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SCIENTIFIC REVIEWS

Preventable Cancer Burden Attributable to Lifestyle.
Cancer risk prevention by cessation of smoking, reduced alcohol consumption, decreased overweight/obesity, daily exercise and healthier diet

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Abstract

Cancer is the second most important cause of morbidity and mortality worldwide. It is estimated by numerous epidemiological studies and statistical surveys of data from most countries that between 40-50% of all cancer cases are preventable by changing into a healthier lifestyle, with special emphasis on smoking cessation, healthier diet, reduced obesity/overweight, decreased alcohol consumption and avoid sedentary life with daily exercise. Prevention offers the most cost-effective long-term strategy for the control of cancer and national policies should aiming to raise awareness, to reduce exposure to cancer risk factors and adopt healthy lifestyle. This review collected and analysed data from various studies on the quantitative reduction of risk for certain cancers associated with five modifiable lifestyle factors:

A. **Cessation of smoking** is an alternative to an unhealthy lifestyle habit. Quitting smoking showed spectacular reduction in lung cancer mortality and other types of human malignancies. Quitting smoking for more than 10 years decreased half of the risk for lung cancer, while more than 20 years of smoking cessation decreased drastically adult morbidity and mortality from cancer and other diseases. B. **Reducing alcohol consumption** is another lifestyle factor that decreases cancer risk. In particular 6 alcohol-related cancers: colorectal, post-menopausal breast, oral cavity and pharynx, liver, larynx and oesophageal squamous cell carcinoma. Heavy drinkers can have as much as a 10-15 times higher risk of developing these cancers than those who do not drink. Light alcohol consumption can be slightly beneficial to health. C. **Reduction of overweight/obesity** can be beneficial to health and decreases the risk of related cancers. Obese people have even higher risk for certain cancers compared to normal-weight people. Overweight/obesity is associated with increased risk for colorectal, breast (in postmenopausal women), endometrium, oesophagus, kidney, liver, multiple myeloma, gastric cardia, ovarian and thyroid. **D. Following daily physical exercise** and an active life can be beneficial to health and reduce the risk for a number of cancers. **E. Healthy eating** is another important factor in the fight against cancer. Increased consumption of fruit and vegetables, whole grains, fat-free dairy products, lean meats, poultry, fish, beans, nuts, seeds, legumes and olive oil is beneficial to health, Avoiding processed meats, saturated and trans fats, sodium, salty and smoked foods, and added sugars control cancer risk. This review contains some very important reviews and epidemiological studies from the international scientific literature.

Introduction: What are the most important causes of cancer?

According to the most authoritative scientific society on cancer, the National Cancer Institute of the USA, the most important causes of cancer in humans are: old age (most cancers appear after 65 years of age), smoking (active and passive), obesity (or overweight), unhealthy diet, alcohol consumption, lack of daily exercising, exposure to carcinogens (mainly in the working environment and from indoor unventilated kitchen cooking), infectious agents (viruses) and genetics. [1]

Why a person develops cancer is difficult to predict, but scientific research in the last decades has shown that certain risk factors and for prolonged exposures, may increase a person's chances of developing cancer. Most cancer risk factors are initially identified in epidemiology studies. Scientists followed for years and collect data (smoking rates, dietary habits, exposure to occupational carcinogens, infections, etc) at large groups of people and compare those who develop certain types of cancer with those who don't. These studies may show statistically, that the people who develop cancer are exposed to certain carcinogenic substances or have a lifestyle (smoking, diet, alcohol, obesity, lack of physical activity) that increase risk to develop certain types of cancer at old age.[1]

A recent epidemiological study in the United Kingdom (UK) calculated the Relative Risks (RRs) from meta-analyses of cohort studies and the prevalence of exposure to risk factors from nationally representative population surveys and cancer incidence data for 2015. The results found that 4 out of 10 (37%) cancer cases in 2015 in the UK were attributable to known risk factors. Tobacco smoking contributed by far the largest proportion of attributable cancer cases (15%), followed by overweight/obesity, accounting for 6.3%, of all cases in the UK in 2015. Researchers concluded that tobacco smoking remains the top contributor to human cancer while overweight and/or obesity, which is linked to unhealthy diet and lack of exercise, is second because it affects a high proportion of the UK population and is also linked with many cancer types.[2]

Another similar study by Parkin et al.,' published in 2011, investigated novel data on the burden of avoidable cancers in the UK in 2010. Tobacco smoking was by far the most important risk factor for cancer, responsible for 60,000 cases (19.4% of all new cancer cases) in 2010. The relative importance of other exposures differs by sex. In men, deficient intake of fruits and vegetables (6.1%),

occupational exposures (4.9%) and alcohol consumption (4.6%) are next in importance,. For women, overweight and obesity (because of breast cancer) are responsible for 6.9% of cancers, followed by infectious agents (3.7%).[3]

A 2013 review of epidemiological studies and survey data in the USA, estimated that a maximum of 60% of cancer deaths in the United States may be attributed to 8 risk factors: tobacco smoking, obesity (as a dietary factor, connected with dietary deficiencies such as lack of sufficient fruit and vegetables, too much red meat and salty foods), physical inactivity (leading to overweight), alcohol consumption, ionizing and solar radiations (exposure to sunlight), occupation exposures (to carcinogens in the working environment) and infectious agents (viruses, such Epstein-Bar virus, Hepatitis B virus, Human Papillomaviruses).[4]

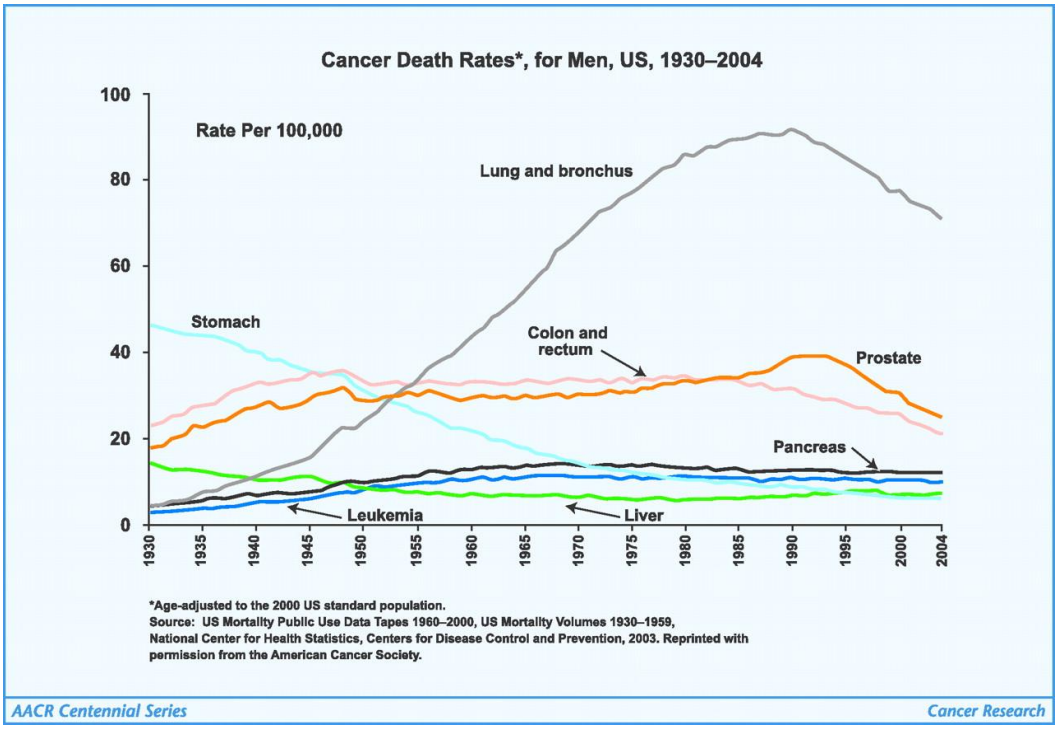

Figure 1. Cancer death rates (age-adjusted) in the USA in the period 1930-2004. In the 1930s stomach cancer was the major type of cancer but it was reduced substantially over the next decades. Preservation by refrigeration of food played an important part. Low intake of fresh vegetables and fruit and high consumption of salted/smoked foods were clearly associated with stomach cancer development. Halving of stomach cancer risk was observed in people who had used refrigerators for more than 30 years. In the other hand lung cancer increased exponentially with increased smoking habits. Colon cancer is connected to red meat consumption.
[Greenwald P, Dunn BK. Landmarks in the History of Cancer Epidemiology. American Association for Cancer Research, AACR, *Cancer Research*, DOI: 10.1158/0008-5472.CAN-09-0416, Published March 2009].

