衞生防護中心
Centre for Health Protection

Cancer Expert Working Group on Cancer Prevention and Screening
2017 Recommendations on Prevention and Screening for Colorectal Cancer
For Health Professionals

Local epidemiology

CRC is the commonest cancer in Hong Kong. According to the Hong Kong Cancer Registry, there were 5,036 newly registered CRC cases in 2015, representing 16.6% of all new cancer cases[1]. The age-standardised incidence rates (ASIR) were 41.5 for male and 26.2 for female per 100,000 standard population[1]. The median age at diagnosis of CRC was 68 in male and 70 in female[1]. The age-specific incidence rates increased significantly from age 50 onwards. CRC is more common in males with the male to female ratio for new cases in 2015 of 1.3:1[1].

The Death Registry registered 2,089 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 death rates (ASMR) were 18.0 for male and 10.5 for female per 100,000 standard population[2].

After adjusting for the effect of population ageing by using age-standardised rates, the ASIRs for both sexes still showed an upward trend, while the ASMRs for both genders have remained stable over the past three decades[2].

Risk factors

Risk factors for developing CRC may be modifiable or non-modifiable.

Modifiable risk factors 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 (IARC) on Cancer had classified 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 gram 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, IARC considered that there is sufficient evidence to classify alcoholic beverage and tobacco smoking as carcinogenic to humans in the

development of colorectal cancer[5]. Separately, the World Cancer Research Fund/ American Institute for Cancer Research (WCRF/AICR) reported that being overweight or obese can increase the CRC risk while 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 (FAP), Lynch Syndrome (previously known as hereditary non-polyposis colorectal cancer), colonic polyp and ulcerative colitis.

Based on local epidemiology, CRC is more common in males and its risk increases significantly from age 50 onwards[1]. Regarding family history, according to a local study, 80-90% of colorectal cancer cases are sporadic while the remaining 10-20% are familial cancers[7]. The cancer risk of individuals with a positive family history may vary according to (a) the age of diagnosis of CRC in the index patient and (b) the number of affected first-degree relatives. The younger the age of diagnosis of CRC in the index patient, the higher the CRC risk of his/her family members. In a meta-analysis, the relative risk of individuals with relatives diagnosed with CRC before 50 was estimated to be 3.55, while the relative risk for relatives diagnosed with CRC at or above 50 years of age was 2.18[8].

On the other hand, FAP is an autosomal dominant disorder caused by germline mutation of the Adenomatous Polyposis Coli (APC) located on the short arm of chromosome 5 (5q21-22)[9] and people with such mutation will have 95% chance of developing CRC by age 50[10]. Lynch Syndrome is another dominantly inherited colorectal cancer syndrome. It is caused by germline mutation in one of the genes responsible for the repair of mismatches during DNA replication. The lifetime CRC risk for those carrying such mutation is estimated to be 50-80%[10].

Ulcerative colitis has been associated with an increased risk of developing CRC, probably caused by long-standing chronic inflammation[11]. Moreover, as CRC arises predominantly from adenomatous polyps which can develop into CRC after 10 or more years[12], the development of polyp with larger size, villous histology and severe dysplasia are important indicators for progression into CRC[13].

Primary prevention

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

- Increase intake of dietary fibre (e.g. fibre from at least five servings of fruits and vegetables

daily);

- Decrease consumption of red and processed meat;
- Take part in moderate-intensity aerobic physical activities for at least 150 minutes per week;
- Maintain a healthy body weight with body mass index between 18.5 to 22.9 and waist circumference less than 80 cm for women and 90 cm for men;
- Avoid or quit tobacco smoking; and
- Avoid alcoholic drinks.

Secondary Prevention

Secondary prevention means screening, i.e. examining people without symptoms in order to detect disease or identify people 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 organized and evidence-based screening. In general, subjects to consideration for colorectal cancer screening, people can be classified into "average risk" and "increased risk" groups.

