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Understanding the Global Cancer Statistics 2018: implications for cancer control

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Cancer incidence and mortality increase rapidly worldwide, making cancer the major cause of death in most regions. Understanding the current cancer burden in different regions is necessary to find out potential risk factors and generate strategies for cancer control. The International Agency for Research on Cancer (IARC) has recently provided a status report about the global burden of cancer by estimating the incidence and mortality for 36 cancers in 185 countries (Bray et al., 2018). In this article, we will summarize the distribution of the major cancer types in different regions and reveal the global cancer pattern. In addition, we will stress the potential risk factors responsible for the increase of cancer burden and the importance of medical allocation for cancer control.

Current cancer burden worldwide

According to the increasing cancer incidence and mortality, the IARC predicts that new cancer cases and cancer deaths will be 18.1 million (17.0 million without nonmelanoma skin cancer) and 9.6 million (9.5 million without nonmelanoma skin cancer), respectively. The global cancer burden profile is closely associated with lifestyle factors and the level of socioeconomic development. Europe has less than 10% of the world's population but over one fifth of new cancer cases and nearly one fourth of cancer deaths of the globe. America also has a high cancer incidence of 21% but less mortality of 14.4%. On the other hand, although it accounts for only 5.8%, the cancer incidence in Africa causes much more deaths (7.3% in mortality). Nearly half of the new cancer cases and over half of the cancer deaths arise in Asia because of its large population (Bray et al., 2018).

In combination of both sexes, lung cancer ranks first in both incidence and mortality for 11.6% and 18.4%, respectively. Other cancers with high incidence include breast cancer (11.6%), colorectal cancer (10.2%), prostate cancer (7.1%) and stomach cancer (5.7%). Colorectal cancer causes 9.2% of cancer death and ranks second in mortality, followed by stomach cancer (8.2%), liver cancer (8.2%) and breast cancer (6.6%). Despite the fact that the top eight cancer types bring about the majority of new cancer cases and deaths, the pattern of each cancer is different by gender, regions and development levels. Here we will discuss the epidemiology of the eight major cancers and their underlying risk factors in order to generate strategies for cancer control.

1. Lung cancer. For males, lung cancer is still the most common type of new cancer cases in 37 countries, ranking second after prostate cancer, and is the leading cause of cancer deaths in 93 countries. For females, the mortality of lung cancer ranks first in 28 countries and high incidence occurs in North America and North/West Europe. Smoking is considered as the most important risk factor for lung cancer. Tobacco control in the United States contributes to 45% of the decline in mortality among men and 8% among women (Byers et al., 2016). Over 50% of Chinese men are smokers and smoking tends to be increasingly prevalent among young adults. The burden of lung cancer in China is

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likely to increase in the next 20–30 years due to the delayed effect of smoking. Although only 2.8% women smoke in China, the incidence and mortality of lung cancer are still at a high level, which may be attributed to the exposure to second-hand smoking and harmful gas from heating and cooking (Xia et al., 2018).

2. Female breast cancer. Among women, breast cancer accounts for 24.2% of new cancer cases and 15.0% of cancer deaths. Globally, the incidence and mortality of breast cancer rank first in 154 and 104 countries, respectively. In high/very high Human Development Index (HDI) regions, although the incidence age-standardized rates (ASR) of breast cancer is much higher than the low/medium HDI regions (54.4 per 100,000 vs. 31.3 per 100,000), the mortality ASR is lower in high/very high HDI regions than the low/medium HDI regions (11.6 per 100,000 vs. 14.9 per 100,000). Genetic mutation, such as BRCA1 and BRCA2, may be explanations for only 5%–10% of breast cancer cases, particularly for those with family history (Tung et al., 2016). The increasing trend of breast cancer incidence in transitioning countries like China may be attributed to a so-called westernized lifestyle, which causes higher obesity rate and physical inactivity. Other potential risk factors include transition in reproductive behavior, prevalence of breast cancer screen and increase of awareness. Reduced postmenopausal hormone treatment, prevalence of mammography and more effective therapy contribute to the decline in incidence and mortality in developed countries like the United States (Byers et al., 2016).

3. Colorectal cancer. In combination of both sexes, colorectal cancer causes over one tenth of new cancer cases and nearly one tenth of cancer deaths, ranking third in cancer incidence and second in cancer mortality. In consistence with the socioeconomic development, the regions with high incidence of colorectal cancer include Europe, Australia/New Zealand, and Northern America and Eastern Asia. Despite the high incidence, the mortality in developed regions, such as the United States, has decreased steadily for decades, partly because of the improved lifestyles and diets, the prevalence of endoscopic screening and progress in therapy (Byers et al., 2016). In developing countries like China, however, the incidence and mortality of colorectal cancer are increasing, which may be the result of westernized lifestyle.