According to the American Cancer Society (ACS) the dramatic decline of stomach cancer in the past several decades is the result of greater use of refrigeration for food storage rather than preserving foods by salting, pickling, and smoking. Meat, fish, fresh vegetables and fruit are better preserved by refrigeration. A diet high in fresh fruits and vegetables can also lower stomach cancer risk. Citrus fruits (such as oranges, lemons, and grapefruit) may be especially helpful. The ACS recommends that people eat a healthy diet, with an emphasis on plant foods. This includes eating at least 5 portions of vegetables and fruits every day. Choosing whole-grain breads, pastas, and cereals instead of refined grains, and eating fish, poultry, or beans instead of processed meat and red meat may also help lower your risk of cancer.[5]

In the United States of America (USA), the overall cancer death rate has declined since the early 1990s as a result of systematic anticancer campaigns and widespread information on prevention measures and in particular cessation of smoking, better diet and reduction of obesity. The most recent Surveillance, Epidemiology and End Results (SEER Cancer Statistics Review,) released in April 2018, showed that cancer death rates in the USA decreased because of reduction of smoking, early diagnosis, healthier diet, and other preventative measures, by:

- 1.8% per year among men from 2006 to 2015
- 1.4% per year among women from 2006 to 2015
- 1.4% per year among children ages 0–19 from 2011 to 2015

Although death rates in the USA for many individual cancer types have also declined, rates for a few cancers have stabilized or even increased. As the overall cancer death rate has declined, the number of cancer survivors has increased. These trends show that progress is being made against the disease, but much work remains. Although rates of smoking, a major cause of cancer, have declined, the U.S. population is aging, and cancer rates increase with age. Obesity, another risk factor for cancer, is also increasing in the USA, especially among young.

[**The Surveillance, Epidemiology, and End Results (SEER) Program collects and publishes cancer incidence and survival data from population-based cancer registries that cover approximately 28% of the U.S. population, National Cancer Institute, https://seer.cancer.gov/].

China is another country of importance because in the last decades witnessed dramatic changes in its socioeconomic development and changes in the causes of morbidity and mortality of its citizens. Many aspects of Chinese modern life have been influenced by the dramatic changes of lifestyle (movement of large populations from villages to big cities), changes in diet, increases in smoking, rising obesity and exposure to carcinogenic substances (e.g. urban air pollution). Statistical data in China showed that mortality of all cancers declined steadily in urban areas, but not in rural areas. Decreasing mortality from cancers of the stomach, esophagus, nasopharynx, and cervix uteri was observed, while lung and female breast cancer mortality increased. Mortality from leukemia remained relatively stable, and cancer of liver, colorectal, and bladder had different trends between the rural and urban areas. Scientists concluded that observed trends in cancer for the Chinese reflected urban population increases, social and economic improvements, air pollution, but mainly lifestyle changes over the past decades (such as diet).[6]

Figure 2. According to the Chinese (2013) Cancer Registry Annual Report, 3.09 million Chinese developed cancer and 1.96 million died in 2010. Lung cancer alone killed 490,000 Chinese in 2010. According to Chinese scientists, the most important risk factors for cancer were smoking, obesity, sedentary lifestyle, unhealthy diet and air and water pollution [http://www.chinadaily.com.cn/m/chinahealth/2014-06/12/content_17507666.htm].

China with around 25% of the world's population witnessed substantial changes in income of its population, urban housing, car ownership, new occupational industrial jobs, new eating habits. China inevitably in the last decades is going through a transition to become a more westernized country in terms of lifestyle, diet and smoking habits. Compared to the USA and UK, China has lower cancer incidence (morbidity) but 30% and 40% higher cancer mortality than the UK and USA respectively. The Chinese population has a substantial 36% of the cancer-related deaths from the digestive tract cancers (stomach, liver, and esophagus cancer due to particular diets and high consumption of salty foods). In comparison, the digestive cancer deaths only took up ≤ 5% of the total cancer deaths in either USA or UK. An estimated 40% of the risk factors can be attributed to environmental and lifestyle factors in China. Chinese men are heavy smokers while in western countries smoking has been reduced substantially due to active antismoking campaigns in the last decades. Tobacco smoking is the single most important carcinogenic risk factor in China, contributing to ~ 25% of cancers in males. Chronic infection is another important preventable cancer contributor which is responsible for ~ 17% of cancers in China.[7]

France is another westernized country which showed interesting cancer mortality statistics. A study estimated the proportion of cancer deaths which occurred in France in 2000 attributable to known risk factors, based on data on frequency of exposure around 1985. In 2000, tobacco smoking was responsible for 23.9% of cancer deaths (33.4% in men and 9.6% in women), alcohol drinking for 6.9% (9.4% in men and 3.0% in women) and chronic infections for 3.7%. Occupation exposures were responsible for 3.7% of cancer deaths in men. The lack of physical activity, overweight/obesity and use of exogenous hormones were responsible for 2%-3% of cancer deaths in women. Other risk factors, including air pollutants, are responsible for <1% of cancer deaths. Scientists concluded that known cancer risk factors explained around 35% of cancer deaths in France with tobacco smoking as a predominant cause of cancer mortality. Data showed that in the last decades cancer mortality is decreasing in France, due to changes in smoking habits and healthier diet.[8]

Smoking cessation and decreased risk of cancer mortality

The World Health Organization (WHO, Geneva) has declared many decades ago that tobacco use is the single greatest avoidable risk factor for cancer mortality in humans. Statistical data worldwide showed that active and passive smoking kills (prematurely) approximately 6 million people each year from cancer and other diseases (mainly cardiovascular diseases, CVDs). Studies have identified in tobacco smoke more than 4,000 carcinogens and other toxic substances in smoke and tar that every smoker breaths deep into its lungs. Further studies proved that at least 250 of these chemical substances are known to be harmful to the respiratory system and more than 50 are highly carcinogenic and are known to cause cancer to humans, not only in the lungs but also in other human organs.[9-11]

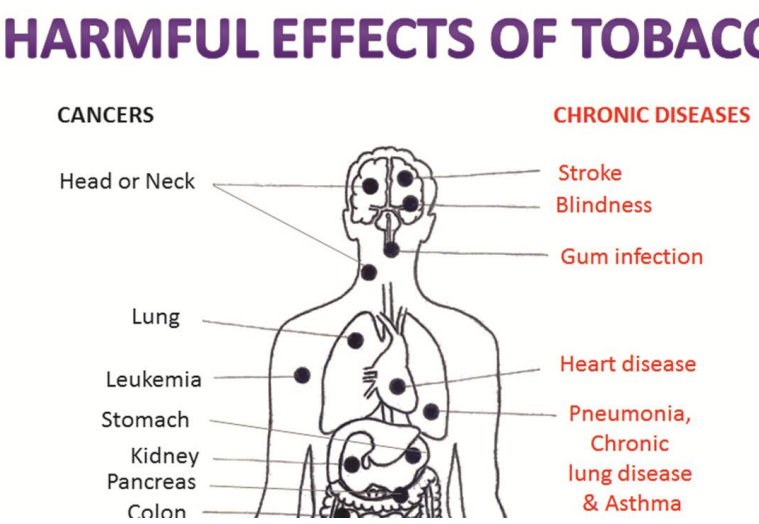

Figure 3. Tobacco use is a risk factor for many diseases; especially those affecting the heart, liver, and lungs, as well as many cancers. In 2008, the World Health Organisation (WHO) named tobacco as the world's single greatest preventable cause of death. Reducing smoking can save millions of premature deaths, in particular lung cancer.

