A Critical Review of *Madia et al.* (2019) 'Carcinogenicity assessment: Addressing the challenges of cancer and chemicals in the environment.

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1.0 INTRODUCTION

The aim of this critical review is to discuss the study by Madia et al., (2019) 'Carcinogenicity assessment: Addressing the challenges of cancer and chemicals in the environment, Environment international, Volume 128 pp.417-429. The study under review discusses the measures that can be taken to better assess the carcinogenic properties of chemicals and manage their risks. To describe Cancer, it is the disease that results when uncontrolled growth and division of cells cause cellular changes. While some types of cancer result in rapid cell growth, there are others that cause cells to grow and divide at a slower rate. The study noted that cancer is the second leading cause of morbidity and mortality globally after cardiovascular diseases, and the prevalence, incidence and mortality rates of cancer continues to increase while in Europe, it is the most frequently occurring form of non-communicable disease. The World Health Organization (WHO) has recognized the impact of cancer on health and its social and economic consequences on a global scale. Cancer is a major public health risk that requires increasing attention, prioritization, and funding, according to the WHO's 70th World Health Assembly, which adopted a resolution on cancer prevention and control in 2017. (WHO Assembly Resolution, 2017). The first part of this review will look at the epidemiological causes of cancer, as well as environmental factors. Second, the evaluation will discuss cancer's global economic consequences. Third, to assess the ethical concerns surrounding cancer. Finally, a review of a cancer-prevention strategy.

1.1 BACKGROUND

According to a global estimate including 36 different diseases in 185 countries in 2018, there were 18.1 million new cancer cases and 9.6 million cancer-related deaths in 2018. (Bray et al., 2018). According to estimates, the number of new cancer cases would increase to 24.1 million per year by 2030 and 29.5 million by 2040. Furthermore, more than 32 million people are already living with a cancer diagnosis (5-year prevalence), putting a significant strain on health-care systems (Ferlay et al., 2018). However, when this is compared to another report in the same year 2018 (Global Cancer Observatory, 2018), cited by Madia et al, we see a record of 10 million people living with a cancer within 5 years of being diagnosed. Looking at the factors that could be responsible for the development of cancer in an individual, Madia et al was able to recognize a common theme across different studies in Europe which include 1) lifestyles which are common

in industrialized countries (WHO); 2) high urbanization and dense distribution of aged population, with long-term exposure to occupational and environmental carcinogens and medicines (EEA Chemicals for a sustainable future, 2018 pp. 1-47); 3) chronic exposure to particulate matter, ozone, and other pollutants that are above European standard limits and WHO air quality guidelines which have been linked to significant increase of respiratory NCD and cancers (EEA Air quality, 2018 pp. 1-88); 4) the deployment of early detection and screening programs that contribute to a documented increase of cancer incidence due to the detection of precursor lesions (Jönsson et al., 2016 pp. 162-170). Following the Council's advice on cancer screening (EU Council Recommendation, 2003) and the establishment of a European Partnership to support Member States in their efforts to combat cancer, a number of initiatives have been put in place during the last two decades (EU Commission Communication, 2009; EU Parliament Resolution, 2008).

1.2 CANCER AS A PUBLIC HEALTH ISSUE

The overall global burden of the incidence and mortality of cancer continues to increase at an alarming rate and this reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer, many of which are linked with socioeconomic development (Omran, 1971). The global incidence rate for all cancers combined in 2020 was 19% higher in men than in women, however rates varied widely across regions. Despite accounting for 9.7% of the global population, Europe contributes for 22.8 percent of all cancer cases and 19.6 percent of cancer deaths, followed by the Americas with 20.9 percent of incidence and 14.2 percent of mortality. Because of disparities in cancer type distributions and substantially higher case fatality rates in the same regions, the percentage of cancer fatalities in Asia (58.3%) and Africa (7.2%) is larger than the share of cancer incidence (49.3 percent and 5.7 percent, respectively). In their study, Madia et al. bolstered these figures, emphasizing the devastating impact of cancer on all aspects of human life, leaving no region unaffected. The authors also stated that low- and middle-income countries, as well as those undergoing rapid industrial expansion, have the biggest impact in terms of mortality, and that many of these countries are almost unprepared to deal with the disease's quickly expanding burden and cost.

