Journal of Cancer Research, Treatment and Prevention

Obafemi F A, et al., 2023- J Cancer Res Treat Prev
Review Article

A Review of Global Cancer Prevalence and Therapy

Faith Ayobamidele Obafemi* **and Grace Umahi-Ottah**

Department of Physiology, Faculty of Basic Medical Sciences, Ebonyi State University, Abakaliki, Nigeria

***Corresponding Author:** Faith Ayobamidele Obafemi, Department of Physiology, Faculty of Basic Medical Sciences, Ebonyi State University, Abakaliki, Nigeria.

Received Date: 05-17-2023

Accepted Date: 05-25-2023

Published Date: 06-02-2023

Abstract

Cancer remains a major contributor to mortality and hinders the increase in life expectancy worldwide, while stroke and coronary heart disease deaths have seen a global decline compared to cancer mortality rates. There are significant disparities in cancer incidence rates between regions and genders, primarily due to varying exposure to risk factors, cancer types, and early detection and prevention challenges. Egypt experienced the highest rate of new cancer diagnoses and cancer-related fatalities in Africa, with prostate cancer being the most prevalent cancer in men and breast and cervical cancers having the greatest impact on women. In North African countries, breast cancer had greater incidence and fatality rates than cervical cancer, however, the trend was the opposite in sub-Saharan African countries. Nigeria had a high number of new cancer cases and deaths due to limited awareness, restricted access to screening and treatment facilities, and the prevalence of risk factors like infectious diseases, tobacco use, and unhealthy lifestyles. Therefore, African countries, including Nigeria, need to take measures to increase awareness, invest in early detection and screening programs, and improve access to treatment and supportive care.

Keywords: Cancer; Global; Cancer therapy; Africa; Nigeria.

Introduction

Why cancer? global cancer burden

Globally, cancer is the leading cause of death and a substantial barrier to raising life expectancy in every nation. According to World Health Organisation (WHO) data from 2019, cancer is the leading or second cause of death before the age of 70 in 112 out of 183 countries, and third or fourth in another 23 (Fig. 1) (WHO, 2019). This trend can be partially explained by the fact that stroke and coronary heart disease death rates are on the decline globally in comparison to cancer mortality rates (WHO, 2019). Figure 2 and 3 provide information on the most

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

recurrently diagnosed malignancies and the top causes of cancer mortality at the national level, respectively. The findings reveal a large diversity in the most prevalent cancer types around the world, particularly for incidence in males with 8 different cancer types and for death in both men and women with 8 and 7 types, respectively. Men are most frequently diagnosed with prostate cancer in 112 of those countries, followed by lung cancer in 36, and colorectal and liver cancer in 11 (Fig. 2A) [2]. Regarding mortality (Fig. 3A), liver cancer is the third-foremost cause of death for males globally (after prostate cancer and liver cancer, respectively, in 48 and 23 nations, respectively). The two cancers most frequently diagnosed in women are breast cancer (159 countries) and cervical cancer (23 of the 26 remaining countries) (Fig. 2B) [2]. According to Bray et al., The mortality profile for women is more diverse (Fig. 3B), with lung cancer ranking third in 25 countries and breast and cervical cancer placing first and second in 110 and 36 countries, respectively.

Cancer incidence and death rates

In 2020, males had a 22% higher global incidence rate of all malignancies than women (186 per 100,000), however, there were significant regional differences. From 494.2 per 100,000 in Western Africa to 100.6 per 100,000 in Australia/New Zealand, the incidence rates for men varied by about 5-fold. Women's incidence rates varied from 405.2 per 100,000 in Australia/New Zealand to 102.5 per 100,000 in South Central Asia, with a nearly 4-fold disparity between each location. The discrepancies in incidence rates are primarily brought about by differences in risk factor exposure and cancer mix, additional challenges to accurate early cancer detection and prevention.

The increased risk of non-melanoma skin cancer owing to excessive sun exposure in a mostly light-skinned population and enhanced disease identification contribute to Australia's and New Zealand's highest overall incidence rates. The prevalence rate for all malignancies combined was, according to statistics (2020), 19% higher in men than in women globally, with males experiencing an incidence rate of 222.0 per 100,000 and women experiencing a rate of 186 per 100,000. Men's incidence rates varied by region, with rates in Western Africa being 100.6 per 100,000 and Australia/New Zealand being 494.2 per 100,000. Women's incidence rates varied between 102.5 per 100,000 in South Central Asia to 405.2 per 100,000 in Australia/New Zealand, a difference of about four times. These geographical variances can be attributable to differences in risk factor exposure, the mix of cancers, and obstacles to cancer prevention and early diagnosis. Male death rates are 43% higher than female death rates globally, with the gender disparity in total cancer mortality being twice as large as the gender discrepancy in incidence rates. Different patterns in the distribution of cancer types contribute to the variation in death rates. Women's mortality rates per 100,000 people ranged from 118.3 in Melanesia to 63.1 in Central America and South-Central Asia, while men's mortality rates per 100,000 people ranged from 165.6 in Eastern Europe to 70.2 in Central America. It is notable that in 2020, female cancer deaths in Eastern Africa were at a higher cumulative risk (11.0%) than in Northern America (8.2%), Western Europe (8.8%), or Australia/New Zealand (7.4%).

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

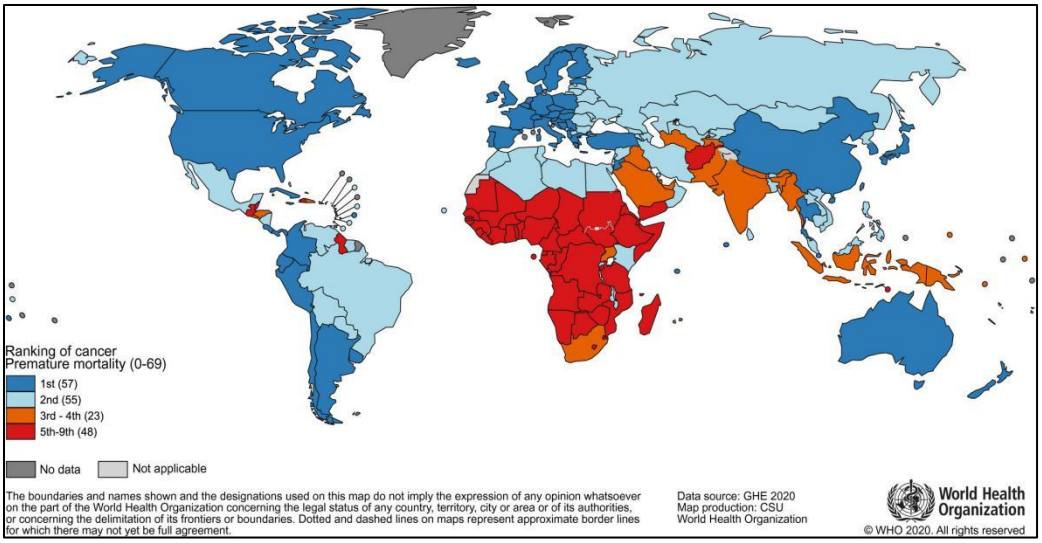

Figure 1: GLOBOCAN estimates of global incidence and mortality for 36 cancers in 185 countries, Global Cancer Statistics 2020 [1].