According to screening recommendations made by the CEWG, people with "increased risk" refer to individuals who have a significant family history, such as those with an immediate relative diagnosed with colorectal cancer at the age of 60 or below; or those who have more than one immediate relatives diagnosed with colorectal cancer irrespective of age at diagnosis; or those who have immediate relatives diagnosed with hereditary bowel diseases. People with "average risk" refer to individuals aged 50 to 75 who do not have the aforesaid family history.

Screening for general population at average risk

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

- annual or biennial faecal occult blood test (FOBT);
- sigmoidoscopy every 5 years;
- colonoscopy every 10 years.

The CEWG made the above recommendations after taking into consideration local epidemiology, research evidence as well as overseas 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 effectiveness and cost-effectiveness of screening tests, local epidemiology as well as anticipated benefits and harms to the screened population. In Hong Kong, the risk of CRC increases significantly from age 50 onwards[1]. Guidelines in U.S.[14,15] and Singapore[16] recommend the starting age of screening at 50 while U.K. recommends screening to start at above 50 years of age[17].

Regarding screening modalities, faecal occult blood test (FOBT), sigmoidoscopy and colonoscopy have been shown to reduce mortality from CRC based on research evidence. FOBT could reduce CRC mortality ranging from 15 to 33 % according to findings from large-scale randomized control trials (RCTs)[18,19,20]. A Cochrane review showed that screening by FOBT might reduce CRC mortality in average risk population by 16%[21]. Sigmoidoscopy was shown to lead to 28% risk reduction in overall CRC mortality and 43% risk reduction in distal CRC mortality in a meta-analysis[22]. Colonoscopy was associated with 61% reduction in CRC mortality in a meta-analysis[23].

Also, overseas 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 burden arising from CRC, the Government launched the three-year Colorectal Cancer Screening Pilot Programme ("Pilot Programme") on 28 September 2016 to provide subsidized screening by phases to average risk Hong Kong residents born in 1946 to 1955. The screening workflow comprises two stages. Participants would first receive subsidised Faecal Immunochemical Test (FIT, a new version of FOBT) from enrolled Primary Care Doctor (PCD). If the FIT result is positive, the participant would receive subsidised colonoscopy examination service from enrolled Colonoscopy Specialist. Persons at average risk who are not currently covered by the Pilot Programme may consult their family doctors about the need for colorectal cancer screening. Details of the Pilot Programme are available at www.colonscreen.gov.hk.

Screening for individuals at increased risk

The CEWG updated in 2017 the CRC screening recommendations for individuals at increased risk, with the key change relating to the interval for colonoscopy screening among individuals with significant family history of CRC but without mutated gene:-

- For carriers of mutated gene of Lynch Syndrome, the CEWG recommends screening for colorectal cancer (CRC) by colonoscopy every one to two years from age 25 onwards.

- For carriers of mutated gene of FAP, the CEWG recommends screening by sigmoidoscopy every two years from age 12.
- For individuals with one first-degree relative[i] diagnosed with CRC at or below 60 years of age or more than one first-degree relatives with CRC irrespective of age at diagnosis, colonoscopy should be performed every five years (instead of every three to five years) beginning at the age of 40 or ten years prior to the age at diagnosis of the youngest affected relative, but not earlier than 12 years of age.

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

The CEWG made the above recommendations after taking into consideration scientific evidence as well as overseas guidelines and practices.

Persons who are carriers of mutated gene of FAP or Lynch Syndrome and individuals with family history of CRC are at higher risk of colorectal cancer. CRC in these individuals tends to be diagnosed at a younger age and progresses more aggressively than CRC in the general population[24,25].

Overseas recommendations emphasize that CRC screening in high risk individuals needs to start earlier in their lifetime and be repeated at shorter intervals. Recommendations made by countries and by professional organizations on screening for persons at increased risk generally suggest the use of colonoscopy and sigmoidoscopy as the screening methods[15,16,26,27,28,29,30,31,32].

