japan	≥ 40	FIT_2	1	CSY or DCBE	Yes (but not for endoscopic sedation)	1992
Korea	≥ 50	FIT_1	1	CSY or DCBE	Total subsidy for low-income population and 90% subsidy for others	2004
Singapore	≥ 50	FIT_2	1	CSY	No	2009
		CSY	10	–		
Taiwan	50–75	FIT_1	2	CSY or DCBE plus FS	Yes (but not for endoscopic sedation)	2004

CSY colonoscopy, *FS* flexible sigmoidoscopy, *DCBE* double-contrast barium enema, *FIT_1* one-sample FIT, *FIT_2* two-sample FIT

In addition, the optimal surveillance interval after baseline colonoscopy in FIT screening programs has yet to be determined and may be different from that in colonoscopy-based screening scenario. A study from Taiwan has shown that the incidence of colorectal cancer after baseline colonoscopy in a FIT screening program was higher than that observed in the colonoscopy-based screening studies [29]. Insufficient colonoscopy quality, which is reflected by cecal intubation rates or adenoma detection rates, may have played an important role in the occurrence of cancer after colonoscopy, FIT-positive patients theoretically have a much higher likelihood of having advanced adenoma (5 times) and invasive cancers (20 times) as compared with general population thus may benefit from a shorter surveillance interval, especially for those with negative colonoscopy results, for whom a 10-year surveillance interval is usually recommended. Further study is necessary.

Piloting, Infrastructure Development, and Monitoring the Screening Program

Screening is not a single test but rather is a continuous process. FIT screening, for example, includes invitation (engagement) of the target population for FIT screening, reporting and notifying patients about FIT results, referral of FIT-positive patients for verification colonoscopy, treatment of detected adenomas or cancers, and subsequent surveillance. Accordingly, setting up an invitation or screening test delivery system, establishing a laboratory for FIT testing, securing sufficient colonoscopy capacity and staff resources, and developing a healthcare team for disease treatment are indispensible steps to ensure the success of a program. Moreover, monitoring and evaluation of the screening program are of utmost importance for securing good quality at every step so that screening organizers can maximize the effectiveness of the program. (Table 2) Ideally, a pilot program should be conducted before the implementation of the full screening program so that those who organize the screening can test the feasibility of screening in the community, identify potential problems, improve infrastructure, or allocate resources beforehand.

In Taiwan, a pilot CRC screening program was conducted in Keelung City in 1999 before the implementation of the national screening program, which was launched in 2004. In this pilot program, we observed good public acceptance of FIT (82% screening uptake) and acceptable compliance with colonoscopy in FIT-positive subjects (80% colonoscopy rate). The positivity rate of 4% among subjects screened also confirmed the affordable level of colonoscopy required following FIT screening [30]. Using the empirical data from this pilot program, the optimal cutoff level for FIT (20 μg hemoglobin/g of feces), which is currently applied in the national program, was then determined based on the results of the receiver operating curve analysis and cost-effectiveness analysis taking into account the clinical scenario and medical costs in Taiwan [31]. We can also use the empirical data from the pilot program in a Markov natural history model to simulate the long-term effectiveness of the screening program. [30] Currently some Asian regions, such as Thailand and Hong Kong, have started pilot programs in preparation for the full program [32–34].

In organized CRC screening programs, several screening indicators should be implemented and regularly monitored [23]. Theoretically, CRC mortality or incidence is the most robust outcome to represent the effectiveness of the screening program. However, mortality or incidence rates require long-term follow-up before healthcare providers can observe significant changes; therefore, implementation of corrective actions based on indictors that are relevant to those outcomes is mandatory [35].

Early Indicators

For organized FIT screening programs, early indicators include screening participation rates, FIT positivity rates, colonoscopy rates after positive FIT, detection rate for neoplasms (invasive cancer, advanced adenoma, or non-advanced adenoma), and the positive predictive value of various categories of neoplasms in FIT-positive patients [23]. Regarding the safety of the screening, it is also important to monitor the rate of significant complications, including perforation and bleeding that require hemostasis or transfusion.

