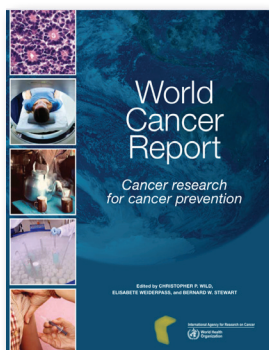




## BOOK REVIEWS, NOTES AND COMMENTS

Edited by  
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### WORLD CANCER REPORT Cancer research for cancer prevention

Wild CP, Weiderpass E,  
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The 2019 *World Cancer Report* (WCR) entitled “Cancer research for cancer prevention” by the International Agency for Research on Cancer (IARC) has been recently published. This five-year publication is unique in its characteristics since it is not based on assessments made by IARC or by any other authority but is a collection of peer reviewed papers prepared by recognized investigators worldwide. In particular, this new WCR is focused on a topic that is highly relevant also for the mission of our Institute (Istituto Superiore di Sanità, ISS, Italian National Institute of Health), i.e. prevention. Because of the specific goal of IARC, cancer prevention is tackled but we are all aware that prevention is the only way to decrease the burden of all types of diseases and to promote public health.

This volume, which is organized in six sections, is structured to guide the reader on how all the information on statistics, causes and mechanisms of cancer can be conveyed into implementation of prevention strategies. Moreover, one section (section 4) is focused on inequalities and cancer. Below I provide a brief summary of the content of these sections.

Section 1 provides an updated picture of cancer impact on human health. Of the 15.2 million premature deaths from noncommunicable diseases worldwide in 2016, almost 30% were due to cancer, thus confirming that cancer is among the most relevant public health issue. A great variation of incidence rates for several types of cancer between countries over time is observed. Although the cancer incidence burden is currently highest in countries with very high human development index (HDI), the predicted increases in the cancer burden will have the greatest impacts on countries with low and medium HDI. Moreover, cancer mortality is declining in most higher-income countries, but not in lower-income countries. The understanding of the causes of variation in cancer incidence rates is key for designing effective cancer prevention strategies.

Section 2 gives a detailed description of the correlation between life style and environmental factors with cancer outcome. Tobacco products (chapter 2.1), in-

fectious agents such as *Helicobacter pylori* and human papilloma virus (HPV) (chapter 2.2), alcohol consumption (chapter 2.3), physical agents such as UV radiation (chapter 2.4) and ionizing radiation (chapter 2.5), dietary patterns particularly those associated with overweight/obesity (chapter 2.6), lack of physical activity (chapter 2.7), dietary contaminants (chapter 2.8), environmental pollutants including air pollution and polluted water from contaminated soils (chapter 2.9), occupational carcinogens (2.10) and hormone-based drugs (2.11) are all potential cancer risk factors. The good news is that exposure to most of these factors is a preventable contributor to the global cancer burden being amenable to interventions by behavioral, technological and regulatory means.

Section 3 shows how important is the understanding of the mechanisms of carcinogenesis for cancer prevention and therapy. About 5-10% of all cancers are estimated to be due to highly penetrant inherited mutations. The remaining cancers are due to environmental/endogenous agents or the interaction between these agents and weak genetic susceptibility due to low-penetrance gene variants (chapters 3.1 and 3.2). New generation sequencing has allowed to identify high density mutations in cancer types that correlate with distinct environmental exposures (e.g. skin cancer and UV mutational signature) (chapter 3.3). Faulty regulation of pathways controlling genetic stability (chapter 3.4) or constitutive activation of pro-inflammatory transcription factors (chapter 3.5) can mediate cancer development. Precision therapies targeted to cancer-specific DNA repair defects, either by synthetic lethality or by immunotherapy, are presented as promise in the treatment of a significant subgroup of human cancers. Reproductive and hormonal factors appear to be important contributors to several cancer sites (chapter 3.6). Metabolomics of human biospecimens (chapter 3.7) as well as the analysis of epigenetic changes (chapter 3.8) can be a useful tool for a cancer prevention strategy. Immune cells are essential components of the tumour microenvironment (chapter 3.9). Targeting the immune system has the potential to become the new frontier in the fight against cancer. Microbiota-targeted cancer prevention strategies (chapter 3.10) appear also promising, but they have yet to be evaluated in prospective studies. To stress the relevance of mechanistic evidence, the key characteristics of human carcinogens have been recently applied in IARC Monographs evaluations (chapter 3.11). Data on the key characteristics can provide independent evidence of carcinogenicity when data from studies in humans are lacking and can help in establishing biological plausibility. This approach is being increasingly applied by agencies throughout the world.