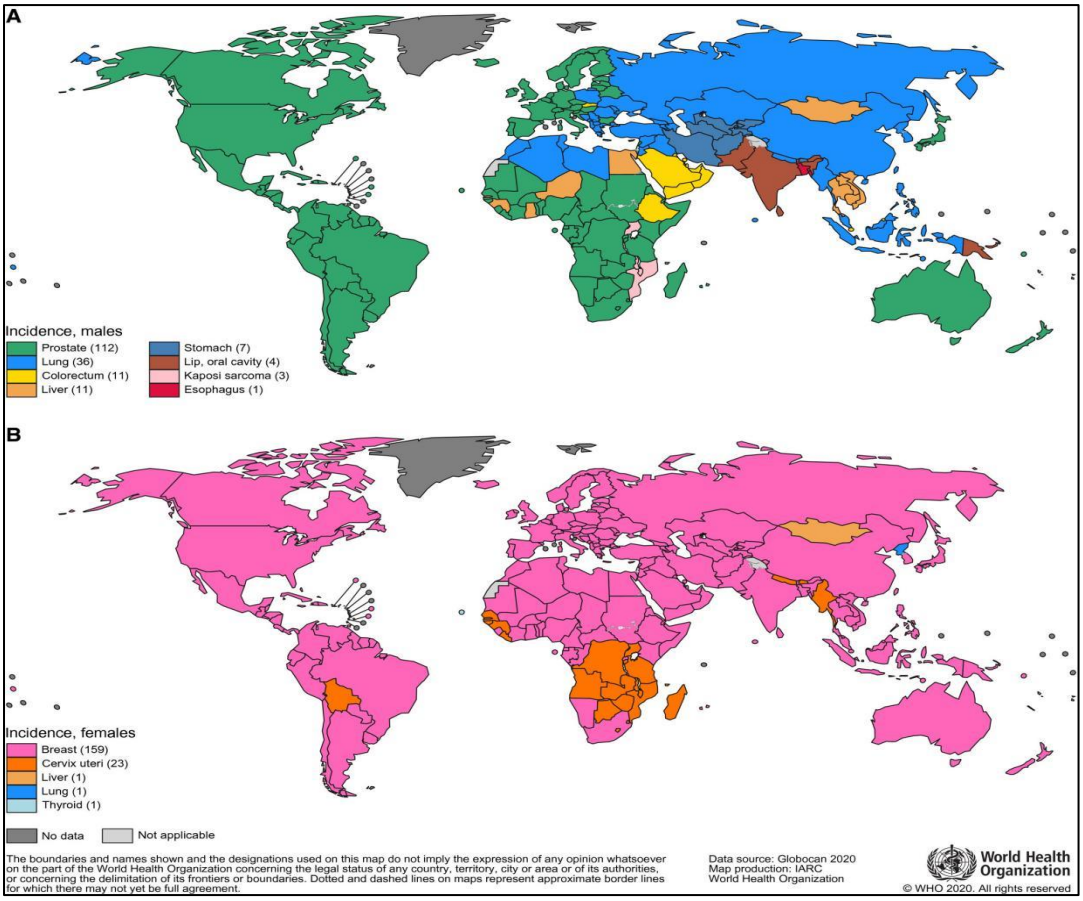

Figure 2a-2b: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, Global Cancer Statistics 2020 [1].

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

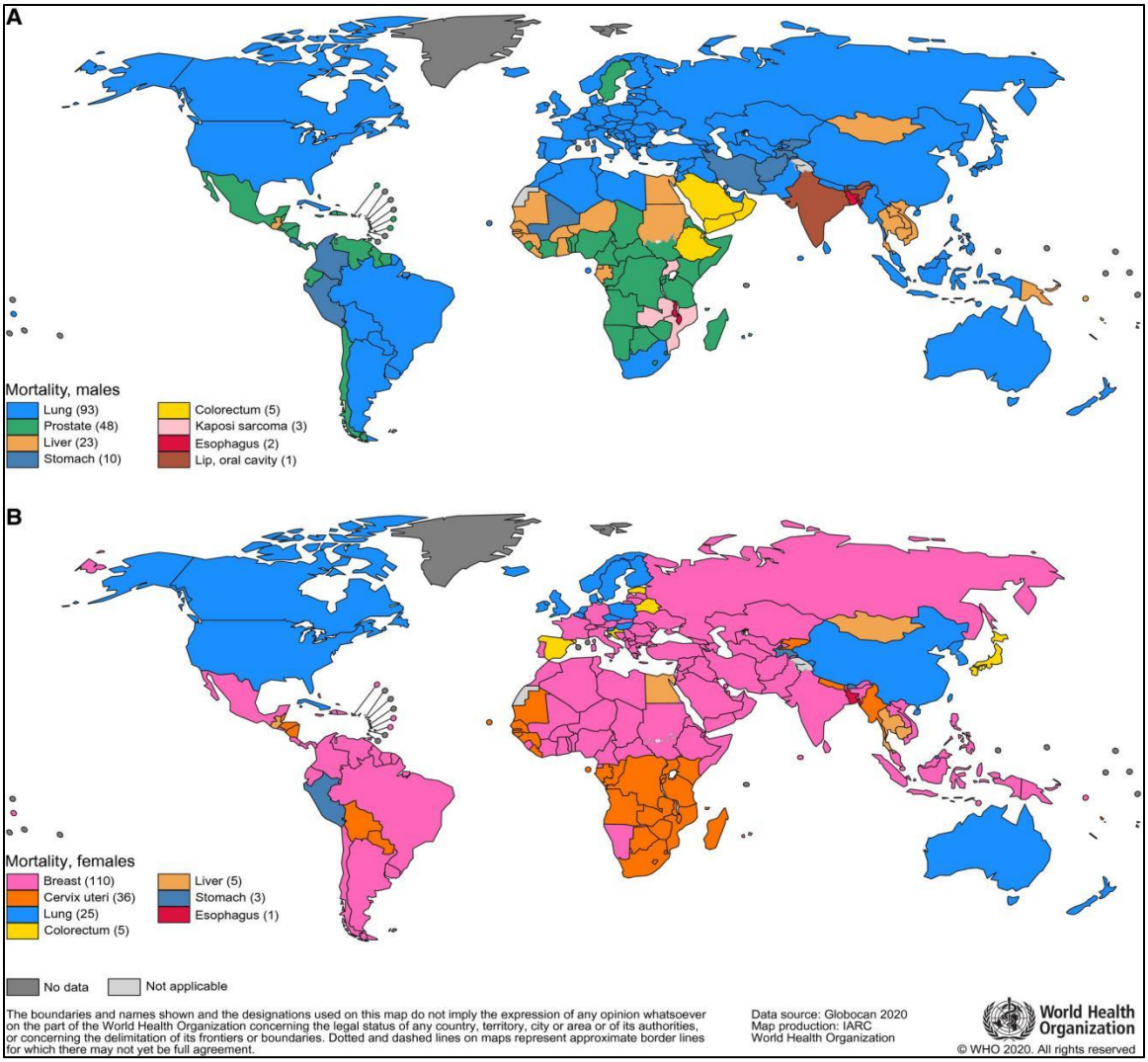

Figure 3a-3b: GLOBOCAN estimates of global incidence and mortality for 36 cancers in 185 countries, Global Cancer Statistics 2020 [1].