Table 2 Indicators and relevant infrastructures that are necessary for quality assurance and evaluation of organized population CRC screening program

Period	Indicators	Infrastructures
Short-term indicators	• FIT screening rate (uptake rate/coverage rate of eligible population) • FIT positivity rate • Verification exam rate (colonoscopy or other exam for FIT-positive subjects) • Detection rate for cancers, advanced adenoma and non-advanced adenoma (for those who received FIT kits) • Positive predictive values for cancers, advanced adenoma and non-advanced adenoma (for those who received colonoscopy) • Indicators relevant to colonoscopy quality (complete rate, adenoma detection rate, bowel cleansing rate, etc.) • Severe complication rate (bleeding and perforation)	• Legislation or development of laws to ensure cancer screening • Household registry system (to identify eligible population or to generate invitation list) • Screening test (FIT) kit delivery system • Laboratory for FIT testing and pathology • Colonoscopy capacity (facility and manpower) • Competency to manage screening-detected neoplasms • Standardized colonoscopy reporting format • Public health professionals/workers • Reasonable subsidization and payment systems
Mid-term indicators	• Interval cancers (FIT IC or colonoscopy IC) • Stage shifting	• Territory-wide cancer registry system • Expert committee to judge IC cases
Long-term indicators	• CRC incidence • CRC mortality	• Territory-wide cancer registry system • Territory-wide death registry system

Intermediate Indicators

Intermediate indicators include stage shift (changes in the proportion of early- or advanced-stage cancers in screening-detected cancers compared with non-screening-detected cancers) and interval cancer rate [including "FIT interval cancers (FIT IC)" that occur within the inter-screening interval after a negative FIT and "colonoscopy interval cancers (Colonoscopy IC)" that occur after a verification colonoscopy but before the next recommended surveillance examination] [36••]. The former (stage shift) is an early surrogate endpoint of mortality reduction, the latter (interval cancer rate) is an indicator of program sensitivity, and both are closely associated with screening effectiveness. Ascertainment of cancer stage or interval cancer, however, requires a comprehensive cancer registry system with a high coverage rate.

Long-Term Indicators

As for long-term indicators, changes in CRC mortality and incidence are the ultimate endpoints to observe, and both cancer and death registry systems are required for such an analysis. Because of the slow natural history of colorectal neoplasms, it usually requires 5 to 10 years before we can observe changes in CRC mortality and incidence. Moreover, adjustment for changing CRC epidemiology is also necessary to yield a more precise estimate of screening effectiveness. In addition, population service screening is different from RCT and self-selection bias (e.g., those who sought screening may have more healthful lifestyles or dietary habits) may exist and may affect the estimate of effectiveness that is actually attributable to screening.

Colonoscopy Quality Assurance

Colonoscopy plays a pivotal role in a CRC screening program as a final verification examination, and its quality is closely associated with the effectiveness of the screening program. Several colonoscopy quality indicators have been proposed, including cecal intubation rate (complete colonoscopy rate), adenoma detection rate (ADR), and bowel cleansing level. Previous studies have demonstrated that some of those indicators are closely associated with future risk of colonoscopy IC (or postcolonoscopy CRC) or even mortality associated with CRC [37•, 38•, 39].

Of these, ADR is probably the most important and is considered to be a surrogate of other quality indicators. Kaminski et al. first demonstrated that ADR is inversely associated with the risk of interval CRC [37•]. Corley et al. further reported that not only was ADR inversely associated with the incidence of CRC, but it also was inversely associated with the risk of advanced-stage CRC and CRC mortality: Each 1% increase in ADR was associated with a 3% decrease in CRC incidence and a 5% decrease in CRC mortality [38•]. The only report from a FIT-based screening program in Taiwan demonstrated that ADR, together with cecal intubation rate, was associated with colonoscopy IC [29]. Although the American Society for Gastrointestinal Endoscopy/American College of Gastroenterology Task Force on Quality in Endoscopy has recommended a benchmark threshold of ADR for screening colonoscopy (30% for males and 20% for females), the optimal ADR for the FIT-positive population remains to be elucidated, because FIT-positive patients actually represent a high-risk population with a much higher prevalence of significant neoplasms compared with the general average-risk population [40, 41]. Here, too, further study is necessary.

