



Cancer Prevention - How Well is this Working?

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Abstract

Many potential causes of cancer have been identified, and many attempts have been made to inhibit cancer initiation and progression. It is unrealistic to expect that all environmental causes of cancer can be eliminated. We should work towards making and keeping our environment clean, however, cancer prevention will not be realistic until the key, unique and primary mechanism(s) that direct cells to undertake cancerous division are identified, and the ways of inhibiting such mechanisms are found.

Keywords: Cancer Prevention; Environment

Can cancer really be prevented? The signing of the National Cancer Act of 1971 by president Richard Nixon can be seen as a formal beginning of cancer-prevention effort in the USA. Subsequently, a National Cancer Prevention Day was established through the USA House of Representatives on February 4, 2013, recognizing the need to prevent and reduce cancer "as much as possible through healthy lifestyles and clean environments".

A recent search of PubMed for "cancer AND prevention" showed some 202,297 publications; a search of Grants.gov showed 54 open grant solicitations on "cancer AND prevention" out of the total of 171 on "cancer" alone (some 31%). Clearly, much time, money and effort are being directed to "war on cancer". After some 50 years, it may be appropriate to examine how well has "cancer prevention" been performing in practice.

Lung cancer

Lung cancer incidence has been decreasing for several years, particularly in males, however it is still the second most common cancer in both females and males, only behind breast and prostate cancer, respectively. Smoking, a main cause of small cell and non-small cell lung cancer, contributes to 80 percent and 90 percent of lung cancer deaths in women and men, respectively [1] and remains the main cause of lung cancer-related death in the US, representing about 27.4% of all cancer deaths [2,3]. The American Cancer Soci-

ety's estimate that in 2018 in the United States there will be some 234,030 new cases of lung cancer (121,680 in men and 112,350 in women), and 154,050 deaths from lung cancer (83,550 in men and 70,500 in women) [4]. Despite the very serious prognosis (outlook) of lung cancer, some people with earlier stage cancers are cured. More than 430,000 people alive today have been diagnosed with lung cancer at some point [1].

It has been estimated that active smoking is responsible for close to 90 percent of lung cancer cases [5], hence it would seem obvious that the best lung-cancer prevention would be not to continue selling tobacco products. Tiffin [6] asked: "Why do we still permit tobacco use?" Taking his example, Canadian government collect \$2.81 billion in tobacco sales taxes federally while in 2012 the direct and indirect cost of lung cancer, asthma and chronic obstructive pulmonary disease (for all of which of smoking is considered to be the number one cause) in Canada was \$12.0 billion. Even considering just the economics, this is not a good trade-off. Sadly, the best available measure to prevent lung cancer is not being used.

Some 10 - 15% of all lung cancers are caused by factors other than active smoking [7]. Importantly, lung cancers in never-smokers exhibit a different molecular profile and response to therapy from that found in smokers. It might make more sense to focus prevention on defining the genetic and environmental factors responsible for the development of lung cancer in never-smokers.

Breast cancer

About 1 in 8 U.S. women (about 12.4%) will develop invasive breast cancer over the course of their lifetime. In 2018, an estimated 266,120 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S., along with 63,960 new cases of non-invasive (in situ) breast cancer [8]. Numerous ways of decreasing the risk of developing breast cancer have been listed [9]. Preventing breast cancer presents even stiffer challenge since the key factors that influence developing the condition include "being a woman and getting older" [10]. The presence of inherited gene mutations such as BRCA1 and BRCA2 may indicate a higher risk of developing breast and ovarian cancer but it does not offer a way to prevent it.

Prostate cancer

It is not known what causes prostate cancer. In common with other cancers, recommendations are made about possible risks that increase the likelihood of developing prostate cancer - age, ethnicity, family history that a man can do nothing about, or are so vague as being practically useless - obesity, exercise, diet [11].

Other cancers

The American Cancer Society expects an estimated 1,658,370 new cancer diagnoses and 589,430 deaths from cancer a year [12]. While some progress has been made in treating successfully some cancers when diagnosed early, progress towards "preventing" cancers has been slow if any. For example, some 56% people diagnosed with early-stage lung cancer live for at least five years after diagnosis. Compared to late-stage lung cancer diagnosis (i.e. when the disease has spread to other areas of the body), the five-year survival is 5% [13].

All this begs a question: "Can cancer really be prevented?" The current Oxford Dictionary defines "prevention" as "The action of stopping something from happening or arising." "Avoidance" is defined as "The action of keeping away from or not doing something." It would appear that the best the current efforts can do is to aim at cancer avoidance.

It has been suggested many years ago that cancer is a preventable disease [14]. How realistic is cancer prevention? Let me propose a notion that until the actual first step that initiates cancer is known at the cellular level, it will not be possible to prevent cancer happening. Our current knowledge can suggest biological predispositions and external factors that are likely to play a role in the

overall process, but not as yet the actual first step. We do know that DNA replication is not perfect but we are not as yet fully able to pinpoint errors and defects in DNA that inevitably lead to cancer generation.

Only about 5% to 10% of all cancers result directly from gene defects inherited from a parent, with the abnormal gene being passed along from generation to generation (for example, Hereditary Breast and Ovarian Cancer (HBOC) syndrome, Lynch syndrome (hereditary non-polyposis colorectal cancer), Li-Fraumeni syndrome) [15].

