

Recommendations on prevention and screening for colorectal cancer in Hong Kong

Cancer Expert Working Group on Cancer Prevention and Screening

ABSTRACT

Colorectal cancer is the commonest cancer in Hong Kong. The Cancer Expert Working Group on Cancer Prevention and Screening was established in 2002 under the Cancer Coordinating Committee to review local and international scientific evidence, assess and formulate local recommendations on cancer prevention and screening. At present, the Cancer Expert Working Group recommends that average-risk individuals aged 50 to 75 years and without significant family history consult their doctors to consider screening by: (1) annual or biennial faecal occult blood test, (2) sigmoidoscopy every 5 years, or (3) colonoscopy every 10 years. Increased-risk individuals with significant family history such as those with a first-degree relative diagnosed with

colorectal cancer at age ≤ 60 years; those who have more than one first-degree relative diagnosed with colorectal cancer irrespective of age at diagnosis; or carriers of genetic mutations associated with familial adenomatous polyposis or Lynch syndrome should start colonoscopy screening earlier in life and repeat it at shorter intervals.

Hong Kong Med J 2018;24:521–6

DOI: 10.12809/hkmj177095

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Introduction

In Hong Kong, the Cancer Coordinating Committee is a high-level committee chaired by the Secretary for Food and Health to steer the direction of work on prevention and control of cancer. Under the Cancer Coordinating Committee, the Cancer Expert Working Group (CEWG) on Cancer Prevention and Screening was established in 2002 to review local and international scientific evidence and practices with a view to making recommendations on cancer prevention and screening suitable for Hong Kong.

This article details the local burden and prevention of colorectal cancer (CRC), and explains the rationale underpinning the current CEWG recommendations on CRC screening, which were reaffirmed and updated in 2017.

Local epidemiology

Colorectal cancer is the commonest cancer in Hong Kong. According to the Hong Kong Cancer Registry, there were 5036 newly registered CRC cases in 2015, representing 16.6% of all new cancer cases.¹ The age-standardised incidence rates were 41.5 per 100 000 population for men and 26.2 per 100 000 population for women.¹ The median age at diagnosis of CRC was 68 years in men and 70 years in women.¹ The age-specific incidence rates increased significantly from age 50 years. Colorectal cancer is more common in men with the male-to-female ratio of 1.3:1 for new cases in 2015.¹

The Death Registry registered 2089 deaths caused by CRC in 2016, representing 14.7% of all cancer deaths and ranking it the second leading cause of cancer deaths in Hong Kong.² The age-standardised mortality rates were 18.0 per 100 000 population for men and 10.5 per 100 000 population for women.² After adjusting for the effect of population ageing, the age-standardised incidence rates for both sexes still showed an upward trend, whereas the age-standardised mortality rates for both sexes have remained stable for more than 30 years.²

Risk factors

Risk factors for developing CRC may be modifiable or non-modifiable. Modifiable risk factors are those that are related to lifestyle, such as physical inactivity, low fibre intake, consumption of red meat or processed meat, overweight or obesity, smoking, and alcohol use. The World Health Organization's International Agency for Research on Cancer classifies consumption of processed meat as "carcinogenic to humans (Group I)," and consumption of red meat as "probably carcinogenic to humans (Group 2A)" and indicated that every 50-g portion of processed meat eaten daily increases the risk of CRC by about 18%.³ Conversely, the risk of CRC is inversely associated with intake of fibre.⁴ In addition, the International Agency for Research on Cancer considered that there is sufficient evidence to classify alcoholic beverage and tobacco smoking

香港的大腸癌預防及篩查建議

癌症預防及普查專家工作小組

大腸癌是香港最常見的癌症。「癌症事務統籌委員會」轄下的「癌症預防及普查專家工作小組」（專家工作小組）於2002年成立，負責檢視本港及國際間的科學證據，以便評估和制定適用於本地情況的癌症預防及普查建議。現時，專家工作小組建議年齡介乎50歲至75歲及沒有明顯家族史的一般風險人士應與醫生商討，考慮使用以下任何一種方法進行大腸癌篩查：（1）每1至2年接受一次大便隱血測試、（2）每5年接受一次乙狀結腸鏡檢查，或（3）每10年接受一次大腸鏡檢查。至於有明顯家族史的較高風險人士，例如有一位直系親屬於60歲或之前患上大腸癌、多於一位直系親屬患上大腸癌（不論確診時的年齡），或帶有家族性大腸腺癌肉病或連氏綜合症突變基因的人士，應及早及更頻密地進行大腸癌篩查。

as carcinogenic to humans in the development of CRC.⁵ Separately, the World Cancer Research Fund/American Institute for Cancer Research reported that being overweight or obese can increase the risk of CRC, whereas increased physical activity is associated with reduction in risk.⁶

Non-modifiable risk factors include ageing, male gender, positive family history, history of familial adenomatous polyposis, Lynch syndrome (previously known as hereditary non-polyposis CRC), colonic polyp, and ulcerative colitis.