Implementation of a standardized colonoscopy reporting format is indispensible for monitoring colonoscopy quality indicators [42, 43]. The Dutch Bowel Cancer Screening Program was launched in 2014, and at the mean time, they implemented a standardized colonoscopy reporting system. All items that are relevant to colonoscopy quality indicators are included in this system, and thereby, the screening organizer can monitor the quality of colonoscopy either at the endoscopist, hospital, regional, or national level [44]. In Asia, Taiwan and Japan are now constructing similar systems to ensure the quality of colonoscopy. In Japan, the Japan Endoscopy Database project was launched in 2015 under the supervision of the Japanese Gastroenterological Endoscopy Society. Colonoscopy data for all purposes, including screening, diagnostic, and therapeutic, were collected in this project's database, which included a total of 16,799 total colonoscopies conducted from July to December 2015, as the first period of this project [45]. In Taiwan, the colonoscopy quality assurance project has been in operation since 2011 within the framework of a national screening program. Since 2015, endoscopists performing verification colonoscopy for FIT-positive patients have been asked to record the endoscopic findings using a standardized format, and currently, 89,645 procedures (colonoscopies only for FIT-positive patients from January 2015 to February 2017) have been documented in this database. In the future, via this platform, individual endoscopy units or even individual endoscopists can periodically obtain feedback regarding their own cecal intubation rates, bowel cleansing levels, and adenoma or cancer detection rates that can be used for further quality improvement.

Challenges and Future Perspectives

Nevertheless, the increasing incidence of CRC in Asia, many people in this region still are not aware of the threat of CRC. Currently, the screening rate in Asian programs is still low, and the verification examination rate (colonoscopy or other) is also unsatisfactory in comparison with Western programs (Table 3). The Asia-Pacific working group on CRC previously conducted a survey in the Asia-Pacific region and demonstrated that the public awareness of CRC and the perceived need for CRC screening are lacking, and some potential barriers are present, including financial and access barriers [49]. This study in the Asia-Pacific region also revealed that a physician's recommendation was the most significant factor that motivated people to seek screening; therefore, educational interventions for both the public and physicians are important to improve screening uptake. In this respect, several approaches can be considered. First, in areas without population screening services, risk stratification is important to identify the population at risk of CRC or advanced adenoma. The Asia-Pacific risk score is a useful and validated tool that uses simple population demographics such as age, sex, smoking status, and family history of CRC to triage people who may require early colonoscopy [50]. In areas without a population screening program but with an increasing trend of CRC, clinicians can use this tool to make the most efficient use of available colonoscopy resources, whereas in areas with a screening program but insufficient screening uptake, such a risk scoring system is also expected to enhance public awareness [51]. Second, educational interventions to enhance public awareness and physician knowledge about CRC and CRC screening may also be helpful. Currently, studies of such interventions are very limited in Asia.

Another barrier to CRC screening in Asia is the subsidization system, because lack of financial support has been studied and now is recognized as an important barrier to screening [52, 53]. In Korea, previously only 50% of the cost of CRC screening is subsidized by the government (initial 2 years since the launch of the national program), except for low-income patients for whom the screening cost is totally subsidized but later subsidizes most of the screening fee (80% from 2006 to 2009 and 90% since 2010) for the sake of improving screening rate. In Taiwan, although the cost for screening, including FIT and colonoscopy after positive FIT, is subsidized by the government, the fee for conscious sedation is not subsidized and thus is considered to be one of the contributing factors in unsatisfactory colonoscopy compliance (approximately 70% in 2016). The level of reimbursement for colonoscopy per se in some Asian countries is obviously too low (US$60 in Korea, US$75 in Taiwan, and US$134 in Japan), especially when compared with that in Western countries, even taking into account the level of economic development, the standard of living, and the similar or even higher payments for other noninvasive procedure in the same country. Low levels of medical coverage or reimbursement for