Female breast cancer

Female breast cancer is predicted to surpass lung cancer as the most common kind of cancer globally in 2020, accounting for 2.3 million new cases and 11.7% of all cancer cases globally. With 685,000 fatalities, it is also the ninth most common cause of cancer mortality globally. Breast cancer is the most common cancer in women, accounting for 1 in 4 cases worldwide and 1 in 6 cancer-related deaths (159 out of 185). In sub-Saharan Africa, cervical cancer occasionally accounts for the majority of cancer-related mortality rather than breast cancer.

The highest rates (>80 per 100,000) were found in Australia/New Zealand, Western Europe, North America, and Northern Europe, while the lowest rates (40 per 100,000) were found in Central America, Eastern and Middle Africa, and South-Central Asia. Breast cancer incidence rates are higher

in transitioning nations. However, due to high fatality rates, transitional nations have mortality rates that are 17% greater than transitioned countries. Melanesia, Western Africa, Micronesia/Polynesia, and the Caribbean all have the highest death rates, with Barbados having the highest mortality rate.

The disparities in risk factor exposure, access to healthcare and early detection, and the accessibility of efficient therapies account for a substantial portion of the discrepancies in incidence and death rates between nations. These elements emphasize the value of international initiatives to enhance cancer prevention, early diagnosis, and treatment in order to lessen the burden of breast cancer and other malignancies globally.

The increased incidence rates of breast cancer in countries with higher HDI can be attributed to a long-standing higher prevalence of reproductive and hormonal risk factors, such as early menarche, late menopause, advanced maternal age, less breastfeeding, menopausal hormone therapy, and oral contraceptives, as well as lifestyle risk factors. This trend has also been aided by more mammograms being detected through planned or opportunistic screening [3].

Women of Ashkenazi Jewish origin also have an abnormally increased frequency of mutations in genes with strong penetrances, like BRCA1 and BRCA2, which explains the high incidence of breast cancer in Israel and several subpopulations of Europe [4]. In several nations in Northern America, Oceania, and Europe, breast cancer incidence rates climbed evenly and quickly during the 1980s and 1990s. This comes on by an increase in detection spurred on by thorough mammographic screening, together with an increase in the frequency of risk factors. The incidence rates, on the other hand, stabilized or dropped in the early 2000s, mostly because fewer women were using menopausal hormone therapy and because screening participation may have peaked [5]. Less than 0.5% each year has increased the incidence rates in the United States since 2007, and several other countries in Europe and Oceania have also experienced moderate but significant rises [6,7].

According to recent research, estrogen receptor-positive breast cancers are only seeing rising incidence rates, whereas estrogen receptor-negative tumors are experiencing declining incidence rates [7]. Studies utilizing data from cancer registries and tumor marker information have shown this tendency in the US, Denmark, Ireland, and Scotland [8-11].

Mammographic screening, which preferentially detects slow-growing oestrogen receptor-positive tumors, and the greater and longer-lasting relationship between high body weight and oestrogen receptor-positive cancer are two explanations for this trend [12]. As a result of improvements in effective treatment, countries in historically high-risk regions have benefited the most from a decline in death rates throughout the late 1980s and early 1990s [13].

In transitional South American, African, and Asian nations as well as previously low-risk Asian nations like Japan and the Republic of Korea, breast cancer incidence rates are rising

quickly [14,15]. Growing economies, a rise in the share of women in industrial labor, and changes in lifestyle, sociocultural, and physical environments are all credited with this growth. These adjustments have caused a convergence toward the risk factor profile of Western nations and a lessening of the global disparities in the morbidity of breast cancer.

The largest increases are seen in sub-Saharan Africa, where incidence rates in Malawi, Nigeria, and Seychelles have climbed by more than 5% annually between the mid-1990s and the mid-2010s [15]. Sub-Saharan African areas have some of the highest mortality rates in the world, which is a reflection of the region's subpar health infrastructure and therefore dismal survival rates. Since 77% of all staged patients were in stage III or IV at the time of diagnosis, late-stage presentation is primarily to blame for low survival rates [15,16].

The key to increasing survival rates is promoting early identification through increased breast cancer awareness and clinical breast examination by trained medical professionals, followed by prompt and suitable treatment. In low-resource environments, organized, population-based mammography screening programs might not be practical or cost-effective [17].

According to a recent study, early detection of symptoms and appropriate treatment might avoid 28% to 37% of breast cancer fatalities in five sub-Saharan African nations. In order to facilitate progressive incorporation into everyday practice, the Breast Health Global Initiative has created a number of evidence-based, resource-based guidelines [8].

Lung cancer

In 2020, lung cancer is expected to be the second most often diagnosed condition and the leading cause of cancer mortality, accounting for approximately 11.4% of all cancers diagnosed and 18.0% of all cancer deaths globally. Males have greater cancer-related morbidity and death than women do, with males experiencing rates of occurrence and death that are almost twice as high. Additionally, there are regional differences in these ratios, with a range of 1.2 in North America to 5.6 in North Africa. According to WHO (2018), the rates of occurrence and demise of smoking are highest in transitioning nations, where 80% of smokers under the age of 15 lived in 2016.

In 36 nations, the most often diagnosed cancer in men is lung cancer. Lung cancer is the main cause of cancer-related death in 93 different nations. The regions with the greatest occurrence rates globally include Turkey, Micronesia/Polynesia, Eastern and Southern Europe, and Asia. Incidence rates remain normally low in both Southern and Northern Africa, despite the possibility that they could vary from moderate to high. In 25 nations such as Northern America, Oceania, and portions of Europe, lung cancer is the most common cancer in women and the leading cause of cancer mortality.

The largest rates of occurrence are in Northern America, Northern and Western Europe, Micronesia/Polynesia, Australia/New Zealand, and Hungary and Hungary with maximum rates per nation. Rates are particularly high in Eastern Asia, particularly among Chinese women who, due to the low

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

prevalence of smoking, are exposed to high levels of indoor ambient air pollution and inhalable pollutants from household solid fuel burning for cooking and heating. According to Mu et al. [18]and Turner et al. [19], outdoor ambient PM2.5 air pollution was to blame for 14.4% of lung cancer deaths globally in 2017, with 4.7% of those deaths occurring in the USA and 20.5% in China.

The maturation of the tobacco pandemic is primarily reflected in the diversity in lung cancer rates and trends throughout the world, with patterns in death mirroring those in incidence due to the high death toll. Smoking was initially made popular among men in several high-income countries, including the UK, USA, Finland, Australia, New Zealand, Singapore, Germany, Uruguay, and Nordic nations. This was followed by a sharp rise in lung cancer cases [2,20]. The maximal level of smoking was followed by a number of decades of subsequent decreases in lung cancer, which were initially noted in young birth cohorts. These trends offer vital information for public health initiatives and worldwide tobacco control legislation.

Colorectal cancer

According to projections, colorectal cancer accounted for around one in ten new cases of cancer and fatalities in 2020, including 935,000 fatalities and more than 1.9 million new cases (including anus). Colorectal cancer is second in terms of mortality but third in terms of incidence. While mortality rates vary less because there are more fatalities in transitioning nations, incidence rates in developing nations are around 4 times greater than those in transitional countries.

There is a roughly 9-fold global range in the incidence rates of colon cancer, with the greatest rates seen in Northern America, New Zealand or Australia, and European areas. For women, Norway comes in #1, and for males, Hungary. Similar regional differences may be seen in rectal cancer incidence rates, while Eastern Asia has some of the highest rates. In much of Africa and South-Central Asia, incidence rates of colon and rectal cancer are normally low [21].

