# Chapter 10: Major Cancer Problems and Prospects for Prevention in Asia

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Rengaswamy Sankaranarayanan discusses major cancer problems and prospects for prevention in Asia by showing, on the one hand, the diverse cancer incidence in various countries and, on the other hand, strategies to prevent, screen, diagnose, and treat that are implemented in various nations. To address, reduce, and eliminate the glaring inequities in cancer prevention and care between states, political commitments should allow to allocate adequate resources, implement targeted programs, improve health infrastructures, strengthen human resources, provide universal healthcare, promote efficient and socially conscious public-private partnerships, and develop efficient monitoring systems.

Cancer has become an important health problem in Asia due to aging, growing populations, and changes in lifestyle associated with economic development and epidemiologic transition. Asia accounts for almost two-thirds of the global population and almost half the world burden of cancer. The incidence of cancer cases is estimated to have increased from 6.1 million in 2008 to 9.5 million in 2020. Striking variations in cancer patterns are seen in this vast continent due to different ethnicity, sociocultural practices, human development index, habits, and dietary practices. Seven cancers—namely in lung, breast, large bowel, stomach, liver, prostate, and oral cavity—account for 59 percent of the total burden in Asia. The prevention and early detection linked with appropriate

<sup>&</sup>lt;sup>1</sup> Hyuna Sung, Jacques Ferlay, Rebecca L. Siegel, Mathieu Laversanne, Isabelle Soerjomataram, Ahmedin Jemal, and Freddie Bray, "Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries," *CA: A Cancer Journal for Clinicians* 71, no. 3 (2021): 209–249.

treatment of these cancers will have a telling effect on the cancer burden in Asia.<sup>2</sup>

Given the massive disease burden, prevention and control of cancer require urgent political action and commitment of resources to implement a phased time-bound action plan for improving public and professional awareness, cancer healthcare infrastructure, and human resources.<sup>3</sup> Prevention as well as early detection of cancers lead to both better health outcomes and considerable savings in treatment costs. The still evolving or stagnant cancer health services require substantial investments to ensure equitable access to cancer care for all sections of the population.

## The Status of Cancer Healthcare Services in Asia

Cancer management requires a comprehensive framework and multidisciplinary care. The cancer health services encompass mechanisms for awareness creation, appropriate referral pathways, patient and subject navigation integrated in primary, secondary, and tertiary hospitals, comprehensive cancer centers, and apex centers. These services should provide advanced care, trained human resources to staff the preventive and clinical services, procurement services for drugs, mechanisms for healthcare financing that reduce or avoid catastrophic out-of-pocket expenditure, data systems including cancer registries, quality assurance, on-going monitoring and evaluation of services rendered, and improved services based on the outcome. The main drivers of cost across the cancer continuum of care are the cancer workforce, medical devices and technology, cancer medicines, infrastructure utilization costs, and capital investments.

There are substantial differences in the adequacy and responsiveness of availability, affordability, and access of cancer health services between Asian countries as well as between different regions in vast countries such

<sup>&</sup>lt;sup>2</sup> Sung et al., "Global Cancer Statistics 2020."

<sup>&</sup>lt;sup>3</sup> Rengaswamy Sankaranarayanan, Kunnambath Ramadas, and You-lin Qiao, "Managing the Changing Burden of Cancer in Asia," *BMC Medicine* 12 (2014): doi.org/10.1186/1741-7015-12–3.

as China, India, Indonesia, and the Philippines. Cancer health services are still evolving in most Asian low- and middle-income countries (LMICs). A substantial variation in the development of the various cancer control components is observed between and within countries, corresponding to their level of income and development. Whereas all components of cancer care are well developed in high-income countries (HICs) such as Singapore and the Republic of Korea, services are underdeveloped in many LMICs such as Bangladesh, Cambodia, China, India, Indonesia, Laos, Myanmar, Pakistan, Vietnam, and Yemen. In high-income countries such as Singapore and South Korea, a low mortality to cancer incidence ratio is seen as opposed to a high ratio in countries like India, Mongolia, the Philippines, Tajikistan, and Kyrgyzstan due to lack of adequate health financing, substantial out-of-pocket costs by patients, and widening gap between affordable cancer care and increased cancer mortality.