Based on local epidemiology, CRC is more common in men and its risk increases significantly from age 50 years.¹ Regarding family history, according to a local study, 80% to 90% of CRC cases are sporadic, and the remaining 10% to 20% are familial cancers.⁷ The cancer risk of individuals with a positive family history may vary according to the age of diagnosis of CRC in the index patient and the number of affected first-degree relatives. The younger the age of diagnosis of CRC in the index patient, the higher the risk of CRC of family members would be. In a meta-analysis, the estimated relative risk of individuals with relatives diagnosed with CRC at age <50 years was 3.55, whereas that for relatives diagnosed with CRC at age ≥50 years was 2.18.⁸

Familial adenomatous polyposis is an autosomal dominant disorder caused by germline mutation of the adenomatous polyposis coli gene located on the short arm of chromosome 5 (5q21-22).⁹ Individuals with this mutation have a 95% chance of developing CRC by age 50 years.¹⁰ Lynch syndrome is another dominantly inherited CRC syndrome. It is caused by germline mutation in one of the genes responsible for the repair of mismatches during DNA replication. The lifetime risk of CRC for those carrying this mutation is estimated to be 50% to 80%.¹⁰

Ulcerative colitis has been associated with an increased risk of developing CRC, likely caused by long-standing chronic inflammation.¹¹ Moreover, CRC arises predominantly from adenomatous polyps, which can develop into CRC after ≥10 years.¹² Development of larger polyps, villous histology, and severe dysplasia are important indicators for progression into CRC.¹³

Primary prevention

Primary prevention is of utmost importance for the prevention of CRC as many of the risk factors are modifiable. For preventing CRC, the CEWG recommends:

- increasing intake of dietary fibre (eg, fibre from at least five servings of fruits and vegetables daily);
- decreasing consumption of red and processed meat;
- taking part in moderate-intensity aerobic physical activities for ≥150 minutes per week;
- maintaining a healthy body weight with body mass index between 18.5 to 22.9 and waist circumference <80 cm for women and <90 cm for men;
- avoiding or quitting tobacco smoking; and
- avoiding alcoholic drinks.

Secondary prevention

Secondary prevention involves screening individuals without symptoms in order to detect disease or identify individuals who are at increased risk of disease. Since CRC arises predominantly from precancerous adenomatous polyps developed over a long latent period, it is one of the few cancers that can be effectively prevented through organised and evidence-based screening. In general, for CRC screening, individuals can be classified into “average risk” and “increased risk” groups.

According to screening recommendations made by the CEWG, increased-risk individuals are those with a significant family history, such as an immediate relative diagnosed with CRC at age ≤60 years; more than one immediate relatives diagnosed with CRC irrespective of age at diagnosis; or immediate relatives diagnosed with hereditary bowel diseases. Average-risk individuals are those aged 50 to 75 years who do not have the aforesaid family history.

Screening for general population at average risk

Since 2010, the CEWG has recommended that average-risk individuals aged 50 to 75 years should consult their doctors to consider one of the following screening methods:

- annual or biennial faecal occult blood test (FOBT);

- sigmoidoscopy every 5 years; and
- colonoscopy every 10 years.

The CEWG made the above recommendations after taking into consideration local epidemiology, research evidence, as well as international guidelines and practices.

The age range recommended for CRC screening in the general population should be defined to capture the largest number of CRC cases while taking into account the efficacy and cost-effectiveness of screening tests, local epidemiology, and anticipated benefits and harms to the screened population. In Hong Kong, the risk of CRC increases significantly from age 50 years.¹ Guidelines in US^{14,15} and Singapore¹⁶ recommend starting screening at age 50 years, whereas guidelines in the UK recommend starting screening at age >50 years.¹⁷

Regarding screening modalities, FOBT, sigmoidoscopy and colonoscopy have been shown to reduce mortality from CRC. Faecal occult blood tests can decrease CRC mortality by 15% to 33%, according to findings from large-scale randomised control trials.¹⁸⁻²⁰ A Cochrane review showed that screening by FOBT might reduce CRC mortality in the average risk population by 16%.²¹ Sigmoidoscopy has been shown to lead to a 28% risk reduction in overall CRC mortality and a 43% risk reduction in distal CRC mortality in a meta-analysis.²² Colonoscopy was associated with 61% reduction in CRC mortality in another meta-analysis.²³