Changes in dietary habits and lifestyle variables are probably to blame for the rise in the incidence rates of colorectal cancer in nations going through a substantial transformation. Increased consumption of foods derived from animals and a more sedentary lifestyle result in a decline in physical activity and an increase in excess body weight prevalence, which are both independently associated with an increased risk of colorectal cancer. Additional risk factors include drinking a lot, smoking, and consuming red or processed meat. The risk seems to be reduced by eating enough whole grains, fiber, dairy products, and calcium supplements. The most effective method for lowering the rising worldwide burden of colorectal cancer is primary prevention [22].

Colorectal cancer screening utilizing less invasive and more affordable methods, like guaiac testing and fecal immunochemical tests, may be cost-effective in particular scenarios of emerging nations and offer opportunities to reduce the disease's mounting toll. However, due to the high cost of colonoscopy and the subpar delivery of diagnostic and therapeutic services, launching a mass screening effort is presently

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

not financially viable in the majority of low-income and middle-income nations.

Prostate cancer

According to recent projections, there will be over 1.4 million new instances of prostate cancer and 375,000 fatalities globally in 2020. It is the second most prevalent malignancy and the fifth most common reason for cancer-related mortality among males. With rates of 37.5 and 11.3 per 100,000, respectively, transitioned nations experience an incidence rate that is three times greater than transitional countries. Less variation may be found in mortality rates, which are 8.1 and 5.9 per 100,000 in transitioned and developing nations, respectively. Among men, the most common cancer diagnosed is prostate cancer, based on 112 out of 185 countries in the globe. Geographically, incidence rates range from 6.3 to 83.4 per 100,000 men, with Northern and Western Europe, the Caribbean, Australia/New Zealand, Northern America, and Southern Africa having the greatest rates. Asia and Northern Africa have the lowest rates. In contrast to incidence rates, trends of regional fatality rates typically don't adhere to the same pattern. The Caribbean, sub-Saharan Africa, and Micronesia/Polynesia have the highest fatality rates. In 48 nations, including some in sub-Saharan Africa, the Caribbean, Central, and South America (such as Ecuador and Venezuela), as well as Sweden, prostate cancer is the most common malignancy that claims the lives of males.

Liver cancer

The third most prevalent cause of cancer mortality globally in 2020 is liver cancer and the sixth most often diagnosed cancer, it is an important global health concern. It is a specific kind of cancer that starts in the liver and spreads to other bodily organs. Males are more likely than females to develop liver cancer and pass away from it in most places, and Liver cancer has the second-highest death rate among males and the fifth-highest prevalence rate globally.

Although liver cancer incidence rates are 2.4 times higher in transitioned countries, the greatest rates are mostly seen in these nations. Eastern Asia (including Mongolia, which has rates significantly higher than any other country), South-East Asia (including Thailand, Cambodia, and Viet Nam), and Northern and Western Africa (including Egypt and Niger) are the 11 geographically different nations where the illness is the most prevalent malignancy. In Guatemala, Thailand, Cambodia, Egypt, Mongolia, and another 18 countries, liver cancer kills more males from the disease than any other type. Alcohol intake, Hepatitis B or C virus infection with non-alcoholic fatty liver disease are common risk factors for liver cancer. However, primary preventative measures such as hepatitis B vaccination, alcohol consumption reduction, and management of obesity and diabetes can lower the incidence of liver cancer. The survival percentage of people with liver cancer can be increased by the early discovery of the disease through screening programs and efficient treatment.

Cervical cancer

With an expected 604,000 new cases and 342,000 deaths globally from cervical cancer

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

in 2020, the disease is a serious global health concern. It is the fourth most frequently diagnosed malignancy and the fourth most lethal cancer in women. In 36 nations, including the great majority in sub-Saharan Africa, Melanesia, America, and Asia, cervical cancer is the most often diagnosed malignancy and the leading cause of cancer mortality.

Sub-Saharan Africa has the greatest regional incidence and fatality rates for cervical cancer, with Eastern Africa having the highest rates. The incidence and fatality rates of cervical cancer are greatest in Malawi. Cervical cancer rates are very high in Middle and Southern Africa. While death rates can vary by up to 18 times, they are 7 to 10 times lower in Northern America, Australia/New Zealand, and Western Asia (including Saudi Arabia and Iraq).

The human papillomavirus (HPV), which is spread through sexual contact, is the main cause of cervical cancer. HPV vaccination, precancerous lesion screening, and treatment of precancerous lesions and early-stage disease are all part of the prevention of cervical cancer. The HPV vaccine, screening, and treatment of precancerous lesions and early-stage cancer are all part of the World Health Organization's comprehensive cervical cancer prevention and control recommendations [23].

Sub-saharan Africa and Nigeria cancer burden

Egypt had the highest number of new cancer cases, at 134,632 [131,480 - 137,860], and the highest number of cancer deaths, at 89,042 [86,773 - 91,371], according to a study by Sharma et al. [24], which sought to comprehensively characterize and compare cancer types in Africa using estimates from GLOBOCAN 2020. South Africa came in second place in terms of newly diagnosed cancer cases, followed by Nigeria. Nigeria came in second place in terms of cancer fatalities, followed by South Africa.

The study also looked at mortality-to-incidence ratios (MIR), age-standardized mortality rates (ASMR), and age-standardized incidence rates (ASIR) in various African nations. The three top nations in terms of ASIR were La Réunion, South Africa, and Zimbabwe, while The Gambia and Niger had the lowest ASIR. Namibia and Zimbabwe have the two highest ASMRs, with the Republic of the Congo having the lowest. MIR was highest in Guinea, Niger, and the Gambia and lowest in Mauritius, La Réunion, and South Africa (indicating improved 5-year survival rates).

This study illustrates the inequalities in cancer incidence, death, and survival rates among the various nations in the area and throws light on the burden of cancer in Africa. The results highlight the need for focused interventions and financial commitments in African nations for cancer prevention, early identification, and treatment.

According to Sharma et al. [24], there were an expected 85,787 [77,648 - 94,779] fatalities and 186,598 [173,041 - 201,217] new cases of breast cancer in Africa in 2020. With an estimated incidence of 117,316 [105,999-129,842] and 76,745 [68,380-86,133] fatalities in women, cervical cancer came in second

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

place. Prostate cancer was the most common kind of cancer among African men, accounting for 93,173 [83,906 - 103,463] cases and 47,249 [41,941 - 53,228] deaths.

The study also discovered that when compared to cervical cancer, breast cancer had higher age-standardized incidence rates (ASIR) and age-standardized mortality rates (ASMR) in every country in North Africa, including Algeria, Egypt, Libya, Morocco, Sudan, and Tunisia. In contrast, the majority of sub-Saharan African nations experienced the reverse. Notably, the top three cancer types in the majority of African nations were breast, cervical, and prostate cancer, with cervical cancer not ranking among the top 10 cancer types in Egypt.

Nigeria had a total population of 206,139,590 in 2020, according to projections from GLOBOCAN. In the same year, 124,815 new instances of cancer within this demographic were documented. There were also 78,899 fatalities brought on by cancer. According to estimates, there are 233,911 prevalent instances of cancer, which are people who have had the disease for at least five years but have not yet received a diagnosis.

