

**Cancer Expert Working Group  
On Cancer Prevention and Screening**

**Recommendations on Colorectal Cancer Screening**

**I. BACKGROUND**

***Burden of Colorectal Cancer in Hong Kong***

Colorectal cancer (CRC) is the second commonest cancer in Hong Kong with 3 706 new cases in 2005.<sup>1</sup> It accounted for 16.3% of all new cases of cancer in 2005. The crude incidence rates for males and females were 64.8 per 100 000 male population and 44.8 per 100 000 female population, respectively. The age-standardised incidence rates were 47.0 for male and 30.3 for female per 100 000 world standard population. Around half of the new cases of CRC were diagnosed at stage III or above<sup>2</sup> and about 90% of new cases occurred in people aged 50 or above. In addition, CRC was the third leading cause of cancer deaths in males and second leading cause of cancer deaths in females with 1 690 deaths in 2007, accounting for 13.7% of all cancer deaths. The crude mortality rates for males and females were 29.6 per 100 000 male population and 19.7 per 100 000 female population respectively. The age-standardised mortality rates were 20.0 for male and 11.6 for female per 100 000 world standard population.

2. The number of new cases and deaths of CRC were on the rising trend over the latest two decades. After adjusting for the effect of ageing population, the age-standardised incidence and mortality rates of CRC were also increasing.<sup>1</sup> The age-standardised incidence rates have increased by 0.7% per year in male and 0.4% per year in female during 1983-2005. The age-standardised mortality rates have increased by 0.8% per year in male, but were relatively stable without statistically significant trend in female. The rising trend of colorectal cancer incidence and mortality was mainly attributed to increase in the population aged 65 or above.<sup>3</sup>

***Natural History of CRC***

3. CRC arises predominantly from adenomatous polyps although many colonic adenomas do not progress to cancer<sup>4</sup>. The

development of a polyp into a cancer can take more than 10 years<sup>5</sup>, with larger size, villous history and severe dysplasia being important indicators of progression to invasive cancer<sup>6</sup>. Early identification and removal of colonic polyps can reduce the chance of developing into invasive cancer.

### ***Risk Factors for CRC***

4. Risk factors for CRC include aging, male gender, low fibre intake, high consumption of red and processed meat and high level of body or abdominal fatness, while smoking is associated with higher risk of developing rectal cancer.<sup>7</sup> In addition, alcohol consumption has been confirmed as causally related to occurrence of colorectal cancer with a relative risk of 1.4 for regular consumption of about 50g of alcohol per day, when compared with non-drinkers.<sup>8</sup> Increased physical activity is associated with reduction in risk of developing CRC.<sup>9</sup> Persons who are carriers of mutated gene of familial adenomatous polyposis (FAP) or hereditary nonpolyposis colorectal cancer (HNPCC) and individuals with family history of colorectal cancer are at higher risk of colorectal cancer. CRC in these individuals tends to be diagnosed at a younger age and develops more aggressively than CRC in the general population.<sup>10,11</sup> About 10-20% of all colorectal cancer cases are familial cancer.<sup>12</sup>

### ***Screening tests for CRC***

5. Since CRC arises predominantly from adenomatous polyps, screening tests for prevention of CRC can detect the presence of cancer and/or colonic polyps. Common screening tests include faecal occult blood test (FOBT), flexible sigmoidoscopy (FS) and colonoscopy.

6. FOBT is easy to be administered and patient can collect stool sample at home. Those screened positive will be further investigated by endoscopy to confirm the diagnosis. Results from meta-analysis<sup>13</sup> on overseas randomised controlled trials<sup>14 – 17</sup> suggested that annual or biennial screening by FOBT might reduce CRC mortality in average risk population by 16%. However, screening by FOBT is associated with considerable false positive and false negative rates in the detection of CRC. Local study using unhydrated guaiac-based FOBT on asymptomatic subjects for detection of advanced colorectal neoplasia<sup>a</sup> demonstrated a sensitivity and specificity of 14.3% and 79.2% respectively.<sup>18</sup> For detection of all colonic neoplasm, the respective rate was 19.1% and 79.6% respectively. While false positives may result in unnecessary anxiety and invasive procedures, false negatives may lead to delay in treatment

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<sup>a</sup> Advanced colonic neoplasm was defined as an adenoma  $\geq 10$  mm in diameter, a villous adenoma (with at least 25% villous architecture), an adenoma with moderate to severe dysplasia, or invasive carcinoma. (Sung, et al. 2003)

of colorectal neoplasms that should have been diagnosed earlier. There is a lack of published data among Chinese populations on whether FOBT screening can effectively reduce the incidence and mortality of CRC.

