



**衛生防護中心**  
Centre for Health Protection

**Cancer Expert Working Group on  
Cancer Prevention and Screening (CEWG)**

**Recommendations on Prevention and Screening for Stomach Cancer  
For Health Professionals**

**Local epidemiology**

Stomach cancer has been one of the most common cancers and leading cause of cancer death in Hong Kong, despite a downward trend in its the incidence and mortality in the locality.<sup>1,2</sup>

2. In 2021, a total of 1,306 new stomach cancer cases (762 in males and 544 in females) were recorded in Hong Kong, accounting for 3.4% of all newly diagnosed cancer cases. It was the sixth most common cancer in Hong Kong. The median age at diagnosis was 71 for male and 70 for female. The age-standardized incidence rates (ASIR)<sup>a</sup> were 9.0 for males and 5.6 for females per 100,000 population. The overall ASIR of stomach cancer has dropped from 11.3 per 100,000 population in 2000 to 7.2 per 100,000 population in 2021.<sup>3</sup>



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<sup>a</sup> Age-standardised rates are age-adjusted to the World Standard Population of Segi (1960).

3. A total of 631 deaths (380 in males and 251 in females) attributed to stomach cancer were recorded in 2021, accounting for 4.2% of all cancer deaths and making stomach cancer the sixth leading cause of cancer death in Hong Kong. The age-standardized mortality rates (ASMR)<sup>a</sup> of stomach cancer were 4.1 for males and 2.2 for females per 100,000 population. The overall ASMR of stomach cancer has dropped from 6.7 per 100,000 population in 2000 to 3.1 per 100,000 population in 2021.<sup>3</sup>

4. ASIR and ASMR of stomach cancer are in general higher in some East-Asian countries, such as Japan, Korea and China, than in the Western countries. Compared with the majority of East-Asian countries, the ASIR and ASMR of Hong Kong were relatively low.<sup>4</sup>

### **Types of stomach cancer**

5. The most common type of stomach cancer is adenocarcinoma, accounting for more than 90% of all cases.<sup>5</sup> Other types of stomach cancer include gastrointestinal stromal tumor, lymphoma and carcinoid tumor. Adenocarcinoma of stomach can be further divided into different types by anatomic classification (cardia and non-cardia) or pathological classification (intestinal and diffuse type).<sup>6</sup>

### **Risk factors**

6. Stomach cancer has a multifactorial aetiology with a well-characterized precancerous process.<sup>7,8</sup> Risk of developing stomach cancer is affected by a number of modifiable and non-modifiable factors.

**(a) Helicobacter pylori (*H. pylori*) infection**

The World Health Organization's International Agency for Research on Cancer (IARC) classified *H. pylori* as a carcinogenic agent with sufficient evidence in causing stomach cancer in humans.<sup>9</sup> Epidemiological studies showed that more than 90% of patients with stomach cancer have had current or past *H. pylori* infection.<sup>10,11</sup>

A meta-analysis of 19 qualified studies estimated the odds ratio (OR) for stomach cancer in *H. pylori*-infected patients is 1.92 (95% confidence intervals [95% CI] 1.32-2.78).<sup>12</sup> Another pooled analysis of 12 prospective studies reported the odds ratio of *H. pylori* infection for non-cardia cancer was 2.97 (95% CI, 2.34-3.77).<sup>13</sup>

**(b) Atrophic gastritis and intestinal metaplasia**

Atrophic gastritis and intestinal metaplasia are precancerous lesions of stomach cancer and are strongly associated with *H. pylori* infection. Studies showed that the adjusted relative risk (RR) of stomach cancer in patients with severe atrophic gastritis was 5.76, while that in *H. pylori*-infected individuals with intestinal metaplasia was 6.4 (95% CI, 2.6-16.1).<sup>14,15,16</sup>

**(c) Dietary factors**

Dietary habits are one of the most important factors in the incidence of stomach cancer.<sup>17</sup> The World Cancer Research Fund/American Institute for Cancer Research's Continuous Update Project Expert Panel concluded there is strong evidence that consuming foods preserved by salting increases the risk of stomach cancer.<sup>18</sup> Multiple meta-analyses and pooled analyses on the association between high salty food intake and risk of stomach cancer were conducted, results from these studies showed positive association between high salty food consumption and stomach cancer (OR 1.55, 95% CI 1.45-1.64).<sup>19,20,21,22,23</sup>