Tobacco smoking causes a variety of cancers besides lung cancer. Oesophagus, larynx, mouth, throat, kidney, bladder, pancreas, stomach and cervix are some of the cancers where smoking play an important part in their development acting in synergy with other external factors. Environmental tobacco smoke (ETS) of passive smoking has been proven to cause lung cancer in non-smoking adults who live for a long time with smoking relatives at home or co-workers in the working environment. Stress, loneliness, depressive symptoms and psychosocial problems were the most common risk factors for starting

tobacco smoking. Young people who abuse other substances, such as alcohol and marijuana, were at risk of tobacco smoking. The majority of studies and epidemiological research focused in the last decades on the role of smoking in the development of cancer.[12-14]

Cessation of smoking and lung cancer reduction

Reduction or cessation of tobacco smoking produces spectacular effects in reducing cancer risk to humans. Most studies until now showed over 50% decrease in lung cancer risk after quitting smoking for more than 10 years.

Chinese scientists investigated the effect of smoking cessation to people who were also Silicotics (workers exposed to crystalline silica in mining, metallurgical industry, etc, with increased risk for lung cancer). Smoking and silica dust are known to act in a synergistic way in the respiratory system increasing the risk for lung cancer. They use 3,185 Chinese silicotics since 1981 and followed-up till 2014. Overall, 1,942 deaths occurred and 188 lung cancer deaths were identified. Compared with never quitters (who never stopped smoking), silicotics who stopped smoking had almost 50% decrease in their lung cancer risk. Also, the study showed that persistent quitters (successful in stopping smoking) had a 53% risk reduction. Lung cancer mortality approximately halved after quitting smoking for 10 years, but did not reverse back to that of never smokers. Scientists concluded that smoking cessation for 10 years reduced the chance for 50% lung cancer mortality among silicotics.[15]

Scientists in the USA used comparative modeling approach using 4 simulation models of the natural history of lung cancer that explicitly relate temporal smoking patterns to lung cancer rates**.** The aim was to project reductions in tobacco use and lung cancer mortality from the next 50 years (2015 to 2065**).** Models were developed using U.S. data on smoking (1964 to 2015) and lung cancer mortality (1969 to 2010). Under the assumption of continued decreases in smoking, age-adjusted lung cancer mortality was projected to decrease by 79% between 2015 and 2065 [the annual number of lung cancer deaths was projected to decrease from 135,000 to 50,000 (63% reduction)]. However, 4.4 million deaths from lung cancer are still projected to occur in the

United States in the next 50 years due to smoking among a lower percentage (from 21% in 2005 to 15% in 2015) of the population.[16]

A South Korean study (2018) investigated the effect of smoking habit change (cessation) on the risk of cancer in Korean men. Scientists used the Korean National Health Insurance Service database (2002-2005). A total of 143,071 men were categorized into baseline heavy (≥ 20 cigarettes per day), moderate (10-19 cigarettes per day), light (< 10 cigarettes per day) smokers, quitters, and never smokers. Compared to heavy continual smokers, heavy smokers who quit had reduced risk of smoking related cancer and tended to have reduced risk of all cancer. Moderate smokers who reduced the amount of smoking to light levels had decreased risk of all cancer but especially lung cancer (55%) compared to heavy continual smokers. The conclusion reach was that smoking reduction decreases the risk of all cancer, smoking related cancer, and in particular lung cancer.[17]

Figure 4. The South Korean government aims to take down male smoking rate to the OECD average of 29% by 2020 by making the country one of the world's most difficult places to smoke (significant increase in cigarette prices, mandatory warning photos on cigarette packs, advertising bans, financial incentives **and** medical help).

Medical experts in the USA agree that smoking is the largest contributor to lung cancer risk, and those who continue to smoke after diagnosis (of having lung cancer) have a worse survival case. In the USA there is a screening programme for lung cancer patients with low-dose computed tomography (LDCT) which reduces mortality in high-risk individuals, but smoking cessation is an essential component of a high-quality screening program. Measurements included self-reported demographics, medical and smoking history, and lung cancer-specific and all-cause mortality. Cox regression was used to study the

association of mortality with smoking status and pack-years. Current smokers had an increased lung cancer-specific and all-cause mortality, compared with former smokers irrespective of screening arm. Former smokers in the control arm abstinent for 7 years had a 20% mortality reduction comparable with the benefit reported with LDCT screening. The maximum benefit was seen with the combination of smoking abstinence at 15 years and LDCT screening, which resulted in a 38% reduction in lung cancer-specific mortality.[18]

In Italy, a scientific study estimated the risks of dying of ischemic heart disease (IHD), lung cancer (LC), stroke, and chronic obstructive pulmonary disease (COPD) for Italian smokers by gender, age and daily number of cigarettes smoked. Also, they estimated the benefit of stopping smoking in terms of risk reduction. Each smoking-related disease was based on Italian smoking data, and risk charts with 10-year probabilities of death were computed for never, current and former smokers. Men aged 45-49 years, current smokers, have a 8, 10, 3 and 1 in 1,000 chance of dying of IHD, LC, stroke and COPD, respectively, whereas women with the same characteristics have a 2, 6, 3 and 1 in 1,000 chance, respectively, for all smokers combined, i.e., independent of the smoking intensity. The risk reduction rates from quitting smoking are remarkable: a man who quits smoking at 45-49 years of age can reduce the risk of dying of IHD, LC, stroke and COPD in the next 10 years by 43%, 53%, 57% and 55%, respectively; a woman can reduce the risk by 49%, 49%, 59% and 57%, respectively.[19]

In Russia, 14% of all deaths, or about 300,000 deaths each year, are attributed to tobacco smoking. Male smoking prevalence is very high (60%), the highest in the European region, and female smoking prevalence increased from 10% to 21% during the last 15 years. Russia has very weak tobacco control policies.[20-22]

Russian scientists from the National Research Center for Preventive Medicine of the Ministry of Health, Moscow, Russian Federation and the International Union Against Tuberculosis and Lung Disease, Moscow, Russian Federation, used a simulation model to examine the effect of tobacco control policies on past and future smoking prevalence and premature mortality in Russia (the model was developed using the SimSmoke tobacco control model, developed for the USA and other nations). The model inputs population size, birth, death and smoking rates specific to Russia. It assesses, individually and in combination, the effect of seven

types of policies consistent with the WHO Framework Convention on Tobacco Control (FCTC): taxes, smoke-free air, mass media campaign, advertising bans, warning labels, cessation treatment and youth access policies. Outcomes are smoking prevalence and the number of smoking-attributable deaths by age and gender from 2009 to 2055. Increasing cigarette taxes to 70% of retail price, stronger smoke-free air laws, a high-intensity media campaign and comprehensive treatment policies are each potent policies to reduce smoking prevalence and smoking-attributable premature deaths in Russia. With the stronger set of policies, the model estimates that, relative to the status quo trend, smoking prevalence can be reduced by as much as 30% by 2020, with a 50% reduction projected by 2055. This translates into 2,684,994 male and 1,011,985 female premature deaths averted in the next 40 years from 2015-2055.[23]