In many countries, cancer diagnostic infrastructure—particularly high-quality pathology including immunohistochemistry, molecular markers, imaging, and endoscopy—is woefully inadequate. Cancer surgery facilities and cancer surgeons are few and are overstretched. There is considerable disparity and inequity in the distribution of radiotherapy services across LMICs. The "barriers to the accessibility of anticancer medicines include the lack of government reimbursement, budget allocation for healthcare and quality-assured generic and biosimilar medicines, as well as shortages and patient rights."<sup>4</sup>

Achieving the United Nations (UN) 2030 Sustainable Development Goal 3.8 on Universal Health Coverage (UHC) requires that everyone, everywhere can access needed healthcare without experiencing financial ruin as a result of that care.<sup>5</sup> Currently, Thailand and South Korea have

<sup>&</sup>lt;sup>4</sup> Alexandru Eniu, Nathan I. Cherny, Melanie Bertram, Sumitra Thongprasert, Jean-Yves Douillard, Gracemarie Bricalli, Malvika Vyas, and Dario Trapani, "Cancer Medicines in Asia and Asia-Pacific: What Is Available, and Is It Effective Enough?," *ESMO Open* 4, no. 4 (2019): doi.org/10.1136/esmoopen-2018-000483.

<sup>&</sup>lt;sup>5</sup> "Target 3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access tosafe, effective, quality and affordable essential medicines and vaccines for all." sdgs.un.org/goals/goal3.

implemented effective UHC. Countries such as China, India, Indonesia, Malaysia, and the Philippines are in various stages of progress towards achieving UHC.

### Cancer Prevention in Asia

Of the estimated 12 million new cancer cases by 2030 in Asia, at least 30–40 percent are avoidable with cancer prevention, which means nearly three or four million lives could be saved. Indeed, the implementation of cancer prevention strategies would result in the reduction of global cancer mortality, supporting the fulfilment of the United Nations 2030 Sustainable Development Goal 3.4 to reduce cancer deaths by one-third by 2030.6 In Asia, substantial lives saved would be in low- and middle-income countries. Moreover, in the continent, more than 20 percent of all malignant tumors can be attributed to tobacco and human papilloma virus, respectively.

Tobacco control is a major cancer preventive action for lung and head and neck cancers among others that needs a complex undertaking of awareness, weaning of tobacco production, and reducing the consumption of tobacco. The World Health Organization Framework Convention on Tobacco Control (WHO FCTC) is an evidence-based public health treaty developed and implemented in response to the growing global tobacco epidemic. Except for Indonesia, all countries in Asia have ratified the WHO FCTC. FCTC focuses on the implementation and evaluation of key measures to reduce the demand for tobacco: monitoring tobacco use; smoke-free laws; tobacco cessation interventions; health warnings; tobacco advertising, promotion, and sponsorship bans; and tobacco tax increases. In most Asian countries, the

<sup>&</sup>lt;sup>6</sup> "Target 3.4: By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being." sdgs.un.org/goals/goal3.

<sup>&</sup>lt;sup>7</sup> Thomas Stubbs, "Commercial Determinants of Youth Smoking in ASEAN Countries: A Narrative Review of Research Investigating the Influence of Tobacco Advertising, Promotion, and Sponsorship," *Tobacco Induced Diseases* 19 (2021): doi.org/10.18332/tid/139124.

FCTC has increased the implementation of measures across several policy domains, in both demand and supply side. These implementations have resulted in measurable impacts on tobacco consumption, prevalence, and other outcomes.8 However, FCTC implementation must be accelerated to meet all the treaty obligations and consider measures that exceed minimum requirements. In Asia, tobacco is grown in an area of around 2.2 million hectares (ha) with the production of 4084 million kg of tobacco, which accounted for 63 percent of global tobacco production, with China and India producing 52 percent and 22 percent of tobacco in Asia respectively. While Singapore has excelled in implementing FCTC regulations, FCTC implementation has not impacted the amount of tobacco produced in Asia, and this needs particular attention. In 1970, Singapore banned tobacco advertising, as well as smoking in the auditoria of cinemas and theatres and on public buses, and, in 1991, Singapore was the first country to ban duty-free incoming cigarettes. Hong Kong banned manufacture, importation, and sale of smokeless tobacco in 1987, being only the second jurisdiction to do so.