Table 3 Current status of Asian colorectal cancer screening programs

Country	Screening rate	Verification rate	Surveillance guidelines	Cancer registry system (population-based)	Reference
Japan	Male: 41.4% (2013) Female: 34.5%	≅ 70%	Yes	Yes (since 2016)	[46]
Korea	35.7% (2016)	47.1% (2016)	Yes	Yes (since 2004)	[47]
Taiwan	38% (2-year rate, 2015–2016)	68% (2016)	No	Yes (since 1979)	[6, 48]

colonoscopy may also hinder the willingness of the physician to spend time on persuading FIT-positive patients who are reluctant to receive colonoscopy to receive exam because the procedure time is expected to be much longer (because of more likely to have multiple adenoma or advanced adenoma) but the payment is equivalent to ordinary colonoscopy.

Finally, all organized screening programs must determine if their programs have really reduced CRC-related mortality. In this regard, some important infrastructure, such as territory-wide cancer and death registries, is indispensible for a population screening program. Japan started a nationwide cancer registry in January 2016. Before that, Japan was not able to evaluate the effectiveness of the national screening program even though Japan has the oldest FIT CRC screening program not only in Asia but also in the world, which was launched in 1992. Obtaining consensus among major stakeholders, screening organizers, and professional bodies is mandatory for the sake of legislative support and setting up the needed infrastructure. Moreover, good communication and joint co-operative efforts among professional societies, public health workers, regional or central governments, and other stakeholders are also important and play a pivotal role in the success of an organized screening program.

Finally, sharing experiences among Asian countries and joining the international screening network are probably the most efficient ways to learn from successful programs worldwide and to orient and improve national screening programs.

Acknowledgements We would like to express our sincere appreciation for the valuable input for regional screening information from professor Hyun-Soo Kim (Yonsei University Wonju College of Medicine, Korea) and professor Yutaka Saito (National Cancer Center Hospital, Tokyo, Japan)

Compliance with Ethical Standards

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

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

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. 2015. http://globocan.iarc.fr. Accessed 16 June 2015.
2. Hewitson P, Glasziou P, Watson E, Towler B, Irwig L. Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update. Am J Gastroenterol. 2008;103(6):1541–9. doi:10.1111/j.1572-0241.2008.01875.x.
3. Edwards BK, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975–2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010;116(3):544–73. doi:10.1002/cncr.24760.
4.• Sung JJ, Lau JY, Goh KL, Leung WK. Asia Pacific Working Group on Colorectal C. Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol. 2005;6(11):871–6. doi:10.1016/S1470-2045(05)70422-8. **A comprehensive review on the current epidemiology of CRC in Asia.**
5.• Gelband H, Jha P, Sankaranarayanan R, Horton S, World Bank. Cancer. Disease control priorities, vol. 3. Washington, DC: The World Bank; 2015. **Chapter 6 is a comprehensive review on current global epidemiology of CRC and effective intervention, especiallly screening, to reduce its disease burden. Various screening modalities and strategies were addressed and compared**
6. Chiu HM, Chang LC, Hsu WF, Chou CK, Wu MS. Non-invasive screening for colorectal cancer in Asia. Best Pract Res Clin Gastroenterol. 2015;29(6):953–65. doi:10.1016/j.bpg.2015.09.015.
7. Zhu J, Tan Z, Hollis-Hansen K, Zhang Y, Yu C, Li Y. Epidemiological trends in colorectal cancer in China: an ecological study. Dig Dis Sci. 2017;62(1):235–43. doi:10.1007/s10620-016-4362-4.
8. Taiwan Cancer Registry. Health promotion administration, Ministry of Health and Welfare 2015. 2011. http://www.hpa.gov.tw/English/ClassShow.aspx?No=201203070002. Accessed 25 June 2015.
9. Registry. HAC. Hong Kong Cancer Registry. 2014. http://www3.ha.org.hk/cancereg/.
10. Giovino GA, Mirza SA, Samet JM, Gupta PC, Jarvis MJ, Bhala N, et al. Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional household surveys. Lancet. 2012;380(9842):668–79. doi:10.1016/S0140-6736(12)61085-X.
11. Arnold M, Pandeya N, Byrnes G, Renehan AG, Stevens GA, Ezzati M, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol. 2015;16(1):36–46. doi:10.1016/S1470-2045(14)71123-4.
12. Elmunzer BJ, Hayward RA, Schoenfeld PS, Saini SD, Deshpande A, Waljee AK. Effect of flexible sigmoidoscopy-based screening on incidence and mortality of colorectal cancer: a systematic review and meta-analysis of randomized controlled trials. PLoS Med. 2012;9(12):e1001352. doi:10.1371/journal.pmed.1001352.
13. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. Am J Gastroenterol. 2006;101(2):343–50. doi:10.1111/j.1572-0241.2006.00390.x.
14. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med. 1993;329(27):1977–81. doi:10.1056/NEJM199312303292701.
15. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366(8):687–96. doi:10.1056/NEJMoa1100370.
16. Nishihara R, Wu K, Lochhead P, Morikawa T, Liao X, Qian ZR, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med. 2013;369(12):1095–105. doi:10.1056/NEJMoa1301969.
17. Inadomi JM, Vijan S, Janz NK, Fagerlin A, Thomas JP, Lin YV, et al. Adherence to colorectal cancer screening: a randomized