Greece is a country with the highest percentage of smokers in the European Union. Overall smoking rates in Greece have decreased slightly from 40% in 2005 to 32.5% in 2014. Despite laws adopted from 2010, prohibiting smoking in public places and TV and press advertising bans, Greece still has one of the world's highest smoking rates. Since 2016, tobacco packaging has required graphic warnings to cover 65% of the cigarette packages. Tobacco taxes increased substantially covering 90% of the cost of cigarette pack. Health experts think that nations such as Greece, should employ taxation as a crucial measure to promote public health and economic development in such dire times of financial austerity. It is estimated that approximately 3 million Greeks (over ages 15 and older) currently smoke. It is estimated that 1 in 4 students aged 13-15 started smoking before the age of 10. Other estimates calculated 19,000 smoking-related deaths to occur each year. Tobacco-attributable disease accounts for nearly 15% percent of all healthcare spending in Greece.[24,25]

Japan has a high proportion of smokers. In 2015, adult smoking rate was 19.3%, of which 29.7% were Japanese men and 9.7% of Japanese women. The number of smokers decreased substantially in the last decade. In 2016, national statistics estimated that over 20 million people still smoked in Japan. Japanese scientists analyzed pooled data from eight population-based prospective cohort studies in Japan with more than 320,000 participants to assess the effect of smoking

cessation on the risk of total cancers and smoking-related cancers (adjusting for potential confounders). Their analysis revealed that cancer risks in men with >21years (more than 21 years) of smoking cessation decreased to the same level as never smokers for total cancer. Even Japanese men who are heavy smokers (more than 20 cigarette pack-years) reported a reduced risk of total cancer. In Japanese women, the risk of total cancer did not differ from that of never smokers after 11 years of smoking cessation before baseline. The conclusion reached from this study was the that longer duration of smoking cessation may attenuate the risk of cancer in both men and women, and that even heavy smokers (more than 20 pack-years) were found to benefit from quitting smoking for more than 10 years.[26]

Reduction in alcohol consumption and risk of cancer

Studies and systematic collection of data established that heavy alcohol consumption is associated with increased risk of certain cancers. Drinking any kind of alcohol can contribute to cancers of the mouth and throat, larynx, esophagus, colon and rectum, liver, and breast (in women). Most epidemiological studies showed that the less alcohol consumption, the lower the risk of cancer in humans. When people drink alcohol, their metabolism in the body breaks it down into a carcinogenic chemical called *acetaldehyde (CH_3CHO) that* damages cellular DNA. When DNA is damaged (mutations), a cell can begin growing out of control and create a cancer tumour. Alcohol intake and associated risk has been investigated by numerous epidemiological studies and meta-analysis.[27-30]

One of the cancers that is prominently associated with alcohol consumption is colorectal cancer. American epidemiologist Giovannucci and colleagues (Associate Professor, Medicine, Harvard Medical School) conducted a meta-analysis of prospective cohort studies to quantitatively assess this association. They analysed data from 12 studies with 32,846 colorectal cancer patients. Compared to no alcohol consumption, light and moderate (pre-diagnostic) alcohol consumption were associated with lower risk of all-cause mortality. Also, light (pre-diagnostic) alcohol consumption was associated with lower risk of colorectal cancer-specific mortality. So, in this respect light alcohol intake is slightly beneficial. However, heavy (pre-diagnostic) alcohol consumption was not significantly associated with colorectal cancer survival. In a dose-response analysis, a non-linear association between pre-

diagnostic alcohol consumption and all-cause mortality was observed, showing the reduction in RR (*Relative Risks*) at (more than) <30 g/day of alcohol consumption. When they analysed data by type of alcohol, wine consumption was associated with lower risk of mortality from all-causes and colorectal cancer, but a positive association was observed between moderate liquor (distilled alcohol, including vodka, gin, rum, tequila, whisky) consumption and all-cause mortality. There was no association between post-diagnostic alcohol consumption and colorectal cancer survival. Conclusion from the study was that light and moderate pre-diagnostic alcohol consumptions were associated with better survival in colorectal cancer.[31]

A very important systematic study was published in 2018 (Lancet) by the Global Burden of Disease 2016 Alcohol Collaborators. The Global Burden of Disease Study 2016 (GBD 2016) was coordinated by the Institute for Health Metrics and Evaluation (IHME, Seattle, WA, USA). The aim was to estimate the burden of diseases, injuries, and risk factors for 195 countries and territories and at the subnational level for a subset of countries. Estimates for alcohol use and the burden attributable to this risk factor were produced by sex, age group, and year for 195 countries and territories for the 25 year period 1990-2016. Estimates for alcohol-attributable deaths and disability-adjusted life-years (DALYs) were calculated available from the GBD Results Tool. Study results were published in *The Lancet* in August 23, 2018 in "Alcohol use and burden: a systematic analysis from the Global Burden of Disease Study 2016 for 195 countries and territories, 1990–2016". [32]

Researchers used 694 data sources of individual and population-level alcohol consumption, along with 592 prospective and retrospective studies on the risk of alcohol use. They estimated prevalence of current drinking, abstention, the distribution of alcohol consumption among current drinkers. Also, the made methodological improvements : adjusted alcohol sales estimates to take into account tourist and unrecorded consumption, they did a new meta-analysis of relative risks for 23 health outcomes and third, developed a new method to quantify the level of alcohol consumption that minimises the overall risk to individual health.[32]

The findings of the study. Globally, alcohol use was the seventh leading risk factor for both deaths and DALYs in 2016, accounting for 2·2% of age-standardized female deaths and 6·8% of age-standardized male deaths.

Among the population aged 15-49 years (relatively young people not affected by cancer or cardiovascular diseases yet), alcohol use was the leading risk factor globally in 2016, with 3·8% of female deaths and 12·2% of male deaths attributable to alcohol use (the 3 leading causes of attributable deaths in this age group 15-49 were tuberculosis, road injuries, and self-harm). For populations aged 50 years and older, cancers accounted for a large proportion of total alcohol-attributable deaths in 2016, constituting 27% of female deaths and 18·9% of male deaths. The level of alcohol consumption that minimised harm across health outcomes was zero standard drinks per week.[32]

Conclusions from the results. Researchers concluded that alcohol use is a leading risk factor for global disease burden and causes substantial health loss. They found that the risk of all-cause mortality, and of cancers specifically, rises with increasing levels of consumption, and the level of consumption that minimises health loss is zero (they accept that even light alcohol consumption causes some type of harm). These results suggest that alcohol control policies might need to be revised worldwide, refocusing on efforts to lower overall population-level consumption of alcohol.[32]

Alcohol in moderation may be good for health but a poison for heavy consumption

Medical experts agree that alcohol is both good for health and a poison depending on the dose. Light or moderate drinking seems to be good for the heart and circulatory system, and probably protects against type 2 diabetes and gallstones. The latest consensus for light or moderate drinking is at no more than 1-2 drinks a day for men, and no more than 1 drink a day for women. In the USA, 1 drink is usually considered to be 336 g of beer, 140 g of wine, or 42 g of spirits (hard liquor such as gin or whiskey).[33]

In the other hand regular and heavy drinking is a major cause of various diseases and premature death in most countries. Alcohol (in the USA and other developed countries) and drunkenness is implicated in about 30% of fatal traffic accidents. Heavy drinking can damage the liver and heart, can harm an unborn child, increase the chances of developing breast cancer and some other cancers,

contribute to depression and violence, and interfere with relationships. In 2012, 10,322 people in the USA were killed in alcohol-impaired-driving crashes. These alcohol- impaired-driving fatalities accounted for 31% of the total motor vehicle traffic fatalities. [U.S.A Department of Transportation. Traffic Safety Facts, 2012 data, https://crashstats.nhtsa.dot.gov/Api/Public/ViewPublication/811870].