International guidelines and practices for CRC screening in the general population mainly recommend annual or biennial FOBT, sigmoidoscopy once every 5 years, or colonoscopy once every 10 years.^{15,16}

To reduce the burden arising from CRC, the government launched the 3-year Colorectal Cancer Screening Pilot Programme (Pilot Programme) on 28 September 2016 to provide subsidised screening by phases to average risk Hong Kong residents born in 1946 to 1955 (aged 61-70 years in 2016). The screening workflow comprises two stages. Participants first receive a subsidised faecal immunochemical test (a new version of FOBT) from an enrolled primary care doctor. If the faecal immunochemical test result is positive, the participant receives a subsidised colonoscopy examination from a colonoscopy specialist enrolled in the Pilot Programme. In August 2018, the government regularised the programme and would progressively extend it to cover individuals aged 50 to 75 years. Details are available at <http://www.colonscreen.gov.hk>.

Screening for increased-risk individuals

In 2017, the CEWG updated the CRC screening recommendations for increased-risk individuals.

The key change was related to the interval for colonoscopy screening among individuals with significant family history of CRC but without genetic mutations.

- For carriers of genetic mutations associated with Lynch syndrome, the CEWG recommends screening for CRC by colonoscopy every 1 to 2 years from age 25 years.
- For carriers of genetic mutations associated with familial adenomatous polyposis, the CEWG recommends screening by sigmoidoscopy every 2 years from age 12 years.
- For individuals with one first-degree relative (offspring, sibling or parent) diagnosed with CRC at age ≤ 60 years, or more than one first-degree relative with CRC irrespective of age at diagnosis, colonoscopy should be performed every 5 years (previously the recommendation was every 3 to 5 years). Colonoscopy should begin at age 40 years or 10 years prior to the age at diagnosis of the youngest affected relative, whichever is earliest, but not earlier than age 12 years.

For patients with CRC with identifiable genetic mutations, including Lynch syndrome and familial adenomatous polyposis, the CEWG recommends two-tier screening for their family members. Genetic testing should be conducted first, followed by endoscopic examination at specified and shorter intervals if the genetic test is positive. This reduces the number of unnecessary investigations among those with strong family history but without proven genetic mutation, decreasing the risk of potential complications arising from repeated endoscopic procedures.

These recommendations were made after considering the scientific evidence and international guidelines and practices.

Individuals who are carriers of genetic mutations associated with familial adenomatous polyposis or Lynch syndrome and individuals with a family history of CRC are at increased risk of CRC. Colorectal cancer in these individuals tends to be diagnosed at a younger age and progresses more aggressively than CRC in the general population.^{24,25}

International recommendations emphasise that CRC screening in increased-risk individuals needs to start earlier in their lifetime and be repeated at shorter intervals. Recommendations made by countries and by professional organisations on screening for increased-risk individuals generally suggest the use of colonoscopy and sigmoidoscopy as the screening methods.^{15,16,26-32}

The recommended endoscopic screening method for carriers of genetic mutations associated with Lynch syndrome is annual or biennial colonoscopy. It is recommended to start screening at age 20 to 25 years in the US^{15,26,27} and Singapore,¹⁶ at age 25 years in UK,²⁸ and at age 25 years or 5 years

earlier than the age at diagnosis of the youngest affected member of the family (whichever is the earliest) in Australia.²⁹ The guidelines issued by the World Gastroenterology Organization (WGO) recommend that screening should start at age 20 to 25 years or 10 years earlier than the youngest age at CRC diagnosis in the family, whichever comes first.³⁰

The recommended endoscopic screening method for carriers of genetic mutations associated with familial adenomatous polyposis is mainly annual or biennial flexible sigmoidoscopy, or annual colonoscopy. It is recommended to start screening at age 10 to 12 years in the US¹⁵ and Singapore,¹⁶ at age 13 to 15 years in the UK,²⁸ and at age 12 to 15 years (later age is recommended) in Australia.²⁹ The guidelines issued by the National Comprehensive Cancer Network suggest screening should start at age 10 to 15 years,^{31,32} whereas the WGO recommendation is to start screening at age 10 to 12 years.³⁰