In the last two decades, Asia has been highly successful in controlling the hepatitis B virus (HBV). Forty-eight countries in WHO Southeast Asia and in the Western Pacific regions have endorsed regional action plans for eliminating hepatitis. All Asian countries incorporated HBV vaccination into their national infant immunization programs, and two-thirds of Asian countries had achieved more than 90 percent coverage of completed (three doses) HBV vaccination. The implementation of the hepatitis B vaccination (HepB) has led to substantial decline in carrier states and hepatitis B related morbidity.<sup>9</sup>

Since perinatal transmission is a major route of HBV infection in endemic Asian countries or regions, the administration of a birth dose

<sup>&</sup>lt;sup>8</sup> Janet Chung-Hall, Lorraine Craig, Shannon Gravely, Natalie Sansone, and Geoffrey T. Fong, "Impact of the WHO FCTC over the First Decade: A Global Evidence Review Prepared for the Impact Assessment Expert Group," *Tobacco Control* 28, no. Suppl. 2 (2019): s119–s128.

<sup>&</sup>lt;sup>9</sup> Jade Pattyn, Greet Hendrickx, Alex Vorsters, and Pierre Van Damme, "Hepatitis B Vaccines," *Journal of Infectious Diseases* 224, no. 12 Suppl. 2 (2021): S343–S351.

(HepB-BD) of the HBV vaccine (within 24 hours after delivery) is the key to preventing perinatal HBV infection. However, timely HepB-BD coverage is still low in many places, especially in LMICs of Asia where the burden is concentrated, and this is the major impediment to eliminating HBV.<sup>10</sup> Unfortunately, such initiatives have been delayed due to the impact of the COVID-19 pandemic. Since unsafe injections and blood transfusions are an important route of transmission of HBV, promoting safe injections (defined as injections that do not harm the recipient, the healthcare worker, or the community) and safe blood banking are critical to prevent HBV infection.<sup>11</sup>

The world's first universal HBV vaccination program was introduced in Taiwan in 1984, reducing the prevalence of HBV infection to one-tenth of the original prevalence. The incidence of hepatocellular carcinoma (HCC) was reduced by 69 percent in the vaccinated birth cohorts of 6–19 year-old children and young adults. The risk of developing HCC for vaccinated cohorts was associated with incomplete HBV vaccination, prenatal maternal hepatitis B surface antigen (HBsAg) seropositivity, and prenatal maternal HBeAg seropositivity.

Cervix cancer is highly preventable by combining human papillomavirus(HPV) vaccination and early detection and treatment of cervical cancer precancerous lesions such as cervical intraepithelial neoplasia Grades 2 and 3 (CIN 2/3) and adenocarcinoma *in-situ* (AIS). Currently licensed HPV vaccines target two to nine HPV types. HPV vaccine is a prophylactic vaccine and to be effective should be given to

<sup>&</sup>lt;sup>10</sup> Margaret J. de Villiers, Shevanthi Nayagam, and Timothy B. Hallett, "The Impact of the Timely Birth Dose Vaccine on the Global Elimination of Hepatitis B," *Nature Communications* 12, no. 1 (2021): 6223, doi.org/10.1038/s41467-021-26475-6.

<sup>&</sup>lt;sup>11</sup> Shan Shan, Fuqian Q. Cui, and Jidong D. Jia, "How to Control Highly Endemic Hepatitis B in Asia," *Liver International* 38 (2018): 122–125.

<sup>&</sup>lt;sup>12</sup> Mei-Hwei Chang, "Hepatitis B Virus and Cancer Prevention," *Recent Results in Cancer Research* 188 (2011): 75–84; Mei-Hwei Chang, San- Lin You, Chien-Jen Chen, Chun-Jen Liu, Chuan-Mo Lee, Shi-Ming Lin, Heng-Cheng Chu, Tzee-Chung Wu, Sheng-Shun Yang, Hsu-Sung Kuo, and Ding-Shinn Chen, "Decreased Incidence of Hepatocellular Carcinoma in Hepatitis B Vaccinees: A 20-Year Follow-up Study," *Journal of the National Cancer Institute* 101, no. 19 (2009): 1348–1355.