More than 3 million people died globally as a result of harmful use of alcohol in 2016, according a report released by the World Health Organization (WHO) today. This represents 1 in 20 deaths. More than 75% of these deaths were among men. Overall, the harmful use of alcohol causes more than 5% of the global disease burden. (World Health Organization, https://www.who.int/news-room/detail/21-09-2018-harmful-use-of-alcohol-kills-more-than-3-million-people-each-year--most-of-them-men].

Figure 5. To keep health risks from alcohol low, the UK Chief Medical Officers has issued low risk drinking guidelines and advise for safe consumption of alcohol. For men and women the advice is: do not to drink more than 14 units a week on a regular basis and restrict your drinking to 1-2 units per day.

Alcohol is more dangerous to women's health

Historically, men have been more likely to drink alcohol than women and to drink in quantities that damage their health. However, in the last decades in developed countries the evidence points to a significant shift in the drinking landscape with rates of alcohol use appearing to converge among men and women. Scientists do not have a definitive answer to what has driven the rise in alcohol consumption among women, but in many developed countries around the world there have seen substantial developments in broader social, cultural and economic factors for women and increasingly accepting societal norms around female drinking.

Research shows that alcohol use and misuse among women are increasing in developed countries.[34,35]

Also, another question that scientist have to answer is why women are in greater danger than men by consuming alcohol. Experts think that women are generally smaller (body size, muscle) than men and have less total body water and more total body fat. Blood alcohol level rises more quickly and stay elevated longer in women, so the harmful effects of alcohol, even if a man and woman drink same amount, will show up sooner in the women. Also, scientists have discovered that women produce smaller quantities of an enzyme called alcohol dehydrogenase (ADH), which is released in the liver and breaks down alcohol in the body.[36]

Women who regularly misuse alcohol are more likely than men who drink the same amount to develop alcoholic hepatitis, a potentially fatal alcohol-related liver condition. This pattern of drinking can also lead to cirrhosis (permanent liver scarring).[37] Long-term alcohol misuse is a leading cause of heart disease. Women are more susceptible to alcohol-related heart disease than men, even though they may consume less alcohol over their lifetime than men. Research suggests that alcohol misuse produces brain damage more quickly in women than in men.[38-40]
Breast cancer in women has many causes, but there is also an association between drinking alcohol and developing breast cancer. Studies demonstrate that women who consume about 1 drink per day have a 5 to 9% higher chance of developing breast cancer than women who do not drink at all.[41-43]

How many cancer cases can be avoided by reducing alcohol consumption

A recent study by scientists in the Nordic countries collected cancer data in order to quantify the proportion of the cancer burden in the Nordic countries (Finland, Sweden, Norway, Denmark, Iceland) linked to alcohol and to estimate the potential for cancer prevention by changes in alcohol consumption (reduction). They used a macro-simulation model (cancer cases in the Nordic countries over a 30-year period, 2016-2045). They used 6 alcohol-related cancers: colorectal, post-menopausal breast, oral cavity and pharynx, liver, larynx and oesophageal squamous cell carcinoma. They used 4 levels of alcohol consumption, a. non-drinkers/occasional drinkers, b. light drinkers (<=12.5 g alcohol/day), c. moderate drinkers (>12.5 and ≤ 50 g/day) and d. heavy drinkers (>50 g/day). Their estimates showed that about 83,000 cancer cases could be avoided in the Nordic countries in a 30-year

period if alcohol consumption was entirely eliminated. Even if there is a 50% reduction with moderate alcohol consumption by year 2025, 21,500 cancer cases could be avoided. The number of avoidable cases was highest for post-menopausal breast and colorectal cancer, but the percentage was even highest for oesophageal squamous cell carcinoma. Scientists concluded that the significance of the reduction in alcohol consumption is very important for cancer risk prevention.[44]

A similar study was contacted in France (2015) to estimate the number of new cases of cancer attributable to alcohol for light, moderate and heavy consumption [light is < 20 g/day (women) and <40 g/day (men), moderate 30-40 g/day (women), 40-60 g/day (men), and heavy drinking is ≥ 40 g/day among women; ≥ 60 g/day among men)]. Scientists assumed a 10-year latency period between exposure and diagnosis. Alcohol consumption in France was estimated by coordinating data from the Baromètre santé 2005, a national representative survey (n = 30 455), with data from the Global Information System on Alcohol and Health. Relative risks were obtained from meta-analyses. Cancer rates were estimated based on data from the French Cancer Registries Network. The number of new cases of cancer attributable to alcohol was between 27-30 thousands for 2015 (estimated 27,894) or 8% of all new cases of cancer. According to their estimate Light, moderate, heavy and former alcohol drinking were responsible for 1.5%, 1.3%, 4.4% and 0.6% of all new cancer cases, respectively. Also, they estimated that a 10% drop (they used a hypothetical small reduction as an example) of alcohol drinking in France would have prevented more than 2,000 new cancer cases in 2015.[45]

Reduction of overweight/obesity and cancer risk

Measurements and statistical health evidence over the past decades revealed that the proportion of people with excess body weight (obese) has been increasing in both developed and less developed countries. From the beginning of 2000 about 50% of men and 35% of women in Europe estimated to be overweight or obese. This evidence was emphasized by an increase in the risk of cardiovascular diseases (CVDs) and type-2 diabetes in most countries. But further research and epidemiological studies showed that excess body weight is directly associated with increased risk of cancer at several organ sites, including colon, breast (in postmenopausal women), endometrium, oesophagus, and kidney. Research in the

last decade revealed changes in metabolic processes of obese bodies which explained mechanisms of cancer initiation and promotion. Association of obesity and cancer can be explained now by alterations in the metabolism of endogenous hormones-including sex steroids, insulin, and insulin-like growth factors-which can lead to distortion of the normal balance between cell proliferation, differentiation, and apoptosis. Medical experts agree that avoidance of overweight/obesity is an important factor for cancer prevention.[46]

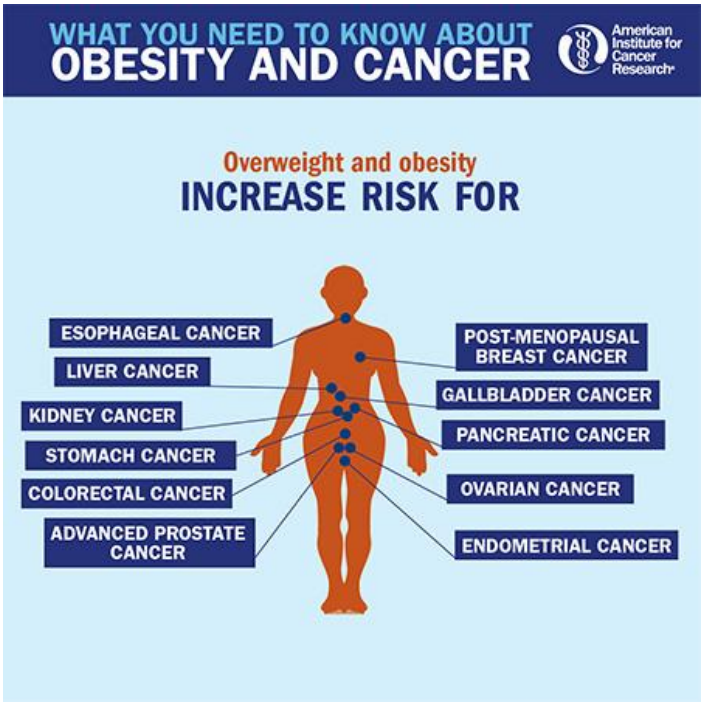

Figure 6. American Institute for Cancer Research. Overweight and Obesity are responsible in the long term for increased risk of certain cancers in humans. The AICR estimates that excess body fat causes around 120,000 additional cancer cases in the USA per year. Now 7 out of 10 Americans are overweight or obese.