According to these figures, cancer affects a sizable portion of the population in Nigeria, which is consistent with a pattern seen in many other African nations. The high rates of cancer incidence and mortality in the area can be attributed to a number of things, including a lack of knowledge about the illness, restricted access to facilities for screening and treatment, and the high prevalence of risk factors like infectious diseases, tobacco use, and unhealthy lifestyles.

The public's knowledge of cancer is being raised, funding for early detection and screening programs is being invested in, and access to treatment and supportive care is being improved in Nigeria and other African nations. In Nigeria, there were a total of 124,815 new cancer cases in 2020, as per GLOBOCAN projections. Breast cancer was the most frequent among these instances, accounting for 28,380 cases, or 22.7% of all new cases. With 15,306 instances (12.3%) of prostate cancer, it was the second most prevalent kind of cancer, after 12,075 cases (9.7%) of cervical cancer. There were 7,478 instances of colorectal cancer and 7,310 cases of non-Hodgkin lymphoma, respectively. Other cancers made up the remaining 54,266 instances or 43.5% of all cancer cases.

According to GLOBOCAN, in 2020, the number of new cancer cases in males of all ages in Nigeria was reported as follows:

- Prostate: 15,306 cases, accounting for 29.8% of all new cancer cases in males.
- Colorectum: 4,306 cases, accounting for 8.4% of all new cancer cases in males.
- Non-Hodgkin lymphoma: 3,769 cases, accounting for 7.3% of all new cancer cases in males.
- Liver: 3,543 cases, accounting for 6.9% of all new cancer cases in males.
- Leukaemia: 1,909 cases, accounting for 3.7% of all new cancer cases in males.
- Other cancers: 22,565 cases, accounting for 43.9% of all new cancer cases in males.

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

According to these statistics, prostate cancer accounts for roughly one-third of all new instances of cancer among men in Nigeria. Leukemia, Non-Hodgkin lymphoma, liver cancer, and colorectal cancer are all serious health issues for males in Nigeria. The report emphasizes the necessity of stepping up efforts in Nigeria for cancer prevention, early detection, and treatment.

GLOBOCAN projections for 2020 show that, with 28,380 new cases (38.7% of all new cancer cases in females), breast cancer was the most prevalent cancer among Nigerian women of all ages. With 12,075 new cases (16.4%), cervical cancer was the second most prevalent malignancy among Nigerian women. Other cancers that were reported were non-Hodgkin lymphoma, ovarian cancer, and colorectal cancer, with 3,541 (4.8%), 3,203 (4.4%), and 3,172 (4.3%) new cases, respectively. The remaining 31.4% (23,046 cases) of new cancer cases among Nigerian women were caused by other forms of cancer.

Cancer therapy/treatments: combination therapy

Apoptosis pathway in cancer

The crucial process of planned cell death known as apoptosis is crucial for healthy growth. This emphasizes the relevance of apoptosis. The buildup of irreversible DNA damage or exposure to toxins can result in tumor growth and eventually cancer. Apoptosis is inhibited during the development of cancer, and pro-survival pathways are activated in addition, to promoting the proliferation and progression of cancer cells. Thus, apoptosis and cell cycle pathways are the targets of numerous therapeutic treatments.

The extrinsic and intrinsic routes are the major apoptotic mechanisms found in the physiology of the human. Death receptors and ligands from the TNF (tumor necrosis factor gene) families, including FasL/FasR, APO-1/Fas (CD95), Apo3L/DR3, Apo2L/DR4, and Apo2L/DR5, are included in the extrinsic route. These receptors for death set off intracellular communication that causes caspases like caspase-3 and caspase-8 to cleave and become active, which causes apoptosis [25]. The most often targeted death receptors during treatment are TNF-related apoptosis-inducing ligand-receptor ½ and CD95. According to Fulda and Debatin [25], CD95 controls immunological function by activating T cells, which triggers a defense mechanism that results in programmed cell death.

Apoptosis is a natural physiological process, but cancer cells have learned ways to thwart it. They achieve this by either reducing surface death receptors such as CD95 and TRAIL receptors are expressed, or by upregulating the expression of dummy receptors that can obstruct the normal apoptotic response [25]. Drug resistance is strongly correlated with this impairment of apoptosis.

Targeting variables that can boost pro-apoptotic processes or block pro-survival pathways is the goal of therapeutic medicines. Therapeutic, economical, and temporal advantages are just a few of the benefits of repurposed pharmaceuticals. Only a small

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

number of repurposed medications with apoptosis-inducing capabilities are presently being studied in clinical trials, though. One repurposed substance that might indirectly because apoptosis is nitroglycerin, which is used to treat angina. In addition to its main function in lowering angiogenesis and downregulating HIF1alpha, nitroglycerin's production of nitric oxide (NO) has been shown to have a secondary impact on inducing apoptosis [26,27].

The overall survival of patients with stage IIIB/IV non-squamous cell lung cancer, not being treated, was increased by the addition of nitroglycerin to the chemotherapy drugs vinorelbine and cisplatin, according to a randomized phase II study [28]. Although concrete solutions have not yet been offered, it was proposed that nitroglycerin may enhance resistance when paired with chemotherapy by enhancing hypoxic conditions. Nitroglycerin enhanced the vinorelbine response rate with acceptable toxicity, according to the study, and it was concluded that a phase III trial was necessary, however, it has not yet been started.

Histone deacetylase inhibitors in combination therapy

Researchers are employing the understanding of prevalent epigenetic modifier mutations in certain tumors as therapeutic targets in the quest to create innovative therapeutic therapies for cancer. In order to do this, several researchers have altered mouse hematopoietic stem cells' epigenetic modifier genes, which have been proven to improve cancer stem cell characteristics like the ability to self-renew.

The reversible nature of the epigenome has led to a rise in the use of therapeutics that target epigenetic modifiers, such as HDACi. HDACi are a frequent target for cancer treatment since dysregulation of HDACs is linked to a variety of cancer types. HDACi such as trichostatin A, vorinostat, romidepsin, and panobinostat have all had positive clinical trial outcomes; vorinostat was the first HDACi to get FDA approval for the management of chronic, cutaneous T-cell lymphoma that is developing or returning.

A synthetic benzamide HDACi known as MS-275 (also known as entinostat or SNDX-275) has reportedly gone through a number of studies [29].

This medication specifically inhibits HDAC1/2 and has the potential for the treatment of malignancies with increased HDAC1 and HDAC2 expression levels. According to phase 1 clinical studies on solid and hematologic cancers, MS-275 has the advantage of not inducing cardiotoxicity, which is a typical adverse effect of other HDACi [30,31].

But with a half-maximal inhibitory concentration in the micromolar range, it is greater than that of the majority of hydroxamic acid HDAC inhibitors. According to theories put out by researchers [32], the therapeutically necessary dose of MS-275 may be reduced if it is used in conjunction with another therapeutic medication due to potentiation effects.

According to preclinical research, combining AZ with MS-275 for the treatment of neuroblastoma resulted in considerably

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

greater effects on cell viability, a decrease in the ability of the cancer cells to migrate, and growth inhibitory effects than either medication used alone. Clinical research into combination treatment containing MS-275 has also been conducted, and the results show promise for increasing the overall survival rate and progression-free survival in comparison to the existing medicines that provide treatment for non-small cell lung cancer [33,34].

Use of anti-angiogenesis medications in combination therapy

VEGF (Vascular endothelial growth factor) and its receptor are usually expressed in a variety of cells, but they are markedly elevated in a variety of malignancies, including breast angiosarcoma and bladder carcinoma [35,36].