7. Evidence from observational studies demonstrated that both flexible sigmoidoscopy (FS) and colonoscopy might reduce the colorectal cancer risk.<sup>19,20</sup> However, there is currently no randomised controlled trial in the literature demonstrating that screening by FS or colonoscopy can reduce CRC mortality. FS examines only the distal colon and may miss lesions in the proximal colon. The sensitivity and specificity of FS in detecting advanced colonic lesions in a local population were found to be 78% and 84% respectively.<sup>18</sup> For colonoscopy, the sensitivity and specificity for detection of colorectal cancer reported in overseas studies were >90% and 99% respectively.<sup>21</sup>

8. According to findings in overseas randomised controlled trials<sup>19</sup>, screening for colorectal cancer using FS was generally safe when performed by trained and experienced endoscopists. The perforation rate was found to be below 0.01%. A cross-sectional analysis studying 50,148 participants from colonoscopy-based screening programme found that the complication or perforation rate of colonoscopy screening was 0.1-0.2%.<sup>22</sup> These procedures were acceptable to participants of screening trial. A local screening study<sup>18</sup> concluded that colonoscopy was a safe procedure for screening in Chinese. Among 505 Chinese subjects with colonoscopy and 148 with colonoscopic polypectomy, there was no perforation and only one reported case of postpolypectomy bleeding requiring blood transfusion.

9. Newer technologies such as virtual colonoscopy and stool DNA test (sDNA) have been emerging as potential options for CRC screening. According to results of meta-analyses overseas, virtual colonoscopy, which was also known as CT colonography, had a sensitivity of 48% to 93%, depending on the size of polyp.<sup>23-26</sup> The specificity for detection of polyps was 92%-97%.<sup>24</sup> sDNA tests stool for the presence of known DNA mutations in the adenoma-carcinoma sequence of colorectal carcinogenesis. The U.S. Preventive Services Task Force has concluded that there is currently insufficient evidence to assess the benefits and harms of virtual colonoscopy or sDNA as screening modalities for colorectal cancer.<sup>27</sup> More scientific evidence is required to decide whether these new tests should be recommended as screening options for CRC in Hong Kong.

10. For individuals at higher risk of CRC, like carriers of mutated gene of familial adenomatous polyposis (FAP) or hereditary nonpolyposis colorectal cancer (HNPCC) or with family history of

colorectal cancer, most overseas guidelines recommend the use of colonoscopy and flexible sigmoidoscopy as the screening method.

### ***Screening protocol***

11. Overseas guidelines, such as those from the U.S. Preventive Services Task Force, recommend that screening for colorectal cancer needs to be done regularly. The recommended frequency of CRC screening depends on the chosen screening test. The screening modalities studied in clinical trials and adopted in overseas recommendations for CRC screening in the general population mainly include annual or biennial FOBT, FS once every 5 years or colonoscopy once every 10 years.

12. The recommended age range for CRC screening in the general population should be aimed at capturing most CRC cases while taking into account the effectiveness of screening tests. In major clinical trials conducted mainly in Western countries in which effectiveness of CRC screening had been demonstrated, the age of participants was usually in the range of 50-75.<sup>13,14</sup>

13. Currently, there is no local published clinical guideline for screening of the colorectal cancer in the general population from medical professional organizations in Hong Kong. Overseas guidelines vary among countries and professional organizations. For example, the U.S. Preventive Services Task Force recommends screening for colorectal cancer using FOBT, sigmoidoscopy, or colonoscopy, in adults, beginning at age 50 years and continuing until age 75 years.<sup>27</sup> The U.K. National Screening Committee recommends that bowel cancer screening using FOBT should be offered to men and women above 50 years of age.<sup>28</sup> The recommended screening frequency in the NHS Bowel Cancer Screening Programme is once every two years.<sup>29</sup> The NHS Bowel Cancer Screening Programme invites men and women aged 60 to 69 to undertake FOBT. The Programme will be extended to men and women aged up to 75 from 2010.

14. International recommendations emphasize that CRC screening in the high risk individuals needs to start earlier in their lifetime and to repeat in shorter time interval. For carriers of mutated gene of FAP and HNPCC, screening starting at the age of 12 and 25 respectively has been recommended.<sup>7</sup> For a person with one or more first degree relatives diagnosed to have CRC at age 60 or below, overseas guidelines usually recommend screening for colorectal cancer starting at an earlier age than as recommended for general population. The recommended starting age of screening are usually at 40, or 10 years prior to the age at diagnosis of the youngest affected relative, while the usual recommended frequency of screening is once every 3 to 5 years.

### ***Considerations for a population-based screening programme for the Hong Kong general population***

15. From the public health point of view, a number of factors are important in considering launching of a population-based screening programme. These include public acceptance, determination of appropriate screening policies, cost-effectiveness of screening, and the readiness and capacity of the health care system in coping with screening and management of positive screening test results.

16. Acceptability of FOBT is an important factor for launching a population-based CRC screening programme. In Australia, the pilot participation rate in eligible population was 45%<sup>30</sup>, while in the UK, the participation rates in the two rounds of screening pilot were 52%-58%<sup>31,32</sup>. According to local studies, knowledge on and uptake of CRC screening were low among the general public.<sup>33</sup> Besides, the Population Health Survey conducted in 2003-04 also found that only around 7% – 11% of local population aged 55 years and above had ever undertaken a FOBT, sigmoidoscopy or colonoscopy.<sup>34</sup> In population in which screening uptake is potentially low, the cost-effectiveness of population-based screening needs to be ascertained. Currently, there is a community CRC screening project and there are local studies about cost-effectiveness of CRC screening underway. More local data will be available in the coming years.