The World Health Organization has published a list of the most frequent cancers in 2020. (in terms of new cases of cancer). There were 2.26 million cases of breast cancer, 2.21 million cases of lung cancer, 1.93 million cases of colon and rectum cancer, 1.41 million cases of prostate cancer, 1.20 million cases of skin cancer (non-melanoma), and 1.20 million cases of stomach cancer (1.09 million cases). Despite the fact that breast cancer had the biggest number of diagnoses in 2020, lung cancer had the highest number of deaths (1 million), followed by colon and rectum cancer (935,000). Surprisingly, breast cancer, which had the most instances, had the fewest deaths, with 685,000 deaths, trailing stomach cancer with 769,000 deaths.

1.3 SUMMARY OF STUDY

Madia et al., (2019) study points out the specific associations between chemical exposures and certain cancer which have been previously reported by different studies and reports. Scientific research has led to considerable insights into the many ways exogenous chemicals can adversely affect human health and cause cancer. The authors noted that there are several variables that should be considered, among which are duration of exposure, demography, geography, environment, and individual susceptibility. The study also expressly mentioned there are measures that can be taken to better assess the carcinogenic properties of chemicals and manage their risks. Furthermore, the study discusses how these measures can be informed not only by the traditional data streams of regulatory toxicology, but also by using new toxicological assessment methods, alongside indicators of public health status on the basis of biomonitoring. In agreement with other reports, the authors discussed how the diverse evidence streams have the potential to form the basis of an integrated and more effective approach to cancer prevention.

2.0 CRITICAL REVIEW

The study's structure demonstrates transparency and evidence-based analysis that is well-justified, with extremely explicit and well-defined objectives. The search method and specific sources of information have also been highlighted. The study's key statements have been adequately and correctly supported by accurate references. The study's data has been beautifully displayed aesthetically and in a logical arrangement. This critical analysis will look at the epidemiological

causes of cancer, the worldwide economic cost of cancer, surveillance, and initiatives to enhance cancer health outcomes, which are all important topics in the discussion.

2.1 EPIDEMIOLOGICAL CAUSES OF CANCER.

While cancer cannot be totally avoided, there is good evidence that lowering the influence of certain risk factors can significantly reduce susceptibility to the illness. Biological agents (infections), exposure to synthetic chemicals through work or consumer products, and lifestyle variables are all examples of risk factors that may be mostly avoided. According to reports, these risk factors have a role in the development of 70–95 percent of all malignancies (Wu et al., 2016).

Because of the comparatively high percentage of cancer cases that can be explained by recognized risk factors, accessible public health initiatives for reducing cancer incidence and mortality have a better chance of being effective. Around 43% of cancer cases in the UK in 2010 were connected to a total of twelve different lifestyle and environmental variables (Parking et al, 2011). In 2020, estimates for the Brazilian population predict that known lifestyle and environmental risk factors will be responsible for around 35 percent of all cancer cases and between 39 percent (women) and 46 percent (men) of fatalities (Azevedo et al, 2016).

This study was successful in linking environmental factors to cancer onset and incidence. Other investigations have successfully linked Madia et al's claim to the development of cancer (Arnold et al., 2015). When comparing the findings of Madia et al. with those of other researchers, it becomes clear that while chemical exposure is one of the risk factors for cancer, the specific contribution of chemicals to cancer is difficult to quantify with certainty; however, a number of estimates have been made in this regard. Anand et al., for example, estimated that nutrition contributes 30–35 percent to cancer development, followed by cigarettes (25–30 percent), infections (15–20 percent), obesity (10–20 percent), alcohol (4–6 percent), and others, such as pollution and radiation (10–15 percent). Surprisingly, Belpomme and colleagues, as well as WHO, published estimations that backed with their findings (Belpomme et al., 2007; WHO Cancer Report, 2014). Furthermore, without taking cigarettes into account, Colditz and Wei estimated that chemicals contribute 4–10% of the total (Colditz and Wei, 2012). Madia et al. also point out that as people get older, their stress resistance and ability to repair cellular and DNA damage decreases.