clinical trial of competing strategies. Arch Intern Med. 2012;172(7): 575–82. doi:10.1001/archinternmed.2012.332.

18. Quintero E, Castells A, Bujanda L, Cubiella J, Salas D, Lanas A, et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. N Engl J Med. 2012;366(8):697–706. doi:10.1056/NEJMoa1108895.
19. Park DI, Ryu S, Kim YH, Lee SH, Lee CK, Eun CS, et al. Comparison of guaiac-based and quantitative immunochemical fecal occult blood testing in a population at average risk undergoing colorectal cancer screening. Am J Gastroenterol. 2010;105(9): 2017–25. doi:10.1038/ajg.2010.179.
20.• van Rossum LG, van Rijn AF, Laheij RJ, van Oijen MG, Fockens P, van Krieken HH, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. Gastroenterology. 2008;135(1):82–90. doi: 10.1053/j.gastro.2008.03.040. **This is a benchmark literature demonstrating the superiority of fecal immunochemical test over guaiac test in public participation/uptake.**
21.•• Chiu HM, Chen SL, Yen AM, Chiu SY, Fann JC, Lee YC, et al. Effectiveness of fecal immunochemical testing in reducing colorectal cancer mortality from the One Million Taiwanese Screening Program. Cancer. 2015;121(18):3221–9. doi:10.1002/cncr.29462. **The first report of FIT on reducing colorectal cancer mortality in a service screening program.**
22.•• Schreuders EH, Ruco A, Rabeneck L, Schoen RE, Sung JJ, Young GP, et al. Colorectal cancer screening: a global overview of existing programmes. Gut. 2015;64(10):1637–49. doi:10.1136/gutjnl-2014-309086. **A comprehensive review of current colorectal cancer screening program worldwide.**
23. Benson VS, Atkin WS, Green J, Nadel MR, Patnick J, Smith RA, et al. Toward standardizing and reporting colorectal cancer screening indicators on an international level: The International Colorectal Cancer Screening Network. Int J Cancer. 2012;130(12):2961–73. doi:10.1002/ijc.26310.
24. Chiu HM, Lee YC, Tu CH, Chang LC, Hsu WF, Chou CK, et al. Effects of metabolic syndrome and findings from baseline colonoscopies on occurrence of colorectal neoplasms. Clin Gastroenterol Hepatol. 2015;13(6):1134–1142.e8. doi:10.1016/j.cgh.2014.10.022.
25. Chung SJ, Kim D, Song JH, Kang HY, Chung GE, Choi J, et al. Comparison of detection and miss rates of narrow band imaging, flexible spectral imaging chromoendoscopy and white light at screening colonoscopy: a randomised controlled back-to-back study. Gut. 2014;63(5):785–91. doi:10.1136/gutjnl-2013-304578.
26. Matsuda T, Chiu HM, Sano Y, Fujii T, Ono A, Saito Y. Surveillance colonoscopy after endoscopic treatment for colorectal neoplasia: from the standpoint of the Asia-Pacific region. Dig Endosc. 2016;28(3):342–7. doi:10.1111/den.12622.
27. Meester RG, Zauber AG, Doubeni CA, Jensen CD, Quinn VP, Helfand M, et al. Consequences of increasing time to colonoscopy examination after positive result from fecal colorectal cancer screening test. Clin Gastroenterol Hepatol. 2016;14(10):1445–1451 **e8**. doi:10.1016/j.cgh.2016.05.017.
28. van Heijningen EM, Lansdorp-Vogelaar I, Steyerberg EW, Goede SL, Dekker E, Lesterhuis W, et al. Adherence to surveillance guidelines after removal of colorectal adenomas: a large, community-based study. Gut. 2015;64(10):1584–92. doi:10.1136/gutjnl-2013-306453.
29. Chiu SY, Chuang SL, Chen SL, Yen AM, Fann JC, Chang DC, et al. Faecal haemoglobin concentration influences risk prediction of interval cancers resulting from inadequate colonoscopy quality: analysis of the Taiwanese Nationwide Colorectal Cancer Screening Program. Gut. 2017;66(2):293–300. doi:10.1136/gutjnl-2015-310256.