Section 4 deals with inequalities that affect cancer

prevention. Cancer inequalities are driven by the interplay of many factors, including educational status, financial income or specific living environments (chapter 4.1). The impact of these factors on cancer burden within certain countries is described. The example of a preventable disease such as cervical cancer is taken to show the impact of services for prevention, early detection, and treatment on its incidence and mortality rate in Africa (chapter 4.2). Women in developing countries, where these services are rare, present cervical cancer incidence rates 2-fold higher and cervical cancer mortality rates 3-fold higher than those for women in developed countries. There is an urban-rural difference in the incidence and spectrum of cancer types in China that could be partially explained by differences in lifestyles and dietary patterns between urban and rural communities along with rapid economic development, urbanization, and the ageing of the population (chapter 4.3). The rapid economic development of India has given rise to vast socioeconomic changes and, consequently, to significant disparities in access to cancer prevention and control services (chapter 4.4). Basic differences are present between screening practices followed in European Union countries (chapter 4.5). Research shows that achieving relatively high participation rates in cancer screening will reduce health inequalities. Disparities in cancer prevention services in the USA is a long-standing, persistent cause of inequity (chapter 4.6). The cancer burden and, more generally, the health of Indigenous peoples are significantly affected by the broader social, political, and economic environments as well as by the legacy of colonization and racism (chapter 4.7).

Section 5 deals with prevention of particular tumor types. Lung cancer (chapter 5.1), head and neck cancer (chapter 5.2), oesophageal cancer (chapter 5.3), stomach cancer (chapter 5.4), colorectal cancer (chapter 5.5), liver cancer (chapter 5.6), pancreatic cancer (chapter 5.7), skin cancer (chapter 5.8), breast cancer (chapter 5.9), cervical cancer (chapter 5.10), endometrial cancer (chapter 5.11), ovarian cancer (chapter 5.12), prostate cancer (chapter 5.13), testicular cancer (chapter 5.14), bladder cancer (chapter 5.15), kidney cancer (chapter 5.16), brain and other primary central nervous system tumors (chapter 5.17), thyroid cancer (chapter 5.18), Non-Hodgkin lymphoma (chapter 5.19) and leukaemia (chapter 5.1) are specifically addressed. The general take home message is that knowledge of cancer causation and prevention must be qualified according to the tumour type or subtype being considered. For example, since exogenous causes of prostate cancer have not been identified, its prevention must focus on

detection of precancerous lesions and screening procedures can be meaningfully explored only with respect to particular cancer sites.

Section 6 presents the basis for, and outcomes from, prevention strategies. The burden of death from the multiple different cancer types can be decreased in all communities and countries. The WHO perspective for tobacco cessation is presented. Cessation support can more than double the chance of successfully quitting. Interventions to change behavior (chapter 6.1) related to nutrition, exercise, and weight gain (chapter 6.2) are key factors in the design of programmes and policies. In some low-income countries, up to one third of all cases of cancer are directly associated with various infections. Vaccination against hepatitis B virus and HPV is effective for liver and cervical cancer, respectively (chapter 6.3). As shown by the use of anti-estrogenic agents in breast cancer, deaths from sporadic cancer may be decreased through chemoprevention (chapter 6.4). Early detection of cancer is a critical component of cancer control. Emerging genomic tools (chapter 6.5) together with screening programmes (chapter 6.6) are an important opportunity for cancer reduction by diagnosis of early-stage disease. The presence of circulating tumour cells is highly predictive of metastatic outgrowth and worse outcome in patients with both early- and late-stage disease (chapter 6.7). Governmental action has been effective in reducing exposure to known and suspected carcinogens (chapter 6.8) particularly by hazard-based regulation (examples include reduction of tobacco use and elimination of persistent organic pollutants). Prevention strategies common to noncommunicable diseases should focus on tobacco, alcohol, obesity, and physical inactivity (chapter 6.9).

Finally, it is of note that two chapters of the 2019 WCR, namely chapter 2.9<sup>1</sup> and 3.4<sup>2</sup>, see as authors researchers of our Institute. This testifies the recognition worldwide of the research conducted in our Institute in the field of environmental epidemiology and mechanisms of carcinogenesis.

<sup>1</sup>Pietro Comba, Ivano Iavarone, Manolis Kogevinas “Contamination of air, water, soil, and food. The challenge is to characterize specific risks”

<sup>2</sup>Eugenia Dogliotti, Margherita Bignami “DNA repair and genetic instability. Endogenous and exogenous sources of damage and hereditary syndromes”

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