On the other hand, consumption of fruits and vegetables appears to have protective effect against development of stomach cancer. A meta-analysis of 13 studies demonstrated that fruit consumption was associated with a decreased risk of both cardia (combined OR 0.58, 95% CI: 0.38–0.89) and non-cardia stomach cancer (OR 0.61, 95% CI: 0.44-0.84), whereas vegetable intake also decreased the risk of cardia (OR 0.63, 95% CI: 0.50-0.79) and non-cardia stomach cancer (OR 0.75, 95% CI: 0.59-0.95).<sup>24</sup>

**(d) Tobacco smoking**

It is estimated that 11% of stomach cancer cases worldwide are attributable to tobacco use.<sup>18</sup> A systemic review and meta-analysis of cohort studies estimated the summary RR for current smokers were 1.62 (95% CI 1.50-1.75) in males and 1.20 (95% CI 1.01-1.43) in females.<sup>25</sup> Another meta-analysis of case-control studies reported that the OR for current smokers and ever-smokers were 1.69 (95% CI 1.35-2.11) and 1.48 (95% CI 1.28-1.71) respectively.<sup>26</sup> The risk increased with intensity and duration of cigarette smoked and decreased significantly after 10 years of quitting smoking.<sup>27</sup>

**(e) Heavy Alcohol consumption**

According to the World Cancer Research Fund/American Institute for Cancer Research's Continuous Update Project Expert Panel, there is strong evidence that consuming approximately three or more alcoholic drinks ( $\geq$  45g of ethanol) per day increases the risk of stomach cancer.<sup>18</sup> Positive association between heavy alcohol drinking and stomach cancer was demonstrated in a meta-analysis of 59 studies, with a pooled RR 1.20 (95% CI 1.01-1.44) for heavy drinkers ( $\geq$ 4 drinks per day).<sup>28</sup>

**(f) Overweight and obesity**

IARC working group assessed the relationship of cancer risk and excess body fatness in 2016, and reported that there were significant associations between BMI and certain cancer risk including cardia stomach cancer (RRs

were 1.2 to 1.5 for BMI of 25 to 29.9, and 1.5 to 1.8 for BMI  $\geq$  30 with respect to cardia stomach cancers).<sup>29</sup> Association between risk of stomach cancer and excess body weight i.e. body mass index (BMI)  $\geq$  25 was also reported in a meta-analysis of cohort studies (OR 1.22, 95% CI 1.06-1.41). The strength of the association increases with increasing BMI.<sup>30</sup>

**(g) Other medical conditions**

Individuals with pernicious anemia have a 6.9% chance of developing stomach cancer, the risk is more than 5 times than the general population.<sup>31</sup> Studies have found that those with pernicious anemia were at increased risk for non-cardia stomach adenocarcinoma (OR 2.18, 95% CI 1.94-2.45) and gastric carcinoid tumors (OR 11.43, 95% CI 8.90-14.69).<sup>32</sup>

**(h) Family history and genetic susceptibility**

Around 10% of stomach cancer cases are aggregated within families.<sup>33</sup> Positive family history in first-degree relatives is a reported risk factor for stomach cancer.<sup>17,34</sup> Individuals with a family history of stomach cancer had an OR of 2.5 (95% CI 1.5-4.2).<sup>33</sup>

Some cancer syndromes are known to account for familial stomach cancer, such as hereditary diffuse gastric cancer caused by germline alterations of CDH1. Other hereditary syndromes associated with stomach cancer include Lynch, Li-Fraumeni, Peutz-Jeghers, hereditary breast-ovarian cancer, familial adenomatous polyposis, and juvenile polyposis.<sup>33</sup>

**(i) Increasing age and gender**

Increasing age positively correlates with the risk of stomach cancer. Most people are diagnosed with stomach cancer at the age of 60-80. Only approximately 10% of stomach cancers are detected at the age of 45 or younger.<sup>7</sup> Meanwhile, stomach cancer is more common in male than in

female.