30. Yang KC, Liao CS, Chiu YH, Yen AM, Chen TH. Colorectal cancer screening with faecal occult blood test within a multiple disease screening programme: an experience from Keelung, Taiwan. J Med Screen. 2006;13(Suppl 1):S8–13.
31. Chen LS, Liao CS, Chang SH, Lai HC, Chen TH. Cost-effectiveness analysis for determining optimal cut-off of immunochemical faecal occult blood test for population-based colorectal cancer screening (KCIS 16). J Med Screen. 2007;14(4):191–9. doi: 10.1258/096914107782912022.
32. Trial of colorectal cancer screening in a Thai population (TCTR20160410001). http://www.clinicaltrials.in.th/index.php?tp=regtrials&menu=trialsearch&smenu=fulltext&task=search&task2=view1&id=1787. Accessed 23 Mar 2017.
33. Khuhaprema T, Sangrajrang S, Lalitwongsa S, Chokvanitphong V, Raunroadroong T, Ratanachu-Ek T, et al. Organised colorectal cancer screening in Lampang Province, Thailand: preliminary results from a pilot implementation programme. BMJ Open. 2014;4(1): e003671. doi:10.1136/bmjopen-2013-003671.
34. Hong Kong Colorectal Cancer Screening Pilot Programme. http://www.colonscreen.gov.hk/en/public/index.html. Accessed 23 Mar 2017.
35. Fayad NF, Kahi CJ. Quality measures for colonoscopy: a critical evaluation. Clin Gastroenterol Hepatol. 2014;12(12):1973–80. doi: 10.1016/j.cgh.2013.09.052.
36.•• Sanduleanu S, le Clercq CM, Dekker E, Meijer GA, Rabeneck L, Rutter MD, et al. Definition and taxonomy of interval colorectal cancers: a proposal for standardising nomenclature. Gut. 2015;64(8):1257–67. doi:10.1136/gutjnl-2014-307992. **Current consensus on the definition of interval cancers in colorectal screening program by the international expert panel.**
37.• Kaminski MF, Regula J, Kraszewska E, Polkowski M, Wojciechowska U, Didkowska J, et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010;362(19):1795–803. doi:10.1056/NEJMoa0907667. **Important study linking colonoscopy adenoma detction rate to the risk of interval colorectal cancer.**
38.• Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med. 2014;370(14):1298–306. doi:10.1056/NEJMoa1309086. **Important study linking colonoscopy adenoma detection rate to the risk of interval colorectal cancer and colorectal cancer mortality.**
39. Baxter NN, Sutradhar R, Forbes SS, Paszat LF, Saskin R, Rabeneck L. Analysis of administrative data finds endoscopist quality measures associated with postcolonoscopy colorectal cancer. Gastroenterology. 2011;140(1):65–72. doi:10.1053/j.gastro.2010.09.006.
40. Hilsden RJ, Bridges R, Dube C, McGregor SE, Naugler C, Rose SM, et al. Defining benchmarks for adenoma detection rate and adenomas per colonoscopy in patients undergoing colonoscopy due to a positive fecal immunochemical test. Am J Gastroenterol. 2016;111(12):1743–9. doi:10.1038/ajg.2016.449.
41. Rex DK, Schoenfeld PS, Cohen J, Pike IM, Adler DG, Fennerty MB, et al. Quality indicators for colonoscopy. Am J Gastroenterol. 2015;110(1):72–90. doi:10.1038/ajg.2014.385.
42. Lieberman D, Nadel M, Smith RA, Atkin W, Duggirala SB, Fletcher R, et al. Standardized colonoscopy reporting and data system: report of the Quality Assurance Task Group of the National Colorectal Cancer Roundtable. Gastrointest Endosc. 2007;65(6): 757–66. doi:10.1016/j.gie.2006.12.055.
43. Rembacken B, Hassan C, Riemann JF, Chilton A, Rutter M, Dumonceau JM, et al. Quality in screening colonoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE). Endoscopy. 2012;44(10):957–68. doi:10.1055/s-0032-1325686.
44. van Doorn SC, van Vliet J, Fockens P, Dekker E. A novel colonoscopy reporting system enabling quality assurance. Endoscopy. 2014;46(3):181–7. doi:10.1055/s-0034-1364877.