The VEGF/VEGFR combination is thus the target of several therapeutic treatments. Itraconazole, a regenerated anti-fungal drug, has recently been chosen and tested in clinical trials and has shown encouraging results in inhibiting endothelial cell proliferation and migration as well as inhibiting the activation of VEGFR2 and FGFR3 in vitro and in vivo in non-small cell lung cancer cell lines. Itraconazole and the chemotherapeutic medication pemetrexed were used for the treatment of non-squamous non-small cell lung cancer in phase II clinical study, and the results showed substantial changes in overall survival rates. In HT29 colonic cancer cells, one of the most popular anti-angiogenic drugs, bevacizumab, has been demonstrated to have improved anti-cancer properties when coupled with turmeric ethanolic extract [37,38].

Erlotinib and bevacizumab were utilized as a first-line treatment in phase 2 randomized study for patients with advanced non-squamous non-small-cell lung cancer who had EGFR mutations, and the findings showed encouraging anticancer activity [39].

Adaptive resistance may restrict the effectiveness of single-agent anti-angiogenic drug therapy; however, it can be avoided by the use of combination therapy, as in the case of the neuroblastoma NB1691 cell line, where the inhibition of HIF1alpha by topotecan potentiated the effects of bevacizumab. Oral metronomic topotecan, a topoisomerase inhibitor, and the anti-angiogenic drug pazopanib together prevented tumor development and minimized microvessel formation in neuroblastoma xenografts. Avastin, an anti-angiogenic medication, may potentially enhance chemotherapeutic agents and make cancer cells more susceptible to the lethal effects. Avastin has been found to make cancer cells more susceptible to the cytotoxic effects of metronomic chemotherapy [39,40].

Nonselective toxicity is a frequent adverse effect of chemotherapeutic medicines, claim Staff et al. [45]. Along with cancer cells, this action also eliminates healthy body cells including bone marrow, hair follicles, and cells from other vital organs. It is also possible for the hands and feet's nerve endings or synaptic gaps to be impacted, which can lead to numbness, pain, burning, tingling, sensitivity to cold or heat, or weakening in the limbs.

Drugs	Target	Mode of Action
Doxorubicin/Daunorubicin	DNA, Topoisomerase II	Intercalates between base pairs to bind to DNA and suppresses topoisomerase II activity by keeping the DNA-topoisomerase II complex stable.
Epirubicin	DNA/RNA, Topoisomerase II-a, Chromodomain-helicase-DNA-binding protein 1	It has antimitotic and cytotoxic activity. Inhibits nucleic acid & protein synthesis in many ways. Inhibits DNA helicase activity thus interferes with DNA replication & transcription.
Cisplatin	DNA, DNA-3-methyladenine glycosylase, a-2-macroglobulin, serotransferrin, ATOXI	It's an alkylating agent that adds an alkyl group to DNA bases, preventing DNA and protein synthesis. Forms cross-links in DNA that prevent synthesis or transcription of DNA and induce mutation by mispairing of nucleotides.
Paclitaxel	Tubulin ß-1 chain, Bel-2, microtubule-associated proteins	It's a mitotic inhibitor that interferes with microtubule growth by hyper-stabilization of the structure. Induce apoptosis by inhibiting Bcl-2 activity.
Cyclophosphamide	DNA	Cross-linking and alkylation of DNA prevent DNA synthesis and transcription.

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

Tamoxifen	Estrogen Receptor (ER)	It is a selective estrogen receptor modulator (SERM), which binds to the estrogen receptor (ER) and causes a conformational shift in the receptor, which blocks or alters the production of estrogen-dependent genes in the mammary tissue.
Herceptin/Pertuzumab	Estrogen Receptor (ER)	It's a recombinant humanized IgG1 monoclonal antibody used in protein-based therapies that block the extracellular ligand-binding domain of the HER-2 receptor, subsequently inhibiting HER- 2 mediated signaling cascade.
Gefitinib	Human epidermal growth factor receptor 2 (HER 2)	Inhibits the activity of EGFR tyrosine kinase, subsequently inhibiting the proliferation of malignant cells.
Bevacizumab	Epidermal growth factor receptor	It's a recombinant humanized monoclonal IgG1 antibody that inhibits the activity of human vascular endothelial growth factor by preventing its interaction with VEGFR
Capecitabine	VEGF/VEGFR	It's a prodrug that converts to fluorouracil in cancer cells and inhibits DNA synthesis.
Raloxifene	Thymidylate synthase	Second generation SERM, mode of action is similar to tamoxifen.

Table 1: Drugs commonly used to treat breast cancer, the targets, and mode of action [41].

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

Drugs	Common Side-Effects
Doxorubicin	Cardiotoxicity, infertility, alopecia, nausea and vomiting, low blood count
Daunorubicin	Alopecia, nausea and vomiting, mouth sores, and low blood count; may cause infertility and cognitive heart failure in some cases.
Epirubicin	Increased risk of infectious diseases, hair loss, respiratory problems, and decreased blood count.
Cisplatin	Nausea and vomiting, kidney toxicity, cytotoxicity, and decreased blood count.
Paclitaxel	Alopecia, joint and muscle pains, peripheral neuropathy, nausea, and vomiting.
Cyclophosphamide	Temporary hair loss, nausea and vomiting, poor appetite, discoloration of skin and nails, low blood count and loss of fertility.
Tomaxifen	Cardiotoxicity, respiratory difficulties, abnormal vaginal bleeding, tenderness and numbness in face, hand and legs.
Raloxifen	Hot flashes, flu, joint and muscle pain, rhinitis, and blood clot.
Herceptin/Pertuzumab	Flu-like syndrome, respiratory problems,insomnia, hypersensitivity, cardiotoxicity, peripheral neuropathy,alopecia, low blood count, nausea and vomiting.
Gefitinib	Eye irritation, hypersensitivity, poor appetite, nausea and vomiting, pulmonaryrespiratory problems, liver toxicity.
Bevacizumab	Upper respiratory infection, alopecia, nausea, vomiting, abdominal pain, constipation, nose bleeding, proteinuria, rare cognitive heart failure and nephrotic syndrome.
Capecitabine	Low blood count, risk of infection, hand-foot syndrome, hepatotoxicity, eye irritation, nausea and vomiting, poor appetite and constipation.

Table 2: Commonly prescribed chemotherapeutic medications for the treatment of breast cancer and the adverse effects [41-44].

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

Additionally, according to Galluzzi et al. [46], chemotherapeutic medications can seriously harm immunological and brain cells, making people more susceptible to infectious infections and impairing the cognitive abilities. While some side effects may go away in a few months, others, like infertility, may linger, especially when chemotherapy causes ovaries to become damaged, which can result in menopausal symptoms like hot flashes and vaginal dryness [47].

The use of aromatase inhibitors in adjuvant therapy can also cause early menopause in premenopausal women, which can have an adverse effect on bone density and cause osteopenia or osteoporosis. In addition, long-term damage from chemotherapy can cause heart conditions and lead to cancers such as leukemia or marrow neoplasms as well as secondary cancers [48,49]. Given the high frequency of cardiovascular problems among cancer patients, cardiotoxicity, in particular, is a significant drawback of cancer therapy [50]. As a result, the death rate rises.