The recommended endoscopic screening method for mutated gene carrier of Lynch Syndrome is annual or biennial colonoscopy. The recommended age of onset of screening may vary from 20 to 25 in US[15,26,27] and Singapore[16], 25 in UK[28] , and 25 or five years earlier than the age of diagnosis of the youngest affected member of the family (whichever is the earliest) in Australia[29] . The guideline issued by the World Gastroenterology Organization (WGO) recommended that screening should start at the age of 20 to 25 or 10 years earlier than the youngest age of CRC diagnosis in the family, whichever comes first[30].

[i] First degree relative means offspring, sibling or parent.

The recommended endoscopic screening method for mutated gene carriers of FAP is mainly annual or biennial flexible sigmoidoscopy, or annual colonoscopy. The recommended age to commence screening varies between 10 to 12 years in US[15] and Singapore[16], 13 to 15 in UK[28] and 12 to 15 (later age is recommended) in Australia[29]. The guideline issued by National Comprehensive Cancer Network suggests screening should start at the age of 10 to 15[31,32] while WGO's recommendation is to start at 10 to 12 years of age[30].

Overseas guidelines recommend endoscopic screening for individuals who have one first degree relative diagnosed with CRC between age of 50 and 60[15,16,26,28,29,30,31,32,33]. Moreover, overseas guidelines also consider individuals with more than one first-degree relatives with CRC irrespective of the age at diagnosis being at increased risk and recommend more frequent endoscopic screening[15,16,26,28,29,30,31,32]. The recommended endoscopic screening method is to receive colonoscopy every 5 years[15,16,26,29,30,31,32]. The age to start screening is age 40 or 50, or 10 years prior to the age at diagnosis of the youngest affected relative[15,16,26,29,30,31,32].

Emerging evidence for CRC screening

In the past 12 months, new evidence supporting the effectiveness of CRC screening has emerged which reinforces the CEWG's recommendations.

A systematic review reported that while sigmoidoscopy is associated with 27% reduction in CRC-specific mortality in 4 randomized control trials (RCTs), biennial FOBT screening could reduce CRC-specific mortality by 9% to 22% at 19.5 to 30 years of follow up in 5 RCTs compared with no screening in average risk population[34,35].

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

In addition, the US Preventive task force[37], U.S. Multi-Society Task Force of Colorectal Cancer[38] and American Cancer Society[39,40] updated the 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 to be appropriate screening modalities for average risk individuals.

Conclusion

After taking into consideration local epidemiology, scientific evidence, local and overseas screening guidelines and practices, **the CEWG reaffirms in 2017 the CRC screening recommendations for average risk and updates the screening interval relating to the recommendations for increased risk individuals with significant family history of CRC as summarized in Table 1 below.** Leaflet and booklet on the CEWG recommendations are available at www.chp.gov.hk/en/content/9/25/31932.html for downloading and dissemination to the public to empower them in making informed choices. The CEWG will continue to keep in view emerging local and overseas evidence and practice to formulate evidence-based CRC prevention and screening recommendations.

Table 1: CEWG recommendations on colorectal cancer screening

For asymptomatic population at average risk	For persons at increased risk
● Individuals aged 50 to 75 years should consider screening by one of the screening methods including : ➢ annual or biennial faecal occult blood test (FOBT); or ➢ sigmoidoscopy every 5 years; or ➢ colonoscopy every 10 years.	**Recommendation on screening for CRC** 1. For carriers of mutated gene of Lynch Syndrome, the CEWG recommends screening for colorectal cancer (CRC) by colonoscopy every one to two years from age 25 onwards. 2. For carriers of mutated gene of familial adenomatous polyposis (FAP), the CEWG recommends screening by sigmoidoscopy every two years from age 12. 3. For individuals with one first degree relative diagnosed with CRC at or below 60 years of age, or more than one first degree relatives with CRC irrespective of age at diagnosis, colonoscopy should be performed every five years beginning at the age of 40 or ten years prior to the age at diagnosis of the youngest affected relative, but not earlier than 12 years of age. **Recommendation on genetic testing for CRC** ● For CRC patients with identifiable genetic mutations, two-tier screening by genetic testing followed by endoscopic examination can be offered to their family members to reduce the number of unnecessary investigations, as well as to reduce the risk of potential complications.

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