## Primary prevention

7. Eradication of *H. pylori* among individuals diagnosed with *H. pylori* infection is reported to reduce the risk of developing stomach cancer.<sup>35</sup> The IARC Working Group released a report “*Helicobacter pylori* Eradication as a Strategy for Preventing Gastric Cancer” in 2014, where the working group concluded that randomized clinical trials have shown that *H. pylori* treatment is effective in preventing stomach cancer.<sup>36</sup> A meta-analysis demonstrated that individuals with eradication of *H. pylori* infection had a lower incidence of stomach cancer than those who did not receive eradication therapy (pooled incidence rate ratio 0.53, 95% CI 0.44–0.64).<sup>37</sup> Another pooled analysis showed that the RR of *H. pylori* eradication for stomach cancer was 0.65 (95% CI 0.43 to 0.98).<sup>38</sup>

8. Although there is evidence in supporting treatment for individuals with *H. pylori* infection, there is currently no robust scientific evidence that supports provision of routine screening and eradication for *H. pylori* among asymptomatic individuals with an average risk of stomach cancer, in areas of intermediate to low incidence of stomach cancer, for the prevention of stomach cancer as a cost-effective measure. Several ongoing randomized controlled trials were conducted in China, the United Kingdom and Korea to evaluate if *H. pylori* screening and treatment can reduce stomach cancer. Their results may provide more evidence on the clinical effectiveness of *H. pylori* screening and eradication in reducing stomach cancer in the future.<sup>36,39</sup>

9. In Hong Kong, a consensus recommendation for the screening, diagnosis and management of *H. pylori* infection was published by a panel of medical experts in gastroenterology in 2023. Individuals at high risk of

stomach cancer (e.g. with a family history of stomach cancer) are recommended to be tested and treated for *H. pylori*, whereas screening of *H. pylori* in the general population is not recommended in view of the declining incidence of gastric cancer in Hong Kong.<sup>40</sup>

10. Apart from eradication of *H. pylori* infection, a number of risk factors associated with stomach cancer are modifiable. The CEWG recommends the general population to adopt the following healthy lifestyle and behavioural changes to prevent stomach cancer:

- Do not smoke, current smokers should quit smoking
- Avoid alcohol consumption
- Avoid salt-preserved foods and have a healthy and balanced diet with adequate consumption of fruit and vegetable
- Being physically active and maintain a healthy body weight

### **Awareness of stomach cancer symptoms and early detection**

11. Stomach cancer may not cause any symptoms at its early stage, until the cancer has grown fairly large or have spread outside the stomach. Some common symptoms include indigestion, unexplained weight loss, abdominal pain or discomfort, loss of appetite, early satiety, nausea, vomiting and fatigue.<sup>41,42</sup>

### **Stomach cancer screening by various modalities**

12. There are three main screening tools used in screening of stomach cancer, which include upper gastrointestinal series (UGIS), upper endoscopy and various biomarkers, such as *H. pylori* antibody, pepsinogen I/II, gastrin-17, carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9 and CA125,

etc., which are tested alone or in combination. The effectiveness of various screening modalities among asymptomatic individuals have been assessed largely in observational studies (i.e. cohort or case-control) conducted in areas with a high incidence of stomach cancer, such as Japan and Korea.

13. UGIS has limitations in terms of its low sensitivity, in addition to the harm related to radiation exposure. The sensitivity of UGIS ranged from 60-80%, whereas the specificity and true positive rate were 90% and 0.7 to 2.0% respectively.<sup>43</sup> In a study conducted in Japan, the false-positive and false-negative rates of UGIS were 14.4% and 10.7% respectively in the first round of screening, and in the subsequent round, the false-positive and false-negative rates were 10.9% and 11.5% respectively.<sup>44</sup> Moreover, UGIS may cause complications such as barium meal aspiration, intestinal obstruction. A survey done by the Japanese Association of Gastroenterological Cancer Screening on more than 3 million UGIS has reported in 2013 that UGIS had a complication rate of 42.8 per 100 000 screenings.<sup>45</sup>

14. Sensitivity of endoscopic screening was reported to be 0.955 (95% CI 0.875-0.991) and 0.977 (0.919-0.997) for the first and the subsequent round of screening respectively, whereas the specificity was found to be 0.851 (95% CI 0.843-0.859) and 0.888 (0.883-0.892) for the first and subsequent round of screening respectively.<sup>44</sup> While endoscopic screening has an apparent advantage that tissue biopsy can be taken for lesions during the procedure, it can also give rise to serious harms, including over-diagnosis and complications such as bleeding and perforation. A survey conducted by the Japanese Gastrointestinal Endoscopy Society on more than 7 million upper endoscopies has reported in 2010 that upper endoscopy had a complication rate of 5.02 per 100 000 examinations.<sup>46</sup>