……..

***Body Mass Index** (BMI) has been used in many studies as a good indicator of how overweight or obese is an individual. BMI is a useful measure of overweight and obesity. It is calculated from your height and weight.

[***BMI at an individual level can be used as a screening tool but is not diagnostic of the body fatness or the health of an individual.

BMI is a person's weight in kilograms (kg) divided by the square of height in meters (m). A high BMI can be an indicator of high body fatness.

- BMI less than 18.5, individual falls within the underweight range.
- BMI is 18.5 to <25, individual is normal (weight).
- BMI is 25.0 to <30, individual falls within the overweight range.
- BMI is 30.0 or higher, individual falls within the obese range.

Obesity is frequently subdivided into categories: Class 1: BMI of 30 to < 35

- Class 2: BMI of 35 to < 40
- Class 3: BMI of 40 or higher. Class 3 obesity is sometimes categorized as extreme" or "severe" obesity].

According to the National Cancer Institute (NCI, USA) there is consistent evidence that higher amounts of body fat (in overweight/obese people) are associated with increased risks of a number of cancers.[47,48]

The most important cancers linked to overweight/obesity are listed below. Research on the subject was contacted for years and some important studies investigated and provided positive correlation for the association:

1. **Endometrial cancer** (cancer of the lining of the uterus): Obese and overweight women are 2 to 4 times as likely as normal-weight women to develop endometrial cancer and extremely obese women are about 7 times as likely to develop the more common of the two main types of this cancer.[49,50]
2. **Esophageal adenocarcinoma:** People who are overweight or obese are about twice as likely as normal-weight people to develop a type of esophageal cancer called esophageal adenocarcinoma, and people who are extremely obese are more than 4 times as likely to develop esophageal adenocarcinoma.[51]
3. **Gastric cardia cancer:** People who are obese are nearly twice as likely as normal-weight people to develop cancer in the upper part of the stomach.[52]
4. **Liver cancer:** Overweight/obese people are up to twice as likely as normal-weight people to develop liver cancer with stronger association between overweight/obesity and liver cancer in men.[53,54]
5. **Kidney cancer:** Overweight/obese individuals are nearly twice as likely as normal-weight people to develop renal cell cancer, the most common form of kidney cancer.[55,56]
6. **Multiple myeloma:** Overweight and obese individuals have a 10%-20% increase in the risk of developing multiple myeloma than normal-weight individuals.[57]
7. **Malignant meningioma:** This slow-growing brain tumour arises in the membranes surrounding the brain and the spinal cord. People obese have a 50% more risk to develop this cancer.[58]
8. **Pancreatic cancer:** Overweight or obese people are about 1.5 times as likely to develop pancreatic cancer as normal-weight people.[59]
9. **Colorectal cancer:** Obese are about 30% more likely to develop colorectal cancer than normal-weight people. Also, both men and women with high Body mass index (BMI) have increased risk for colorectal cancer.[60,]

10. **Gallbladder cancer:** Overweight individuals have a 20% increase in risk of gallbladder cancer, and people who are obese have a 60% increase in risk of gallbladder cancer.[61,62]
11. **Breast cancer:** Postmenopausal women, with a higher BMI are associated with a modest increase in risk of breast cancer.[63,64] Those who are obese have a 20% to 40% increase in risk of developing breast cancer compared with normal-weight women. The higher risks are seen mainly in women who have never used menopausal hormone therapy.[64] Obesity is also a risk factor for breast cancer in men.[65]
12. **Ovarian cancer:** Women with high BMI have a slight increase in the risk of ovarian cancer, particularly in women who have never used menopausal hormone therapy. [66]
13. **Thyroid cancer:** Higher BMI (specifically, a 5-unit increase in BMI) is associated with a slight (10%) increase in the risk of thyroid cancer.[67]

What are the possible mechanisms connecting obesity with cancer

Scientists have long suspected chronic inflammation may play some role in cancer's development, but researchers have only recently pinpointed chronic inflammation as a primary risk factor. Investigations pinpointed possible inflammatory mechanisms for the association of obesity and carcinogenic mechanisms of initiation and promotion. Excess fat in obese people was one of the factors investigated and its connection with mechanisms of inflammation that are leading pathways to initiate cellular mutations to DNA. Several possible mechanisms have been suggested to explain how fat in obese people might increase the risks of some cancers.[68-71]

Overweight/obese individuals are more likely than normal-weight individuals to have conditions or disorders that are linked to chronic local inflammation and certain cancers.[72] There are examples that chronic local inflammation induced by gastroesophageal reflux disease (Barrett esophagus) is a likely cause of esophageal adenocarcinoma. Obesity is a risk factor for gallstones (gallstones are pebble-like collections of cholesterol and other substances that form in the gallbladder and can cause chronic inflammation), a condition characterized by

chronic gallbladder inflammation, and a history of gallstones is a strong risk factor for gallbladder cancer.[73]

Ulcerative colitis is an inflammatory bowel disease that causes long-lasting inflammation and ulcers (sores) in digestive tract, affecting the innermost lining the large intestine (colon) and rectum. Chronic ulcerative colitis and hepatitis (a disease of the liver causing inflammation) are risk factors and can cause different types of liver cancer.[74]

Overweight/obese people carry excess amounts of fat tissue (also called adipose tissue) that produces excess amounts of estrogen, high levels of which have been associated with increased risks of breast, endometrial, ovarian, and some other cancers. Further factors influencing breast cancer development via obesity and breast adiposity have included the possible influence of estrogens produced in adipose tissue. These steroids can promote carcinogenesis and add to the lifetime total of estrogen stimulation from oral contraceptives, hormone replacement therapy, and pregnancies.[75,76]

Obese people often have increased blood levels of insulin and insulin-like growth factor-1 (IGF-1). (This condition, known as hyperinsulinemia or insulin resistance, precedes the development of type 2 diabetes). High levels of insulin and IGF-1 may promote the development of colon, kidney, prostate, and endometrial cancers.[77]

Research revealed that fat cells produce adipokines, hormones that may stimulate or inhibit cell growth (an adipokine called leptin, which seems to promote cell proliferation, in the blood increases with increasing body fat). Another adipokine, adiponectin—which is less abundant in obese people than in those of normal weight—may have antiproliferative effects.[78,79]

Other possible mechanisms by which obesity could affect cancer risk include changes in the mechanical properties of the scaffolding that surrounds breast cells and altered immune responses, effects on the nuclear (NF-κB), factor kappa beta system, and oxidative stress.[80-83]

The Cancer Research UK emphasize that being overweight does not mean will definitely develop cancer, but if someone is overweigh/obese is more likely to get cancer in later life. It is estimated that a healthy weight of the United Kingdom (UK) (England, Wales, Scotland, N. Ireland) population could prevent 22 thousand additional cancer cases every year.