International guidelines recommend endoscopic screening for individuals who have one first-degree relative diagnosed with CRC at age 50 to 60 years.^{15,16,26,28-33} Individuals with more than one first-degree relative with CRC irrespective of age at diagnosis are considered at increased risk and endoscopic screening at more frequent intervals is recommended.^{15,16,26,28-32} For these individuals, the recommended endoscopic screening method is to receive colonoscopy every 5 years.^{15,16,26,29-32} It is recommended to start screening at age 40 to 50 years, or 10 years prior to the age at diagnosis of the youngest affected relative.^{15,16,26,29-32}

Currently, patients with CRC may be referred for genetic counselling and testing. These services are provided at centres run by non-governmental organisation, including the Hereditary Gastrointestinal Cancer Genetic Diagnosis

Laboratory (<http://www.patho.hku.hk/colonreg.htm>); the Department of Health's Clinical Genetic Service (<http://www.dh.gov.hk>); and the private sector. Although referral criteria for testing may differ among these testing services, commonly adopted criteria include strong family history, occurrence of multiple cancers in a single individual, early onset of disease, presence of pathogenic mutation in the cancer predisposition gene, and clinically suspected hereditary cancer syndrome.

Emerging evidence for colorectal cancer screening

In the past 2 years, new evidence supporting the effectiveness of CRC screening has emerged which reinforces the CEWG recommendations.

A systematic review reported that sigmoidoscopy is associated with a 27% reduction in CRC-specific mortality in four randomised controlled trials and that biennial FOBT screening reduced CRC-specific mortality by 9% to 22% at 19.5 to 30 years of follow-up in five randomised controlled trials compared with no screening in the average-risk population.^{34,35}

Separately, a prospective study in Sweden found that colonoscopic surveillance for increased-risk individuals with significant family history is a cost-effective intervention to prevent CRC.³⁶

In addition, the US Preventive Services Task Force,³⁷ the US Multi-Society Task Force on Colorectal Cancer Screening,³⁸ and the American Cancer Society^{39,40} updated their recommendations for CRC screening in 2016 and 2017. All continue to recommend annual FOBT, sigmoidoscopy every 5 to 10 years, or colonoscopy every 10 years as appropriate screening modalities for average-risk individuals.

TABLE. Recommendations on CRC screening by the CEWG

For asymptomatic average-risk individuals	For at increased-risk individuals
<p>Recommendation on screening for CRC</p> <ul style="list-style-type: none"> The CEWG recommends that all individuals aged 50 to 75 years should consult their family doctor to consider CRC screening by one of the following methods: faecal occult blood test every 1 or 2 years; sigmoidoscopy every 5 years; or colonoscopy every 10 years. 	<p>Recommendations on screening for CRC</p> <ul style="list-style-type: none"> For carriers of genetic mutations associated with Lynch syndrome, the CEWG recommends screening for CRC by colonoscopy every 1 to 2 years from age 25 years. For carriers of genetic mutations associated with familial adenomatous polyposis, the CEWG recommends screening by sigmoidoscopy every 2 years from age 12 years. For individuals with one first-degree relative diagnosed with CRC at age ≤60 years, or more than one first-degree relative with CRC irrespective of age at diagnosis, the CEWG recommends colonoscopy every 5 years from age 40 years or 10 years prior to the age at diagnosis of the youngest affected relative, but not earlier than age 12 years. <p>Recommendation on genetic testing for CRC</p> <ul style="list-style-type: none"> For patients with CRC with identifiable genetic mutations, the CEWG recommends offering their family members two-tier screening by genetic testing followed by endoscopic examination, to reduce the number of unnecessary investigations and to reduce the risk of potential complications.

Abbreviations: CEWG = Cancer Expert Working Group; CRC = colorectal cancer

Conclusion

After considering local epidemiology, scientific evidence, and local and international screening guidelines and practices, the CEWG reaffirms in 2017 the CRC screening recommendations for average-risk individuals and updates the screening interval relating to the recommendations for increased-risk individuals with significant family history of CRC, as summarised in the Table. A leaflet and booklet on the CEWG recommendations are available (<http://www.chp.gov.hk/en/content/9/25/31932.html>) for downloading and dissemination to the general public to help them make informed choices. The CEWG will continue to monitor emerging local and international evidence and practice to ensure evidence-based CRC prevention and screening recommendations are up to date.

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All authors have made substantial contributions to the concept or design; acquisition of data; analysis or interpretation of data; drafting of the article; and critical revision for important intellectual content.

Declaration

As editors of this journal, DVK Chao, HHH Loong, and MCS Wong were not involved in the peer review process of this article. All authors have no conflicts of interest to disclose. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity. An earlier version of this article was published online on the Centre for Health Protection website (https://www.chp.gov.hk/files/pdf/cewg_crc_professional_hp.pdf).

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