17. The impact of launching a population-based CRC screening programme to the whole health care system must be carefully assessed. Even in countries with population-based CRC screening programme in place, their programmes are being implemented by phase over a number of years in order to alleviate the pressure on local health care services. Based on local population statistics and overseas experience, assuming 50% coverage and 1.77% positivity rate of FOBT screening, one round of FOBT screening in the Hong Kong general population aged 50-75 would generate demands of about 900 000 FOBT samples for laboratory analysis and around 16 000 colonoscopies for follow-up of patients with positive FOBT. Thus, detailed planning is required before implementation of a population-based CRC screening programme to address the constraints in capacity of colonoscopy, laboratory services and further management, including counseling, treatment and follow up in Hong Kong. Taking into account the current capacity of colonoscopy, laboratory and treatment services in the public sector, screening will increase the number of people who need further management and lead to longer waiting time and delay in treatment of symptomatic cases.

## **II. CEWG RECOMMENDATIONS ON CRC SCREENING**

### ***For screening of individuals in the general population***

18. Individuals aged 50 to 75 with average risk in Hong Kong should consider screening for colorectal cancer by one of the screening methods including annual or biennial faecal occult blood test (FOBT), flexible sigmoidoscopy (FS) every five years and colonoscopy every ten years. Based on currently available evidence, there is insufficient information to determine which screening strategy is superior to others in terms of the balance of benefits and potential harms. There is also insufficient evidence to recommend CRC screening using either virtual colonoscopy or stool DNA test.

19. Health care providers are advised to discuss with their clients on the best screening test according to individual risk profile. Taking into consideration of the low sensitivity of FOBT and the potential complications and harms associated with sigmoidoscopy and colonoscopy, health care providers are also advised to provide adequate explanation to their clients, especially on the limitations, and the potential risks and benefits in receiving a screening test, so that their clients can make informed choices.

20. When choosing a CRC screening test, persons should be aware that all screening tests have their limitations, including false positive and false negative results, and be prepared to undergo more invasive procedures in case their initial screening result turns out to be positive. While a false positive test result may induce unnecessary anxiety and physical harm to the patient, a false negative test result may give false reassurance. Potential complications associated with colonoscopy and sigmoidoscopy include perforation, significant haemorrhage and complications related to surgical resection of adenomas.

### ***For population-based screening***

21. The implementation of population-based colorectal cancer screening programme as an important strategy in cancer prevention should take into consideration a number of factors including organization, cost-effectiveness, funding options, service capacity, acceptability and programme logistics and more local research would be needed to address these factors. Centrally organized screening programmes in a number of countries have been shown to be more effective and reduce inequity than opportunistic screening.<sup>35</sup> Currently, a local community-based screening programme is currently underway to test the feasibility of a large-scale programme in Hong Kong. Besides, there is a on-going study analyzing the cost-effectiveness of

implementing CRC screening programme in our locality. The results would provide invaluable information for further deliberation on the implementation of a population-based CRC screening programme in Hong Kong.

### ***For high risk individuals***

22. For carriers of mutated gene of HNPCC, the CEWG recommends screening for colorectal cancer by colonoscopy should be started every 1-2 years from age 25. For carriers of mutated gene of FAP, the CEWG recommends screening by flexible sigmoidoscopy every 2 years from age 12.

23. Based on overseas recommendations, in order to provide effective protection through early detection among high risk population, the CEWG recommends that for persons with one or more first degree relatives diagnosed to have colorectal cancer at or below 60 years of age, colorectal cancer screening by colonoscopy every 3 to 5 years should begin at age 40 or 10 years prior to the age at diagnosis of the youngest affected relative, but not earlier than 12 years of age. In addition, 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.

24. For persons with one or more first degree relatives diagnosed to have colorectal cancer above age of 60, they are regarded as having similar risk as the general population. Screening of these individuals should adopt the same protocol as those in the general population, that is, commencing colorectal cancer screening at age of 50.

### ***Primary prevention of colorectal cancer***

25. Primary prevention is very important in lowering the risk of having colorectal cancer. The public is advised to prevent colorectal cancer by adopting primary preventive measures like increasing intake of dietary fibre (e.g. fibre from fruits and vegetables), decreasing consumption of red and processed meat, increasing physical activities, maintaining healthy body weight, avoiding or quitting tobacco smoking and avoiding or limiting consumption of alcoholic drinks. Health education on colorectal cancer prevention should be enhanced to raise the awareness of CRC in the public.

26. Members of the public are also advised to increase awareness of early symptoms of colorectal cancer, such as change in bowel habit (diarrhoea, constipation, etc.) and blood or copious mucus in

stool. Individuals should seek medical advice early and discuss with their doctors if these symptoms appear.

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