According to Pinder et al. analysis, congestive heart failure (CHF) rates were considerably greater in breast cancer patients 65 to 70 years old who underwent adjuvant anthracycline chemotherapy [51]. Similar findings were made by Mitry et al. [52] and Swain et al. [53] discovered that 26% of patients with breast cancer developed CHF after using the commonly used chemotherapy medication doxorubicin. Additionally, it was shown that chemotherapy increased the likelihood of developing various marrow neoplasms or leukemia, with these illnesses appearing in 0.5% of breast cancer patients after a few years of chemotherapy [54]. In the initial years following chemotherapy, there is an increased chance of marrow neoplasm development. Additionally, in some circumstances, patients' natural psychological states may be disturbed by chemotherapy medications [55,56]. Chemotherapeutic medications' inability to target cancer cells specifically is the primary source of the side effects, which adversely affect normal cells and vital organs and reduce the amount of treatment that may be utilized [57]. Drugs for cancer thus have a poor therapeutic index. The hunt for natural substances that suppress cancer cell development without compromising the functioning of healthy cells is one of the most well-liked ways being examined to increase the efficacy of anticancer medications.

Conclusion

Evidence shows that Nigeria had a considerable number of new cancer cases, with breast cancer being the most prevalent. The high incidence and mortality rates of cancer in Africa can be attributed to a lack of awareness and access to screening and treatment facilities. Therefore, there is a need for focused interventions and financial commitments in African nations for cancer prevention, early detection, and treatment. The public's awareness of cancer is improving in Nigeria, and funding for early detection and screening programs is being invested in, along with improved access to treatment and supportive care.

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249. PubMed | CrossRef
2. Alonso R, Piñeros M, Laversanne M, Musetti C, Garau M, Barrios E, Bray F. Lung Cancer Incidence Trends in Uruguay 1990-2014: An Age-Period-Cohort Analysis. Cancer Epidemiol. 2018;55:17-22. PubMed | CrossRef
3. Hunter K, Boyle D, Kavanagh J, Hanhauser Y, Connolly E, O'Keeffe S. Breast Cancer in Women Under 35 Years. BCR. 2015;17:1-3.
4. Wu L, Shi W, Long J, Guo X, Michailidou K, Beesley J, et al. A Transcriptome-Wide Association Study of 229,000 Women Identifies New Candidate Susceptibility Genes for Breast Cancer. Nat genet. 2018;50(7):968-78. PubMed | CrossRef
5. Torre LA, Islami F, Siegel RL, Ward EM, Jemal A. Global Cancer in Women: Burden and Trends. Cancer Epidemiol Biomarkers Prev. 2017;26(4):444-457. PubMed | CrossRef
6. Breen N, Gentleman JF, Schiller JS. Update on Mammography Trends: Comparisons of Rates in 2000, 2005, and 2008. Cancer. 2011;117(10):2209-18. PubMed | CrossRef
7. DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, et al. Breast Cancer Statistics, 2019. CA Cancer J Clin. 2019;69(6):438-451. PubMed | CrossRef
8. Anderson WF, Katki HA, Rosenberg PS. Incidence of Breast Cancer in the United States: Current and Future Trends. J Natl Cancer Inst. 2011;103(18):1397-402. PubMed | CrossRef
9. Anderson WF, Rosenberg PS, Petito L, Katki HA, Ejlertsen B, Ewertz M, et al. Divergent Estrogen Receptor-Positive and Negative Breast Cancer Trends and Etiologic Heterogeneity in Denmark. Int J Cancer. 2013;133(9):2201-6. PubMed | CrossRef
10. Mullooly M, Murphy J, Gierach GL, Walsh PM, Deady S, Barron TI, et al. Divergent Oestrogen Receptor-Specific Breast Cancer Trends in Ireland (2004-2013): Amassing Data from Independent Western Populations Provide Etiologic Clues. Eur J Cancer. 2017;86:326-333. PubMed | CrossRef
11. Mesa-Eguiagaray I, Wild SH, Rosenberg PS, Bird SM, Brewster DH, Hall PS, et al. Distinct Temporal Trends in Breast Cancer Incidence from 1997 to 2016 by Molecular Subtypes: A Population-Based Study of Scottish Cancer Registry Data. Br J Cancer. 2020;123(5):852-859. PubMed | CrossRef
12. Suzuki R, Orsini N, Saji S, Key TJ, Wolk A. Body Weight and Incidence of Breast Cancer Defined by Estrogen and Progesterone Receptor Status--A Meta-Analysis. Int J Cancer. 2009;124(3):698-712. PubMed | CrossRef
13. Gilliland FD, Joste N, Stauber PM, Hunt WC, Rosenberg R, Redlich G, et al. Biologic Characteristics of Interval and Screen-Detected Breast Cancers. J Natl Cancer Inst. 2000;92(9):743-9. PubMed | CrossRef
14. Bray F, McCarron P, Parkin DM. The Changing Global Patterns of Female Breast Cancer Incidence and Mortality. Breast Cancer Res. 2004;6(6):229-39. PubMed | CrossRef
15. Joko-Fru WY, Jedy-Agba E, Korir A, Ogunbiyi O, Dzamalala CP, Chokunonga E, et al. The Evolving Epidemic of Breast Cancer in Sub-Saharan Africa: Results from the African Cancer Registry Network. Int J Cancer. 2020;147(8):2131-2141. PubMed | CrossRef
16. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global Surveillance of Trends in Cancer Survival 2000-14 (CONCORD-3): Analysis of Individual Records for 37 513 025 Patients Diagnosed with One of 18 Cancers from 322 Population-Based Registries in 71 Countries. Lancet. 2018;391(10125):1023-1075. PubMed | CrossRef
17. Ngan TT, Nguyen NTQ, Van Minh H, Donnelly M, O'Neill C. Effectiveness of Clinical Breast Examination as a 'Stand-Alone' Screening Modality: An Overview of Systematic Reviews. BMC Cancer. 2020;20(1):1070. PubMed | CrossRef
18. Mu L, Liu L, Niu R, Zhao B, Shi J, Li Y, et al. Indoor Air Pollution and Risk of Lung Cancer among Chinese Female Non-Smokers. Cancer Causes Control. 2013;24(3):439-50. PubMed | CrossRef