15. In a nested case-control study using data from the Korean National Cancer Screening Program for gastric cancer since 2002, according to screening



modality, the ORs of death from stomach cancer were 0.53 (95% CI 0.51–0.56) for upper endoscopy and 0.98 (95% CI 0.95–1.01) for UGIS. With more endoscopic screening tests performed per subject, the ORs of death from stomach cancer decreased from 0.60 (95% CI 0.57–0.63) to 0.32 (95% CI 0.28–0.37) and 0.19 (95% CI 0.14–0.26), with screening once, twice and at least thrice respectively.<sup>47</sup> Two case-control studies evaluating mortality reduction were conducted in Japan. Compared with those who had never been screened before diagnosis of stomach cancer, the OR of death from stomach cancer within 36 months from the date of diagnosis were 0.695 (95% CI 0.489-0.986) for endoscopic screening and 0.865 (95% CI 0.631-1.185) for radiographic screening, suggesting a 30% reduction in stomach cancer mortality by endoscopic screening.<sup>48</sup> Currently, there is lack of evidence from randomised controlled trials on the effectiveness and mortality reduction of both endoscopy and UGIS for stomach cancer screening in both general or high-risk population.

16. Serological testing for various biomarkers are also used or studied as an alternative method for screening of stomach cancer, including reportedly *H. pylori* antibody, pepsinogen I/II, gastrin-17, CEA, CA19-9, CA125, CA72-4, etc. However, they are in general limited by low sensitivity and specificity, and are not useful as a stand-alone screening tool for stomach cancer screening.<sup>43,49,50</sup>

### **Recommendations and practices on screening in countries with intermediate to low stomach cancer incidence rate**

17. In areas with an intermediate to low incidence of stomach cancer, including the United Kingdom and Singapore, the guidelines issued by health professional bodies/organisations (e.g the UK National Screening Committee, American Society for Gastrointestinal Endoscopy, Academy of Medicine Singapore, etc.) in general do not recommend screening for stomach cancer among asymptomatic persons at average risk or has no recommendation on

stomach cancer screening.<sup>43,51,52,53</sup>

18. There are some overseas professional guidelines which suggest screening for stomach cancer among individuals who are at a higher risk of developing stomach cancer, although these recommendations differ in the criteria of high-risk individuals and screening regimen, and are largely developed based on expert opinions. The American Society for Gastrointestinal Endoscopy recommended that endoscopic screening for stomach cancer starting at age 50 should be considered for individuals who are first- or second-generation immigrants from high-incidence regions (East Asia, Russia, and South America). Individuals with a family history of stomach cancer are recommended to begin endoscopic screening 10 years before diagnosis in the affected relative.<sup>43</sup> Similarly, the British Society of Gastroenterology recommends that endoscopic surveillance every 3 years should be offered to patients with extensive gastric atrophy or gastric intestinal metaplasia,<sup>51</sup> whereas the Singapore Academy of Medicine recommends targeted endoscopic screening be considered in high-risk individuals  $\geq 50$  years, with 3 or more of the following risk factors: Chinese, male, history of *H. pylori* infection, heavy smoker, first-degree family history of gastric cancer, or pernicious anemia.<sup>52</sup>

### **Recommendations and practices on screening in countries with high stomach cancer incidence rate**

19. Universal screening for stomach cancer has been implemented in some countries or regions with a high incidence and high disease burden of stomach cancer, e.g. Japan, Korea. According to the 2018 Japanese Guidelines for Gastric Cancer Screening, both radiographic and endoscopic screenings are recommended for population-based and opportunistic screenings. Screenings are recommended to individuals aged 50 years or older, with a screening interval of two to three years.<sup>54,55</sup>