45. Society JGE. JED-Project (Japan Endoscopy Database Project). http://www.jges.net/jedproject/. Accessed 24 Mar 2017.
46. Sano Y, Byeon JS, Li XB, Wong MC, Chiu HM, Rerknimitr R, et al. Colorectal cancer screening of the general population in East Asia. Dig Endosc. 2016;28(3):243–9. doi:10.1111/den.12579.
47. Choi KS, Lee HY, Jun JK, Shin A, Park EC. Adherence to follow-up after a positive fecal occult blood test in an organized colorectal cancer screening program in Korea, 2004–2008. J Gastroenterol Hepatol. 2012;27(6):1070–7. doi:10.1111/j.1440-1746.2011.06944.x.
48. Taiwan Cancer Registry. http://tcr.cph.ntu.edu.tw/main.php?Page=N1. Accessed 20 March 2017.
49. Koo JH, Leong RW, Ching J, Yeoh KG, Wu DC, Murdani A, et al. Knowledge of, attitudes toward, and barriers to participation of colorectal cancer screening tests in the Asia-Pacific region: a multicenter study. Gastrointest Endosc. 2012;76(1):126–35. doi:10.1016/j.gie.2012.03.168.
50. Yeoh KG, Ho KY, Chiu HM, Zhu F, Ching JY, Wu DC, et al. The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects. Gut. 2011;60(9):1236–41. doi:10.1136/gut.2010.221168.
51. Chiu HM, Ching JY, Wu KC, Rerknimitr R, Li J, Wu DC, et al. A risk-scoring system combined with a fecal immunochemical test is effective in screening high-risk subjects for early colonoscopy to detect advanced colorectal neoplasms. Gastroenterology. 2016;150(3):617–625 **e3**. doi:10.1053/j.gastro.2015.11.042.
52. Myong JP, Shin JY, Kim SJ. Factors associated with participation in colorectal cancer screening in Korea: the Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV). Int J Color Dis. 2012;27(8):1061–9. doi:10.1007/s00384-012-1428-4.
53. Wools A, Dapper EA, de Leeuw JR. Colorectal cancer screening participation: a systematic review. Eur J Pub Health. 2016;26(1):158–68. doi:10.1093/eurpub/ckv148.