The inference is that, when this is paired with cumulative use of drugs and exposure to stressors, such as toxins, people are more likely to acquire cancer as they get older. In the study of Podolskiy and Gladyshev, (2016), it was discovered that there are some types of cancer, such as esophageal carcinoma, liver hepatocellular carcinoma, pancreatic adenocarcinoma, pheochromocytoma, stomach adenocarcinoma, bladder and colon cancers, in which the effect of ageing has been suggested to outweigh other risk factors.

Tobacco smoking, alcohol use, bad food, physical inactivity, and air pollution have all been identified as risk factors for cancer and other non-communicable diseases in reports and research. Some chronic infections have been identified as cancer risk factors, particularly in low- and middle-income nations. In 2013, carcinogenic diseases such as Helicobacter pylori, human papillomavirus (HPV), hepatitis B virus, hepatitis C virus, and Epstein-Barr virus were associated to approximately 13% of malignancies diagnosed (de Martel et al, 2020). Hepatitis B and C viruses, as well as various other forms of Hepatitis viruses, have been linked to an increased risk of liver and cervical cancer. In addition, HIV infection greatly raises the incidence of malignancies such as cervical cancer.

According to a WHO report (Prüss-Ustün et al., 2016), around 20% of all cancers are caused by environmental factors, with occupational exposure accounting for 2–8% and cancers caused by chemicals in the environment accounting for 1.5–2%. Differences in estimates could be related to research context (target cancer or target pollutant), uncertainties in data collecting, or various techniques to data processing, according to Madia et al. According to the WHO report, household air pollution contributes 17 percent to lung cancer, while ambient air pollution contributes 14 percent, residential radon contributes 7%, occupational exposure contributes 7%, and second-hand tobacco smoke contributes 2% (Prüss-Ustün et al., 2016). According to research, the strongest evidence for cancer occurrences linked to chemical exposure is seen in industrial situations. Characterization of the environment, exposure levels, exposure time-frame, and worker health status may all be tracked precisely and accurately in the workplace. Lung cancer accounts for 54–75 percent of all occupational malignancies, according to the statistics collected (Cogliano et al., 2011)

2.2 GLOBAL ECONOMIC IMPACTS OF CANCER

Cancer has been shown to have the greatest economic impact of any cause of mortality in the world, according to study. In 2008, the entire economic cost of cancer-related premature death and disability was estimated to be $895 billion around the world. This figure is estimated to be roughly 19 percent more than the cost of heart disease ($753 billion). Surprisingly, factors like direct medical bills were left out of the analysis. If such costs had been factored in, the total economic cost of cancer would have increased even more. By 2010, the entire annual economic cost of cancer had increased to US$ 1.16 trillion (Wild et al, 2020). While numerous diseases have an economic impact, it is concerning that cancer alone is responsible for the greatest number of lost years of life and productivity worldwide. Lung cancer, colon/rectal cancer, and breast cancer are the main cancers in terms of death and disability, with lung cancer, colon/rectal cancer, and breast cancer accounting for the highest global economic expenditures. Cancers of the mouth and throat, cervix, and breast, on the other hand, have the highest impact in low-income countries. While the global economic impact of cancer is worrying, the impact on people and families is even greater, particularly in nations classified as low- and middle-income, where a loss of income due to illness or death may quickly devastate family finances. If there are targeted interventions or strategies to prevent and treatment these devastating cancers and other preventable forms of cancer, we could be looking beyond just saving lives, but also improving economic development prospects in many countries.