4. Prostate cancer. Prostate cancer is the most common type of cancer incidence in 105 countries, particularly in Australia/New Zealand, Northern/Western Europe and America. Ranking second in incidence and fifth in mortality among males, prostate cancer is presumed to bring nearly 1.3 million new cancer cases and 0.36 million deaths. Considering both the incidences in low HDI and high HDI countries are high, the etiology of prostate cancer needs to be further explored. The mortality of prostate cancer has declined by over half between 1990 and 2015 in the United States, partly because of the SPA screening and earlier intervention with anti-androgen therapy. Paradoxically, the SPA screening had limited effect in reducing the deaths of prostate cancer (Andriole et al., 2012). Early detection by SPA screening, in some degree, increases the incidence of prostate cancer in developing countries like China (Chen et al., 2016).

5. Stomach cancer. There will be over 1.0 million new diagnosed cases of stomach cancer and 0.78 million deaths in 2018. In combination of both sexes, stomach cancer ranks fourth in incidence for 5.7% and third in mortality for 8.2%. Higher incidence and mortality are found in males. The incidence ASR, both in males and females, was astonishingly high in Eastern Asia, nearly twice that of the second-placed Eastern Europe. In China, stomach cancer is still the second leading cause of new diagnosed cancer cases and deaths, closely after lung cancer, although the incidence and mortality are steadily declining (Chen et al., 2016). The most important risk factor is *H. pylori* infection, which can be found in most cases of stomach cancer. Other high risk factors include hereditary susceptibility, diets, alcohol and smoking.

6. Liver cancer. Liver cancer is going to be the sixth leading cause of new diagnosed cancer cases and fourth of deaths. Similar to lung cancer and stomach cancer, the prevalence of liver cancer is higher in men. More liver cancer cases are found in low/medium HDI regions, including East/South East Asia and North Africa. Infection with hepatitis virus (HBV or HCV) is responsible for a great portion of liver cancer cases. Other high risk factors for liver cancer include aflatoxin contamination in food, alcohol abuse, obesity, tobacco and diabetes. In China, the incidence and mortality of liver cancer have decreased, partly because of the control of infection with HBV and a reducing intake of aflatoxins and cyantoxins in food and water (Chen et al., 2016).

7. Esophageal cancer. It is estimated that there will be over 0.57 million (ranks seventh in incidence) new cancer cases and approximately 0.51 million (ranks sixth in mortality) deaths for esophageal cancer in 2018. High incidence regions are found in East Asia, South/East Africa and North/West Europe, with higher rate in males. In China, esophageal cancer is one of the four most common cancers, closely after lung, stomach and liver cancer, in spite of the declining incidence and mortality (Chen et al., 2016). Smoking, alcohol, betel quid, pickled vegetables and high-temperature food are potential risk factors for esophageal squamous cell carcinoma (ESCC), the major type of esophageal cancer (Abnet et al., 2018). Esophageal adenocarcinoma (EAC) is another major type of esophageal cancer, with a rapid increasing incidence in some high HDI regions. Known and suspected causes for EAC include smoking, overweight, GERD and Barrett's esophagus (Coleman et al., 2018).

8. Cervical cancer. As an infection-associated cancer, cervical cancer is the most common cancer in 28 countries

and ranks first for mortality in 42 countries, most of which are low HDI regions. Infection with human papillomavirus (HPV) has been identified as a necessary cause of cervical cancer (Walboomers et al., 1999). In more developed regions, the incidence and mortality of cervical cancer have decreased for decades thanks to regular screening. HPV vaccination works as a powerful tool to prevent HPV infection and thus reduce cervical cancer (Learman and Garcia, 2018). Because of the lack of access to regular screening and HPV vaccination in less developed regions, the improvement in sanitary condition to reduce exposure to high rick-HPV infection may work.

Potential risk factors and strategies for cancer control

At the global level, cancer is still the second-placed cause of deaths for non-communicable diseases, with an increasing incidence. Considering the cancer burden inequalities in different regions, decline of incidence and mortality of some specific cancer types is also found in some regions, which is attributable to effective measures of cancer control. It has been estimated that 30%–40% new cancer cases and nearly 60% cancer deaths can be avoided by prevention from verified and modifiable risk factors (Islami et al., 2018). Understanding the unequal global cancer profile enables us to explore the etiology and potential high risk factors of cancer and to work out strategies for better cancer prevention, early detection and treatment.