HPV naive girls and women. In Southeast Asia and the Western Pacific region of Asia, although more than 20 countries have introduced HPV vaccination, only Bhutan, Maldives, Sri Lanka, Thailand, Federated States of Micronesia, Marshall Islands, Myanmar, Malaysia, South Korea, and Fiji have implemented HPV vaccination covering the entire countries. <sup>13</sup> Programs cover selected regions/provinces within India, Indonesia, and the Philippines. The challenges for HPV vaccination are similar to elsewhere: lack of awareness, the low standing of cervix cancer elimination in the political agenda, lack of advocacy for women, vaccine misinformation, vaccine hesitancy, anti-vaccine campaigns, perceived excess harms, vaccine costs and affordability, confusion on morality and sexual mores, and lack of strong recommendations from healthcare providers.

Given the vast potential for cervical cancer prevention and its social relevance, the WHO has called for implementation of three interventions with high coverage, namely, HPV vaccination, screening for early detection and treatment of lesions by 2030, and setting incidence-elimination threshold to less than 4/100,000 women. The WHO has proposed this three-pronged approach to be implemented before 2030. Almost all Asian countries need to invest substantially and plan judiciously to meet the implementation targets. Hence, data systems to monitor implementation coverage are critical.

## Cancer Screening in Asia

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<sup>&</sup>lt;sup>13</sup> Laia Bruni, Anna Saura-Lazaro, Alexandra Montoliu, Maria Brotons, Laia Alemany, Mamadou Saliou Diallo, Oya Zeren Afsar, D. Scott LaMontagne, Liudmila Mosina, Marcela Contreras, Martha Velandia-Gonzalez, Roberta Pastore, Marta Gacic-Dobo, and Paul Bloem, "HPV Vaccination Introduction Worldwide and WHO and UNICEF Estimates of National HPV Immunization Coverage 2010–2019," *Preventive Medicine* 144 (2021): 106399,10.1016/j.ypmed.2020.106399; Rei Haruyama, Sumiyo Okawa, Hiroki Akaba, Hiromi Obara, and Noriko Fujita, "A Review of the Implementation Status of and National Plans on HPV Vaccination in 17 Middle-Income Countries of the WHO Western Pacific Region," *Vaccines (Basel)* 9, no. 11 (2021): doi.org/10.3390/vaccines9111355.

Cancer screening is mostly sporadic, without poor organization, coverage, and quality assurance in most Asian countries, with the exception of South Korea, Singapore, Thailand, Taiwan, and the Hong Kong special administrative region. In most countries, the primary screening method is based on cytology with screening activity, except for Bangladesh, India, and Indonesia, where visual inspection of the cervix with acetic acid (VIA) is mainly used as a primary screening method. Thailand has switched over to HPV testing-based screening from cytology recently using COBAS 4800 platform. The high negative predictive value for cervical neoplasia even for a single baseline HPV test is impressive, and it has allowed screening intervals to be extended up to ten years. WHO recommends using HPV DNA detection rather than VIA or cytology as the primary test for screening, management, and treatment approaches, if infrastructure allows.

HPV screening has been recently piloted in Sri Lanka. Screening uptake rates are dismally low (~5 percent) in countries such as Bangladesh, India, and Indonesia, whereas they range between 30 and 60 percent in countries such as Japan, South Korea, Singapore, Taiwan, and Thailand. Cervical cancer incidence rates have substantially declined following screening programs in Singapore, South Korea, Hong Kong, and Taiwan. The linkage between screening and treatment needs to substantially improve in Asian countries with some screening activity. In the future, given the performance profile of different screening tests, the high accuracy, objectivity, reproducibility, and negative predictive value associated with HPV testing makes it the most preferred test to be considered for implementation in new and upcoming screening programs in Asian countries.