Cancer has a global economic impact that is not evenly divided among countries. Consider the United States as an example. While the expense of cancer is highest in absolute terms in the United States, the disease costs the country 1.73 percent of its GDP. When compared to a country like Hungary, which has a smaller population and domestic economy, cancer costs the country about 3.05 percent of its GDP. More than 20 countries are losing more than 2% of their GDP due to cancer-related deaths and disabilities. Furthermore, cancer costs nearly half of all countries more than 1% of their GDP. According to the WHO and global health experts, it is believed that in order to significantly mitigate costs from cancer , interventions or strategies such as targeted, cost-effective interventions that have been deployed and found effective in richer nations can be implemented in many countries. The WHO has also further confirms that the “silent pandemic” of cancer is rapidly penetrating and spreading through low- and middle-income countries. If there is little to no worldwide response to the menace of cancer, it could handicap public health systems, pose enormous dangers to social structures, and shatter efforts geared

towards economic development. On the global scale, specific types of cancers such as the cancers of the lung, bronchus, and trachea are by far responsible for about $180 billion drain on the economy. It's not unexpected that this is the case because smokers die 15 years earlier on average than nonsmokers. If current trends continue, tobacco will kill eight million people per year by 2030, with over 80% of deaths occurring in low- and middle-income nations. Cancer is responsible for around one-third of those deaths.

While smokers are the ones who are most impacted by tobacco, it is unfortunate that thousands of nonsmokers are killed by it every year. According to statistics, 200,000 individuals die each year as a result of being exposed to secondhand smoke in the job. As the number of deaths and disabilities caused by lung cancer continues to rise across all income levels in almost every country, efforts like the WHO Framework Convention on Tobacco Control (FCTC) become increasingly important, as it has the potential to significantly reduce cancer-related economic losses. The World Health Organization's Framework Convention on Tobacco Control (WHO FCTC) is an international convention that was signed by 168 countries with the goal of regulating the sale of tobacco products. If tobacco is successfully controlled, it may have other benefits for both public health and economic development. Furthermore, implementing intervention programs aimed at lowering tobacco use could have a positive impact on the treatment of cardiovascular and respiratory disorders. Another source of concern is the tremendous weight that people in developing nations must suffer as a result of a lack of understanding and efficient treatments for some cancers. While most occurrences of cervical cancer may be prevented or efficiently treated, the illness nonetheless claims the lives of 274,000 women each year. Women from low- and middle-income nations account for around 241,000 of the 274,000. Cervical cancer, which is also common in low-income nations, has a significant economic burden. Cervical cancer, followed by mouth and throat cancers, accounts for more than 10% of the economic loss in countries classed as low income by the World Bank. Unfortunately, one of the key causes is that most women in low-income nations do not have access to medical care that can prevent the start of cervical cancer or even diagnose it early enough. As a result, many women are diagnosed too late and miss out on potentially life-saving therapy. Contrary to popular belief, a considerable proportion of women living in high-income nations have had easy access to and benefited from routine screening and treatment techniques for decades, which has resulted in a dramatic fall in cervical cancer rates in

those countries. However, while this economic impacts exist, the study by Madia et al did not discuss on issues relating to the global economic impact of cancer.

2.3 SURVEILLANCE FOR CANCER

Cancer surveillance is defined as "the continuous, timely, and systematic collecting and analysis of data on new cancer cases, the degree of disease, screening tests, treatment, survival, and cancer deaths." To do so, registries are established, which are made up of cancer registrars who have received training and currently meet specified testing and continuing education requirements.

Case identification is the initial stage in cancer registration. To elaborate, it is the identification of cancer patients who have previously had medical care in hospitals. In most cases, clinicians begin the data collection procedure by noting the cancer's location, type, patient demographics, and illness stage in the medical record. The doctor can also give other details such as the sort of treatment. After that, the patient can be followed up on an annual basis to monitor cancer recurrence and survival.