Despite the failure in meeting its goal to decrease 50% cancer mortality between 1990 and 2015, the American Cancer Society (ACS) makes significant progress in reducing the mortality in lung cancer, colorectal cancer, prostate cancer and breast cancer by high risk factor control, early screening and effective treatment (Byers et al., 2016). The most important high risk factors are smoking, alcohol, westernized lifestyle (overweight, unhealthy diets and physical inactivity), infection and ultraviolet radiation, etc. Considering the fact that China has the largest population of smokers, the burden of smoking-associated cancers, such as lung cancer, will increase in the future (Chen et al., 2016). More strict practices of tobacco control should be carried out, including the implementation of policy and legislation. Alcohol is closely associated with esophageal carcinoma, colorectal cancer, liver cancer and breast cancer. To reduce alcohol exposure has an important role in cancer prevention (LoConte et al., 2018). With the rapid socioeconomic development in China, the rates of breast cancer and colorectal cancer are continuously increasing, partly because of westernized lifestyle. Public education is also needed to make people realize the benefit of a healthy lifestyle, balanced diet and regular exercise in cancer prevention (Carr et al., 2018). Infection-associated cancers, like stomach cancer, liver cancer and cervical cancer, can be reduced by the prevention from carcinogenic infections.

More than a single-cause disease, cancer is a group of related diseases that are related to hereditary, environmental, inflammation and other factors (Wang, 2017). In the majority of cancers, it takes many years or even decades to develop malignant diseases, which provides an opportunity for cancer prevention. Although progress in treatment, like immunotherapy, has largely improved cancer outcomes (Li and Wang, 2017), cancer prevention is so far the cheapest and most effective method for cancer control. The specific practices include regular cancer screening, avoidance of known risk factors, healthy diet, weight management and physical exercise.

Cancer screening. The most important measure for cancer prevention is to detect precancerous conditions and timely intervention. As recommended for many kinds of cancers, particularly in breast cancer, cervical cancer, lung cancer and colorectal cancer, cancer screening makes it possible to identify and cure pre-cancerous lesions or early-stage malignancy (Gapstur et al., 2018). For women older than 40 years, mammogram screening is important, which has been proven to contribute to the decline in breast cancer mortality. Endoscopic screening is the most effective method to reduce death by colorectal cancer, which offers an opportunity for earlier detection and removal of colorectal adenomas (Byers et al., 2016). For adults aged 45 years or older, a regular stool-based test is necessary and any person with positive result should have a timely colonoscopy (Smith et al., 2018). For women at average risk, screening with Pap test (cervical cytology) alone every 3 years is recommended in women aged 21–29 years, and Pap test alone every 3 years or co-test with hrHPV testing every 5 years in women aged 30–65 years (Jin, 2018). HPV vaccination serves as a novel and effective measure to reduce HPV-associated cervical cancers and the targeted age group is among 9–26 years old (Smith et al., 2018). Low-dose helical computed tomography (LDCT) has been proved to effectively lower the mortality of lung cancer, which enables the detection of suspected pulmonary lesions. It is recommended in smokers aged 55–74 years with at least a 30 pack-year smoking history (Smith et al., 2018).

Avoidance of tobacco. Numerous studies have proven that tobacco is still the leading cause of cancer and other non-communicable diseases. Tobacco control is the most important and effective way to reduce cancer deaths than any other cancer control strategies (Gapstur et al., 2018). In the United States, the smoking prevalence in men and women has declined significantly since 1955, followed by the continuous decline in cancer mortality from 1991 (Gapstur et al., 2018). The long-term benefit of tobacco control is often overshadowed by the short-term economic profits, particu-

larly in low-income and middle-income countries or regions. China is the largest cigarette-consuming country, with the consumption continuously increasing from 1998 to 2017 (Gilmore et al., 2015). More efforts for tobacco control are needed, including more health education and stricter policies.

Less alcohol consumption. Harmful alcohol drinking has been shown to associate with over seven types of cancers, including liver cancer, colorectal cancer, breast cancer, stomach cancer, oral cavity/pharynx cancers, larynx cancers and esophageal cancers. The adverse effects of alcohol increase with the amount of intake. Therefore, reducing alcohol consumption is recommended.

Healthy diet, weight management and physical activity. A healthy lifestyle plays an important role in cancer prevention. Eating more fruits and vegetables may reduce the risk of cancer, partly because of such constituents as vitamins, phytochemicals, and dietary fiber. On the other hand, red meat, especially processed meat, is reported to relate with colorectal cancer. Excessive body weight has been shown to be responsible for various kinds of cancers, including breast cancer and colorectal cancer. Weight management and physical exercise are thus good measures for cancer prevention.

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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