20. The Korean National Cancer Screening Program for gastric cancer has been launched in Korea since 1999, providing stomach cancer screening by UGIS or endoscopy once every two years for participants aged 40 or above. The latest guideline published in 2015 recommends biennial stomach-cancer screening for asymptomatic adults from 40 to 75 years using upper endoscopy. Stomach cancer screening using UGIS in asymptomatic adults aged between 40 to 74 years may be recommended based on clinicians' judgment regarding the patient's risk and the patient's preference.<sup>56,57</sup>

21. The current national stomach cancer screening programmes in China follow a modified high-risk population strategy, providing screening service for individuals aged 45 – 75 years in selected high-risk areas, and population selection is generally based on cluster sampling in each area.<sup>58,59</sup> The latest Chinese guideline for the screening, early detection and early treatment of gastric cancer in 2022 issued by the Expert Group of China Guideline for the Screening, Early Detection and Early Treatment of Gastric Cancer recommended that anyone who meets clause 1) and one of the clauses 2) – 6) should be classified as a high-risk group of stomach cancer, and recommended for screening:<sup>59</sup>

- 1) over 45 years old, regardless of gender
- 2) population in areas with high incidence of gastric cancer
- 3) *H. pylori* infection
- 4) previously suffered from chronic atrophic gastritis, gastric ulcer, gastric polyp, residual stomach after surgery, hypertrophic gastritis, pernicious anemia and other pre-gastric cancer diseases
- 5) first-degree relatives of patients with gastric cancer
- 6) with other high-risk factors for gastric cancer (e.g. high salt or pickled diet, smoking, heavy drinking, etc.)

22. Screening methods for stomach cancer in the Chinese guidelines include serological testing for pepsinogen I/II and *H. pylori* antibody, gastrin 17

(for helping diagnosis of atrophic gastritis), and endoscopy. The risk of stomach cancer was stratified according to the results of serum PG test and *H. pylori* serology test which determine further examination strategy. UGIS is not recommended by the Chinese guideline for stomach cancer screening.<sup>59,60</sup>

## Conclusion

23. There is no strong evidence supporting the effectiveness, cost effectiveness, or favorable benefits vs. harms of screening for stomach cancer in areas with intermediate to low incidence of stomach cancer. Since Hong Kong has intermediate to low incidence of stomach cancer in global comparison, screening for stomach cancer (by upper endoscopy, UGIS and serological testing for various biomarkers) is not recommended for persons at average risk of stomach cancer in the local population.

24. There is also a lack of local study or data to establish criteria of at-risk groups in whom the benefits would outweigh the harms from screening in Hong Kong. Primary prevention by practicing healthy lifestyle remains important in reducing the risk of stomach cancer.

25. Screening of *H. pylori* in the local general population is not recommended in view of the declining and relatively low incidence of stomach cancer in Hong Kong. On the other hand, eradication of *H. pylori* in persons known to be infected is important in reducing their risk of developing stomach cancer.

26. In summary, screening for stomach cancer is not recommended in asymptomatic persons at average risk. High-risk individuals are recommended to seek advice from doctors to understand the potential benefit and harms of screening and on their individual need for and approach of stomach cancer

screening. The CEWG will keep in view the latest development and emerging evidence on this issue.

## Recommendations by CEWG

27. Taking local epidemiology, emerging scientific evidence, overseas recommendations and screening practices into consideration, the CEWG has formulated recommendations for stomach cancer screening which were endorsed by the Cancer Coordinating Committee at its 19<sup>th</sup> meeting on 28 June 2024. The recommendations for the local population are given below.

1. Primary prevention remains an important strategy for reducing the risk of stomach cancer. All individuals should adopt a healthy lifestyle which includes no smoking, avoiding alcohol consumption, healthy eating (with adequate intake of fruits and vegetables and avoidance of high-salt and salt-preserved foods) and maintaining healthy body weight.
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<b>For asymptomatic population at average risk</b>
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2. Screening for stomach cancer (by upper gastrointestinal series, upper endoscopy or biomarkers, such as <i>H. pylori</i> serology) is not recommended in asymptomatic persons at average risk. Screening for <i>H. pylori</i> infection (by urea breath test, serology or stool antigen test) among asymptomatic persons in the general population is also not recommended.
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<b>For asymptomatic persons at increased risk</b>
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3. Persons at increased risk, e.g. with precancerous lesion of stomach cancer or family history of stomach cancer, may consider seeking advice from doctors regarding the need for and approach of screening.
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