Daily physical activity and reduction in cancer risk

Medical cancer experts and a growing body of research studies have established the fact that making moderate to vigorous physical activity on a daily basis lowers the risk of cancer in humans. Also, physical activity in connection with healthy diet and avoidance of overweight decrease the risk of other chronic diseases, such as heart cardiovascular diseases and type 2 diabetes. Moderate to vigorous physical activity is exercise that includes walking, swimming, cycling, or running. The types of cancer which are reduced by physical activity are: colon cancer (people who exercise regularly have a 40-50% lower risk, compared with those who do not exercise), breast cancer (long-term studies show that women who engage in moderate to vigorous exercise for more than 3 hours per week have a 30-40% lower risk), Uterine cancer **(**research has linked exercise to lower risk of uterine cancer), Lung cancer **(**people who do not smoke and at the same time exercise are less likely to develop lung cancer) and Endometrial cancer **(**a meta-analysis of 33 studies, showed that the average endometrial cancer risk reduction associated with high versus low physical activity was 20%).[84-89]

Metabolic and biological effects of physical exercise that reduce cancer risk

Scientific research explained various metabolic and biological effects in the human body that explained mechanisms and associations for physical activity and reduced risk of cancer.

Exercising on a daily basis lowers the levels of hormones in the human body, such as insulin (an essential hormone for controlling blood sugar and energy absorption) and estrogen (estrogen, or oestrogen, primary female sex hormone responsible for the development and regulation of the female reproductive system). Also, physical exercise lowers certain growth factors that have been associated with cancer development and progression of breast and colon cancers. Growth factors are defined as polypeptides that stimulate cell proliferation. They are made by the human body and their function is to regulate cell division and cell survival.[90,91]

Physical activity helps people to prevent overweight and obesity which are important factors increasing cancer risk, through the development of insulin resistance (failure of the body's cells to respond to insulin).[92]

Physical activity and exercise on a daily basis prevents the development of inflammatory areas in the human body, a factor that is linked to cancer initiation, especially colorectal cancer.[93]

Physical exercise improves the immune system function in the human body which is beneficial to fight the initiation and progression of various cancer mechanisms.[94]

Physical activity alters the metabolism of bile acids, resulting in decreased exposure of the gastrointestinal tract to these suspected carcinogens, and prevents colon cancer.[95,96] Physical activity reduces the time it takes for food to travel through the digestive system, which decreases gastrointestinal tract exposure to possible carcinogens and increase risk of colon cancer.[97]

Sedentary life and increased cancer risks

Life in the last decades has changed in many developed countries and people do not use much energy or do physical activities to a great extend. Sedentary habits, office jobs, prolonged periods of television viewing, sitting, and lying down for many hours has been proved to be a risk factor for developing chronic diseases, CVDs, cancer and type 2 diabetes. There are plenty of epidemiological and observational studies on these risks and sedentary life.[98,99] Sedentary life is associated with increased risks to health and premature mortality. Some physical exercise does not reverse the risk, but sedentary people with the least physical activity showed the maximum risk in cancer mortality.[100]

All medical experts recommend to their clients and patients to sustain a vigorous life style with some exercise on a daily basis because it provides health benefits. For adults they recommend to engage in at least 150 minutes per week of moderate-intensity aerobic physical activity, or 75 minutes of vigorous-intensity aerobic physical activity, or an equivalent combination every week. For children and adolescents, the guidelines recommend at least 60 minutes of physical activity daily.

Daily physical activity has also some beneficial effects for several aspects of cancer survivorship (people who were diagnosed with cancer), specially for

controlling their weight and for quality of life. Most of the evidence for the potential benefits of physical activity in cancer survivors comes from people diagnosed with breast, prostate, or colorectal cancer.[101-104]

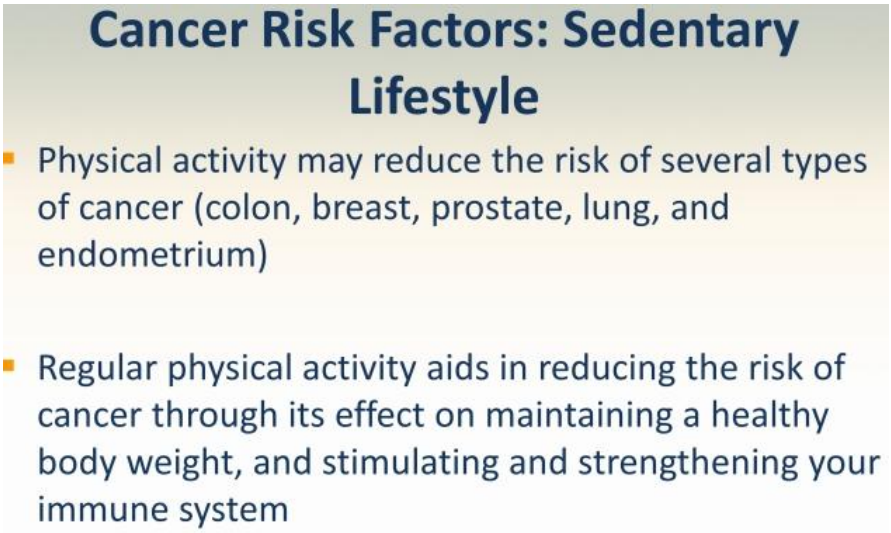

Figure 7. Sedentary lifestyle is a form of life where physical activity is absent or the person does sitting for a long time and does not take vigorous physical exercise. Exercise is beneficial because it reduces body weight and obesity, also exercise enhances the immune system thus reducing risk of cancer.

Association of healthier diet with reduction in cancer risk

For several decades scientists have investigated the association of diet and human cancers. Epidemiologists noticed long time ago the large variations in rates of specific cancers among countries and the dramatic changes in cancer incidence among populations emigrating to regions with different rates of cancer. One of the most interesting examples was the changes in cancer incident trends among Japanese emigrating to Hawaii (USA) between 1960-1997. The migrant effect was strongest for colon and stomach cancers, which are associated with diet. Whereas prostate and breast cancers were affected to a lesser degree, and lung cancer risk showed no difference between Japanese in Japan and Hawaii. Scientists can explain the fact on the changes in the type of diet of emigrating Japanese that led to lower risk of stomach, esophageal, pancreatic, liver, and cervical cancers.[105]

Such observations were obviously crucial for scientists to realize the importance of dietary practices and cancer risk. The role of diet has been suggested by strong correlations between cancer rates and national per capita intake of specific nutrients. In 1981, the famous Oxford University cancer epidemiologists (Prof. R.