Because cancer is comprised of over 100 entities, each of which is characterized by out-of-control cell development and identified by place of origin and kind of cell originally impacted, cancer heterogeneity is currently posing a significant challenge to cancer surveillance. As a result, precise information regarding the affected organ and histological type is required in order to appropriately categorize the nature and extent of disease, as well as plan treatment and assess disease outcomes. According to Wingo et al. (2005), "the development of a simplified surveillance cancer framework at a global level; the natural history of disease from inception through resolution (cure or death) and its associated control measures" are some of the factors that prove critical in developing a US cancer surveillance template (prevention, early detection, treatment, and end-of-life care). As a result, the structure assisted in the identification of four major demographic segments for surveillance. Furthermore, the authors defined cancer control in terms of 1) healthy populations, 2) newly diagnosed populations, 3) cancer-affected populations, and 4) cancer-dead populations.

2.4 ACTIONS TO IMPROVE HEALTH OUTCOMES FOR CANCER

According to the World Health Organization, between 30 and 50 percent of malignancies can currently be avoided by avoiding risk factors and using evidence-based preventative techniques. Another strategy to lessen the cancer burden is to detect cancer early and provide appropriate therapy for cancer patients, because many cancers can be cured if detected and treated properly. It is critical to take into account the type of cancer burden, documented trends, and changes in exposure patterns to environmental chemicals in order to provide effective human protection against cancer and better disease outcomes. As Madia et al. point out, doing so will aid in forecasting how carcinogenicity evaluation should progress. The contribution of different risk factors, the prevalence of certain cancers over others, the evolution of the disease and its link to other morbidities, and exposure to chemicals in occupational or environmental settings, as discussed in this study and many others, must all be taken into account when developing cancer prevention strategies (Madia et al., 2019), which include a proper assessment of chemical carcinogenicity. As a result, it's critical to keep adapting the approaches and testing procedures used in regulatory toxicity testing. Prioritization of carcinogenicity evaluation of chemicals for their potential to contribute directly to the development of malignancies, as advocated by Madia et al, one critical action that can be done is investigating the role of specific biomarkers that describe signaling pathways drive carcinogenesis in the tissues of interest. Sanchez-Vega et al., (2018) also supports this approach. The authors' second recommendation is to make better use of knowledge of human physiology and pathophysiology gained from various research studies on human cancer biology, clinical studies, and human biomonitoring because all of these contribute to large amounts of relevant data that can be used to guide toxicity studies.

The National Initiatives for New Chemicals Screening and Breast Cancer and Chemicals Policy Programs, a 'disease endpoint' strategy that is currently being developed, were mentioned by the authors of the paper under evaluation. Furthermore, a detailed analysis of biological effects of the disease and changes in biological pathways that serve as early indicators of toxicity has led to the development of tailored mechanistic tools that can identify specific breast cancer-inducing traits, based on insights into breast cancer etiology and epidemiology evidence. These novel tools, such as Grashow et al., (2018)'s curated genomic biomarker panel for screening or Schwarzman et al.,

(2015)'s procedure for hazard identification, can be fully integrated into the carcinogenicity assessment processes.

3.0 CONCLUSION

This study successfully outlined and highlighted the common causes of cancer, with emphasis on chemicals in the environment. However, this is not the highlight of the whole study, rather it is the importance of carcinogenicity assessment of chemicals to which humans are exposed which can result in cancer. The rates at which cancer incidence and prevalence is increasing as identified by the World Health Organization are of grave concerns. The authors noted that the scientific advances in the last few years have helped to put light to the most critical properties of cancer, thereby facilitating the development of effective therapeutic options. In agreement with other studies, Madia et al pointed out that managing significant risk factors can also go a long way in reducing the occurrence and incidence of cancer globally. Furthermore, as a result of the increase in global trend of chemical production, there is an expected changes to patterns of chemical exposure, placing more demands on chemical safety assessment. The authors clearly highlighted the importance of ensuring continuous safety assessment of carcinogenicity. While there are many actions being taken globally to tackle cancer, it is important to include further plans for assessing carcinogenicity. Additionally, a major take away from this study is that there is a need for more inclusive method to assess carcinogenicity that will focus on the chemicals of most significant concern, and also use testing methodologies that are relevant to humans to guide the best measures for risk management.

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