Breast cancer screening programs in Asia are fewer than cervix cancer screening initiatives. Large scale mammography-based screening programs

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<sup>&</sup>lt;sup>14</sup> Eiko Saitoh Aoki, Rutie Yin, Kemin Li, Neerja Bhatla, Seema Singhal, Dwiana Ocviyanti, Kumiko Saika, Mina Suh, Miseon Kim, and Wichai Termrungruanglert, "National Screening Programs for Cervical Cancer in Asian Countries," *Journal of Gynecological Oncology* 31, no. 3 (2020): e55, doi.org/10.3802/jgo.2020.31.e55; Bruni et al., "HPV Vaccination Introduction Worldwide."

are on-going in Japan, Hong Kong, Singapore, South Korea, and Taiwan. Singapore was the first country in Asia to offer biennial mammography screening for 50 to 69 year-old women since 2002. In 2014, a formal evaluation indicated that the breast cancer detection rate in the Singapore program was 182.1 per 100,000 women screened, and the positive value was 1.7 percent; the interval cancer rate was 75.1 per 100,000 screen negatives and the sensitivity and specificity were 75.1 percent and 85.7 percent respectively. The Korean National Cancer Screening Program (KNCSP) recommends biennial breast cancer screening through mammography for women aged 40 to 69 years. The KNCSP has been effective in reducing breast cancer mortality by 59 percent among Korean women aged 40 to 69 years. The program has switched over to digital mammography screening from screen film mammography.

South Korea has an ongoing colorectal cancer (CRC) screening program based on annual fecal immunochemical testing (FIT) for adults aged 50 years and above and triage of FIT-positive persons using colonoscopy. The results of Korea's national colorectal cancer screening program from 2006 to 2013, involving 20.6 million people, indicated a 6.4 percent FIT positivity rate and compliance rate of 46.6 percent for diagnostic investigations of FIT positive persons; side effects within three months after colonoscopy accounted for 0.17 percent of all procedures, with bleeding being the most common. In an observational cohort study,

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<sup>&</sup>lt;sup>15</sup> Kunsei Lee, Hyeongsu Kim, Jung Hyun Lee, Hyoseon Jeong, Soon Ae Shin, Taehwa Han, Young Lan Seo, Youngbum Yoo, Sang Eun Nam, Jong Heon Park, and Yoo Mi Park, "Retrospective Observation on Contribution and Limitations of Screening for Breast Cancer with Mammography in Korea: Detection Rate of Breast Cancer and Incidence Rate of Interval Cancer of the Breast," *BMC Women's Health* 16, no. 1 (2016): 72, doi.org/10.1186/s12905-016-0351-1.

<sup>&</sup>lt;sup>16</sup> Eunji Choi, Jae Kwan Jun, Mina Suh, Kyu-Won Jung, Boyoung Park, Kyeongmin Lee, So-Youn Jung, Eun Sook Lee, and Kui Son Choi, "Effectiveness of the Korean National Cancer Screening Program in Reducing Breast Cancer Mortality," *NPJ Breast Cancer* 7, no. 1 (2021): 83, doi.org/10.1038/s41523-021-00295-9.

<sup>&</sup>lt;sup>17</sup> John Hoon Rim, Taemi Youk, Jung Gu Kang, Byung Kyu Park, Heon Yung Gee, Jeong-Ho Kim, and Jongha Yoo, "Fecal Occult Blood Test Results of the National Colorectal Cancer Screening Program in South Korea (2006–2013)," *Scientific Reports* 7, no. 1 (2017): 2804, doi.org/10.1038/s41598-017-03134-9.

a biennial FIT screening program in Taiwan achieved a 62 percent reduction in CRC-related mortality. Singapore launched colorectal cancer screening in 2004, and citizens as well as permanent residents aged 50 or more years were invited to screen for colorectal cancer annually using free FIT kits from the Community Health Assist Scheme annual FIT screening in primary care clinics under the Integrated Screening Program.

In Asia, Taiwan is the only country with an oral cancer screening program.<sup>19</sup> Around 4.6 million people with areca nut and tobacco habits have undergone biennial oral cancer screening in Taiwan. However, the program has yet to impact oral cancer incidence and mortality. A national stomach cancer screening program using upper gastrointestinal imaging or gastroscopy for people aged 40 years has also been on-going since 2002.