Doll and Peto) presented a famous review of avoidable causes of cancer mortality in the U.S.A. Doll and Peto suggested that dietary factors might account for approximately 35% of cancer deaths, similar to the impact of tobacco smoking.[106]

In the 1980s there was a uncertainty among epidemiologists as to the causal contribution to cancer risk of diet and the quantitative aspects. Diet is what people eat with beneficial effects to health (e.g fruit, vegetables, olive oil, etc), or unhealthy diet with excess calories, red meat, saturated fat, salt-preserved processed foods and less fish, poultry and pulses for protein intake. Diet also is connected with overweight/obesity that contributes to cancer risk. Scientists realized that there were large differences in cancer rates among countries, striking changes in these rates among migrating populations, and rapid changes over time within countries by changing diet patterns.[107-109]

For many decades morbidity and mortality statistics and epidemiological studies reflecting the most current scientific evidence, estimated that unhealthy diet represents 30-35% of risk to the onset of human cancer. There is a direct relationship between unhealthy diet and lifestyle with the increase of tumour development and cancer risk. For this reason, a good nutritional status based on a balanced diet constitutes one of the main preventive factors from neoplastic diseases. However the mixed results from epidemiologic studies hinder to get unequivocal and consistent evidence about the interaction between diet and increased risk of various types of cancer.[110]

The most recent extensive review (2017) by Giovannucci and co-workers, investigated the evidence of an association between dietary patterns and decreased risk of cancer. The review investigated in particular the relation between a posteriori-derived dietary patterns, grouped as healthy, unhealthy, and cancer risk diet.

Healthy diet: was characterized by consumption of fruit, vegetables, olive oil , fish, legumes, whole grains, balanced ratio of fatty acids, high fiber content food items, and substantial amounts of antioxidant compounds (vitamins, plant foods), which inhibit multiple cancer-related biological pathways, including carcinogen bioactivation, cell signaling, cell cycle regulation, angiogenesis, and inflammation (dietary antioxidants that act against chronic inflammation may explain the association between their dietary consumption and decreased risk of lung cancer for smokers).

Unhealthy diet was characterized by, but not limited to, red and processed meat, sugary drinks and salty snacks, starchy foods, and refined carbohydrates, saturated fats, excess calorie intake.

Cancer risk diet: Red and, especially, processed meats, salty foods, *N*-nitroso compounds, heterocyclic amines, heme iron, and, following cooking at high temperature, polycyclic aromatic hydrocarbons (PAHs, carcinogens), which have been considered responsible for the carcinogenic effects of meat consumption. Alcohol-related dietary patterns are characterized by a high intake of spirits and fortified wines, demonstrated to increase the risk of cancer.

A total of 93 studies including over 85, 000 cases, 100, 000 controls, and 2, 000, 000 exposed individuals were selected. The most convincing evidence (significant results from prospective cohort studies) supported an association between healthy dietary patterns and decreased risk of colon and breast cancer, especially in postmenopausal, hormone receptor-negative women, and an association between unhealthy dietary patterns and increased risk of colon cancer. Limited evidence was found for a relation between an unhealthy dietary pattern and risk of upper aerodigestive tract, pancreatic, ovarian, endometrial, and prostatic cancers. Dietary antioxidants (fruit, vegetables) that act against chronic inflammation may explain the association between their dietary consumption and decreased risk of lung cancer for smokers. Unhealthy dietary patterns were associated with higher body mass index (BMI) and energy intake, while healthy patterns were associated with higher education, physical activity, and less smoking. Reviewers concluded a healthy diet has potential to modulate cancer risk, especially the risk of colon, breast, and lung cancers. In contrast, unhealthy dietary patterns showed a trend of association with increased cancer risk. Healthy dietary patterns have been found to be part of overall healthier lifestyle choices, which may explain in part their association with decreased cancer risk.[111]

Another recent review (2017) focused on the association of dietary patterns and colon cancer. The review collected 49 studies (28 cohort and 21 case-control) relevant studies. The reviewers produced a synthesis of food group components comprising the different index-based and empirically-derived patterns. They revealed two distinct dietary patterns: a "**healthy" pattern** characterized by high intake of fruits and vegetables, whole grains, nuts and legumes, fish and other seafood, milk and other dairy products, was associated with lower colorectal

cancer risk, and b. the **"unhealthy" pattern**, characterized by high intakes of red meat, processed meat, sugar-sweetened beverages, refined grains, desserts and potatoes associated with higher colorectal cancer risk. The results of the review were: consuming a dietary pattern high in fruits and vegetables and low in meats and sweets is protective against colorectal cancer risk (with stronger associations among men than women). Reviewers concluded that various questions remain about mechanisms underlying differences by sex; life-course timing of exposure to dietary patterns; interaction of dietary patterns with the microbiome or with lifestyle factors including physical activity.[112]

The Mediterranean diet is considered by many scientists as an ideal diet for reducing chronic diseases and in particular overall cancer risk. A recent review (2017) searched the electronic databases PubMed, and Scopus for randomized controlled trials (RCTs), cohort studies, and case-control studies. A total number of 83 studies were evaluated with overall population of 2,130,753 subjects. The results revealed that the highest the adherence to the Mediterranean diet (MedD) the highest in cancer risk reduction. The results showed that the highest adherence score to a MedD was inversely associated with a lower risk of cancer mortality (relative risk, RR, 0.86), colorectal cancer (RR 0.82), breast cancer (RR_{RCT}: 0.43), gastric cancer (RR 0.72), liver cancer (RR 0.58), head and neck cancer (RR 0.49) and prostate cancer (RR 0.96). Among cancer survivors, the association between the adherence to the highest MedD category and risk of cancer mortality, and cancer recurrence was not statistically significant. When reviewers analysed individual dietary components of the MedD the results revealed the protective effects most attributable to higher intake of fruits, vegetables, and whole grains. The updated meta-analysis confirms an important inverse association between adherence to a MedD and cancer mortality and risk of several cancer types, especially colorectal cancer.[113]

Gastric cancer (GC) is malignant type of cancer affecting the cells in the lining of the stomach. Age, diet, and stomach diseases can affect the risk of developing gastric cancer. Changing dietary habits can improve substantially stomach health and reduce gastric cancer. In 2-013 a group of scientists conducted a systematic review and meta-analysis of the literature through Medline and Embase databases. They collected 16 relevant papers. The results showed that “Prudent/healthy' diet, reduced substantially the risk of gastric cancer with an odds

ratio (OR) of 0.75 (reduction of 25%). In contrast, a 'Western/unhealthy' dietary pattern, showed an OR of 1.51 for gastric cancer (increase of 50%) . Reviewers concluded that there is a ~2-fold difference in gastric cancer risk between a 'Prudent/healthy' diet (rich in fruits and vegetables, whole grains, nuts, etc), and a 'Western/unhealthy' diet (rich in starchy foods, meat and saturated fats).[114]

Conclusions

According to the World Health Organization (WHO) cancer is the second leading cause of death globally. Cancer was responsible for worldwide 9.6 million deaths in 2018. Most types of cancer are preventable diseases. The majority of epidemiological and other studies support the fact that around 35% of deaths from cancer are due to the 5 leading modifiable lifestyle factors: tobacco smoking, dietary factors (low fruit and vegetable intake, high consumption of red meat, salty and smoked foods, saturated fat, etc), high alcohol consumption, high body mass index (BMI) leading to overweight/obesity, and sedentary life with lack of physical exercise. The most important cancer risk factor is tobacco smoking, responsible for approximately 22% of cancer deaths globally. This review collected the most important studies from the scientific literature of the last decade, that investigated the reduction of cancer risk by quitting smoking, reducing alcohol consumption, avoiding unhealthy dietary practices, reducing overweight and obesity and finally follow daily physical exercise instead of unhealthy sedentary life. These studies offer a very clear picture of what people can avoid and what type of lifestyle they can follow.

All estimates showed that between 30–50% of cancers can currently be prevented by avoiding 5 risk factors and implementing existing evidence-based prevention strategies. The global cancer burden to humans can also be reduced through early detection of cancer and medical management of cancer patients. Also, many types of cancers have a high chance of to be cured by medical interventions if diagnosed early and treated adequately with the right anticancer drugs and advanced combinations of anticancer strategies.

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