Many potential external causes of cancer have been identified [14]. The authors examined several potentially modifiable risk factors, concluding that smoking and alcohol use were the most frequent causes of cancer across the world, in both high- and low-middle-income countries. Persistent infections with human papilloma virus (HPV) have been found to be a major risk factor for women. However, not all cancers such as prostate, kidney, melanoma, and lymphomas were found not to be associated with any modifiable risk factors, largely because multiple environmental and behavioural risks might be involved. Further, risks associated with occupational exposures, *Helicobacter pylori* and components and additives in food, and exposure to ultraviolet light and environmental tobacco smoke need to be considered. However, evaluation of such is difficult because accurate exposure data (e.g. extent of exposure to environmental tobacco smoke, ultraviolet light, protection used, etc.) are not available. Most such cancers are caused by acquired mutations that starts in one cell, and then is passed on to any new cells as cells divide. One of the reasons that cancer develops is a loss of function of the tumor suppressor genes. When this happens, cells can grow out of control, and this can lead to cancer. Patients with such defect become at high risk for cancer development, so the concept of primary prevention or at least very early detection in a "pre-malignant" state is realistic.

In general, generating a proof of prevention in clinical trials is always difficult. Very large numbers of patients are needed to demonstrate any efficacy, with a statistical significance; proving a null hypothesis in this case, i.e. the absence of carcinogenesis, is a formidable challenge. Further, there will be many confounding, inherently genetic and epigenetic variation and the diversity of environmental exposures among individual patients in such studies. Should we accept that prevention of most cancers is a pipe dream? Perhaps not; but the focus of research must be directed to elucidating the primary events in cancer initiation.

Some argue [16] that “the obsession with curing advanced disease has prevented progress in the war on cancer”. The issue of medical ethics - the patients’ right to refuse or choose their treatment, acting in the best interest of the patient, not be the cause of harm (doing more good than harm), and decisions on who gets what treatment - comes into play here. Working towards finding the primary steps in cancer initiation would support these sentiments.

Advances have been made in diagnosing and treating cancer, notably in case of hematological malignancies. Even with determining a genetic predisposition to the disease, prevalence tends to remain unchanged indicating that prevention of the condition remains ineffective [17].

For cancers for which there are clearly established cause and effect relationships such as for lung cancer and tobacco smoking, measures taken to limit exposure to tobacco do appear to reduce lung cancer incidence [18]. However, not always; for example, in 2013, there were 11,174 new cases of lung cancer diagnosed in Australia (6,627 males and 4,548 females). In 2018, it is estimated that 12,741 new cases of lung cancer will be diagnosed in Australia (7,212 males and 5,529 females) [19]. While even more effective measures could be put in place such as banning tobacco altogether, such might be counter-productive at several levels (personal, commercial).

Taking steps that might lessen the risks of developing cancer need to start at a personal level, by avoiding risks that each individual can eliminate, such as by not smoking, limiting exposure to ultraviolet light, maintaining healthy diet and life style, etc. We need to recognize that ability to do so will much depend on individual financial situation. It is, however, even more important that the society, effectively enabled by governments making the required decisions about policies, implementation, and funding, starts putting measures in place that eliminate, or at least reduce the global presence of harmful, unhealthy environmental, and also behavioural (such as the use of illegal drugs) factors.

Although it is “politically correct” for governments, organizations and environmental groups, and even prominent individuals to spend much time in discussions on how to correct the current environmental conditions, very little effective, if any actions have been suggested and put into practice. Advice given to general public

that comes out from such activities is rather weak: “Go Green and buy products that are environment friendly”; “3Rs - Reduce, Re-use and Recycle”; “Plant trees wherever you can” [20].

What are some of the environmental factors that need to be addressed? It is “comfortable” to “blame” global warming, but our task is to ensure that our air, water, the land, and all-natural resources (including sources of food such as animals) are free of harmful contaminants. The task is getting increasingly challenging as the size of the human population grows, requiring more land, water, and of everything - cars producing emissions, industrial activities generating toxic waste, more carbon emissions - all adding toxins into our environment. Is it realistic to make behavioural and environmental changes to decrease cancer-causing factors while we extract some 55 billion tons of fossil energy, minerals, metals and bio mass from the Earth? While we continue to reduce forested areas at a rate of 375 km² per day? While we have a “garbage island” floating in our ocean the size of India, Europe and Mexico combined? [21].

One might expect that provided cancer prevention works well it would have the biggest impact on the incidence of cancer in the rich, well-developed western countries, however, statistics of cancer does not show this. In fact, developed countries such as Denmark, France, Australia, Belgium, Norway and the United States top the list, and countries such as Yemen, Oman, Namibia, Nepal and Mauritania show the lowest incidence [22]. It has been suggested [23] that the highest rates of incidence such as shown in Denmark has more to do with a high efficiency of diagnosing the disease rather than its frequency. As the connection between improved ways of diagnosing diseases and the apparent disease incidence was observed before, this adds another factor that makes evaluating of any benefits of cancer prevention very inaccurate.

Conclusion

Current activities done under the label of “cancer prevention” have some merit; it is beneficial to keep our environment clean for all, and on an individual level to adopt healthy life style. However, it is very unlikely that such general measures will prevent cancer occurring, or indeed have much impact on incidence of cancer. Our ability to prevent cancer might become more realistic once we acquire knowledge about the key, unique and primary mechanism(s) that direct cells to undertake cancerous division and develop ways of inhibiting such mechanisms. Human and financial resources should be directed to such an effort. Knowledge acquired in this

way would also enable us to develop therapies for treating cancer at its very early stages of development.

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