## The Challenge of the COVID-19 Pandemic for Cancer Control in Asia

The COVID-19 pandemic has dramatically affected cancer healthcare, with substantial impact on health systems around the world and the whole Asia, with emphasis on managing the pandemic at the expense of other essential and elective health services.<sup>20</sup> This situation has put backwards all

<sup>&</sup>lt;sup>18</sup> Han-Mo Chiu, Sam Li-Sheng Chen, Amy Ming-Fang Yen, Sherry Yueh-Hsia Chiu, Jean Ching-Yuan Fann, Yi-Chia Lee, Shin-Liang Pan, Ming-Shiang Wu, Chao-Sheng Liao, Hsiu-Hsi Chen, Shin-Lan Koong, and Shu-Ti Chiou, "Effectiveness of Fecal Immunochemical Testing in Reducing Colorectal Cancer Mortality from the One Million Taiwanese Screening Program," *Cancer* 121, no. 18 (2015): 3221–3229.

<sup>&</sup>lt;sup>19</sup> Shu-Lin Chuang, William Wang-Yu Su, Sam Li-Sheng Chen, Amy Ming-Fang Yen, Cheng-Ping Wang, Jean Ching-Yuan Fann, Sherry Yueh- Hsia Chiu, Yi-Chia Lee, Han-Mo Chiu, Dun-Cheng Chang, Yann-Yuh Jou, Chien-Yuan Wu, Hsiu-Hsi Chen, Mu-Kuan Chen, and Shu-Ti Chiou, "Population-Based Screening Program for Reducing Oral Cancer Mortality in 2,334,299 Taiwanese Cigarette Smokers and/or Betel Quid Chewers," *Cancer* 123, no. 9 (2017): 1597–1609; J.-Y. Lin, "Information System of Nationwide Population-Based Cancer Screening in Taiwan," *Journal of Global Oncology* 4, no. Suppl. 2 (2018): doi.org/10.1200/jgo.18.84500.

<sup>&</sup>lt;sup>20</sup> Mengyuan Dai, Dianbo Liu, Miao Liu, Fuxiang Zhou, Guiling Li, Zhen Chen, Zhian Zhang, Hua You, Meng Wu, Qichao Zheng, Yong Xiong, Huihua Xiong, Chun Wang, Changchun Chen, Fei Xiong, Yan Zhang, Yaqin Peng, Siping Ge, Bo Zhen, Tingting Yu, Ling Wang, Hua Wang, Yu Liu, Yeshan Chen, Junhua Mei, Xiaojia Gao, Zhuyan Li, Lijuan Gan, Can He, Zhen Li, Yuying Shi, Yuwen Qi, Jing Yang, Daniel G. Tenen, Li Chai, Lorelei A.

cancer control efforts, and cancer patients are at great risk of complications and death. In Asia, the impact of COVID-19 on cancer service delivery—such as screening, diagnosis, treatment, follow-up, and end-of-life care—has been substantial. In many countries, the existing few cancer treatment facilities were designated and transitioned to COVID care centers, which had a telling effect on access to diagnosis, treatment, and follow-up care.

#### Conclusion

There is substantial variation across Asian countries in terms of national response to cancer control, efficiency of cancer healthcare services, and the availability and access to cancer early detection programs and the means of healthcare financing. On the one hand, universal healthcare is not available in most LMICs in Asia, leading to financial toxicity and high out of pocket healthcare expenditure wrecking household incomes and stability. On the other hand, high income countries such as Singapore and South Korea have done well compared to Asian LMICs. Political commitments, adequate budgetary allocation of resources, phased implementation of well-thought-out programs, improved infrastructures and human resources, universal healthcare available for all segments of society, efficient and socially conscious public-private partnerships, and development of efficient data systems are urgently needed to avoid the glaring inequity in cancer prevention and cancer care between countries in Asia.

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Mucci, Mauricio Santillana, and Hongbing Cai, "Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study During the COVID-19 Outbreak," *Cancer Discovery* 10, no. 6 (2020): 783–791.

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