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

19. Turner MC, Andersen ZJ, Baccarelli A, Diver WR, Gapstur SM, Pope CA 3rd, et al. Outdoor Air Pollution and Cancer: An Overview of the Current Evidence and Public Health Recommendations. CA Cancer J Clin. 2020;10.3322/caac.21632. PubMed | CrossRef
20. Parkin DM, Bray FI, Devesa SS. Cancer Burden in the Year 2000. The Global Picture. Eur J Cancer. 2001;37 Suppl 8:S4-66. PubMed | CrossRef
21. Arnold M, Abnet CC, Neale RE, Vignat J, Giovannucci EL, McGlynn KA, et al. Global Burden of 5 Major Types of Gastrointestinal Cancer. Gastroenterology. 2020;159(1):335-349.e15. PubMed | CrossRef
22. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, et al. Colorectal Cancer Statistics, 2020. CA Cancer J Clin. 2020;70(3):145-164. PubMed | CrossRef
23. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of Incidence and Mortality of Cervical Cancer in 2018: A Worldwide Analysis. Lancet Glob Health. 2020;8(2):e191-e203. PubMed | CrossRef
24. Sharma R, Aashima, Nanda M, Fronterre C, Sewagudde P, Ssentongo AE, et al. Mapping Cancer in Africa: A Comprehensive and Comparable Characterization of 34 Cancer Types Using Estimates From GLOBOCAN 2020. Front Public Health. 2022;10:839835. PubMed | CrossRef
25. Fulda S, Debatin KM. Extrinsic Versus Intrinsic Apoptosis Pathways in Anticancer Chemotherapy. Oncogene. 2006;25(34):4798-811. PubMed | CrossRef
26. Maeda H. Nitroglycerin enhances vascular blood flow and drug delivery in hypoxic tumor tissues: analogy between angina pectoris and solid tumors and enhancement of the EPR effect. J Control Release. 2010;142(3):296-8. PubMed | CrossRef
27. Zhen H, Sun Q, Zhang M, Wu G, Chen X, Chen C, et al. Efficacy and Safety of Nitroglycerin Combined with Chemotherapy in the Elderly Patients with Advanced Non-Small Cell Lung Cancer Complicated with Coronary Heart Disease. J Clin Experimental Med. 2016;9:1-7.
28. Yasuda H, Yamaya M, Nakayama K, Sasaki T, Ebihara S, Kanda A, et al. Randomized Phase II Trial Comparing Nitroglycerin Plus Vinorelbine and Cisplatin with Vinorelbine and Cisplatin Alone in Previously Untreated Stage IIIB/IV Non-Small-Cell Lung Cancer. J Clin Oncol. 2006;24(4):688-94. PubMed | CrossRef
29. Gojo I, Jiemjit A, Trepel JB, Sparreboom A, Figg WD, Rollins S, et al. Phase 1 and Pharmacologic Study of MS-275, A Histone Deacetylase Inhibitor, in Adults with Refractory and Relapsed Acute Leukemias. Blood. 2007;109(7):2781-90. PubMed | CrossRef
30. Ropero S, Esteller M. The Role of Histone Deacetylases (HDACs) in Human Cancer. Mol Oncol. 2007;1(1):19-25. PubMed | CrossRef
31. Kummar S, Gutierrez M, Gardner ER, Donovan E, Hwang K, Chung EJ, et al. Phase I Trial of MS-275, A Histone Deacetylase Inhibitor, Administered Weekly in Refractory Solid Tumors and Lymphoid Malignancies. Clin Cancer Res. 2007;13(18 Pt 1):5411-7. PubMed | CrossRef
32. Gryder BE, Sodji QH, Oyelere AK. Targeted Cancer Therapy: Giving Histone Deacetylase Inhibitors All They Need to Succeed. Future Med Chem. 2012;4(4):505-24. PubMed | Crossref
33. Juergens RA, Wrangle J, Vendetti FP, Murphy SC, Zhao M, Coleman B, et al. Combination Epigenetic Therapy has Efficacy in Patients with Refractory Advanced Non-Small Cell Lung Cancer. Cancer Discov. 2011 Dec;1(7):598-607. PubMed | Crossref
34. Cetin K, Ettinger DS, Hei YJ, O'Malley CD. Survival by Histologic Subtype in Stage IV Nonsmall Cell Lung Cancer Based on Data from the Surveillance, Epidemiology and End Results Program. Clin Epidemiol. 2011;3:139-48. PubMed | Crossref
35. Wu W, Shu X, Hovsepyan H, Mosteller RD, Broek D. VEGF Receptor Expression and Signaling in Human Bladder Tumors. Oncogene. 2003;22(22):3361-70. PubMed | Crossref
36. Silva E, Gatalica Z, Vranic S, Basu G, Reddy SK, Voss A. Refractory Angiosarcoma of the Breast with VEGFR2 Upregulation Successfully Treated with Sunitinib. Breast J. 2015;21(2):205-7. PubMed | CrossRef
37. Rudin CM, Brahmer JR, Juergens RA, Hann CL, Ettinger DS, Sebree R, et al. Phase 2 Study of Pemetrexed and Itraconazole as Second-Line Therapy for Metastatic Nonsquamous Non-Small-Cell Lung Cancer. J Thorac Oncol. 2013;8(5):619-23. PubMed | CrossRef

Citation: Obafemi FA, Umahi-Ottah G. A Review of Global Cancer Prevalence and Therapy. J Cancer Res Treat Prev. 2023;1(3):128-147.
DOI: https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011

38. Tsubamoto H, Sonoda T, Ikuta S, Tani S, Inoue K, Yamanaka N. Combination Chemotherapy with Itraconazole for Treating Metastatic Pancreatic Cancer in the Second-line or Additional Setting. Anticancer Res. 2015;35(7):4191-6. PubMed
39. Seto T, Kato T, Nishio M, Goto K, Atagi S, Hosomi Y, et al. Erlotinib Alone or with Bevacizumab as First-Line Therapy in Patients with Advanced Non-Squamous Non-Small-Cell Lung Cancer Harbouring EGFR Mutations (JO25567): An Open-Label, Randomised, Multicentre, Phase 2 Study. Lancet Oncol. 2014;15(11):1236-44. PubMed | CrossRef
40. Blagosklonny MV. How Avastin Potentiates Chemotherapeutic Drugs: Action and Reaction in Antiangiogenic Therapy. Cancer Biol Ther. 2005;4(12):1307-10. PubMed | CrossRef
41. Lo EJ. Drug Bank 5.0: A Major Update to the Drug Bank Database for 2018. Nucleic Acids Res. 2017.
42. Shapiro CL, Recht A. Side Effects of Adjuvant Treatment of Breast Cancer. N Engl J Med. 2001;344(26):1997-2008. PubMed | CrossRef
43. Partridge AH, Burstein HJ, Winer EP. Side Effects of Chemotherapy and Combined Chemohormonal Therapy in Women with Early-Stage Breast Cancer. J Natl Cancer Inst Monogr. 2001;(30):135-42. PubMed | CrossRef
44. Tao JJ, Visvanathan K, Wolff AC. Long Term Side Effects of Adjuvant Chemotherapy in Patients with Early Breast Cancer. Breast. 2015;24 Suppl 2(0 2):S149-53. PubMed | CrossRef
45. Staff NP, Grisold A, Grisold W, Windebank AJ. Chemotherapy-Induced Peripheral Neuropathy: A Current Review. Ann Neurol. 2017;81(6):772-781. PubMed | CrossRef
46. Galluzzi L, Buqué A, Kepp O, Zitvogel L, Kroemer G. Immunogenic Cell Death in Cancer and Infectious Disease. Nat Rev Immunol. 2017;17(2):97-111. PubMed | CrossRef
47. Blumenfeld Z. Chemotherapy and Fertility. Best Pract Res Clin Obstet Gynaecol. 2012;26(3):379-90. PubMed | CrossRef
48. Chang HM, Moudgil R, Scarabelli T, Okwuosa TM, Yeh ET. Cardiovascular Complications of Cancer Therapy: Best Practices in Diagnosis, Prevention, and Management: part 1. J Am College Cardiol. 2017;70(20):2536-51. PubMed | CrossRef
49. Keilani M, Hasenoehrl T, Neubauer M, Crevenna R. Resistance Exercise and Secondary Lymphedema in Breast Cancer Survivors—A Systematic Review. Support Care Cancer. 2016;24:1907-16. PubMed | CrossRef
50. Fadol A P. Management of Chemotherapy-Induced Left Ventricular Dysfunction and Heart Failure in Patients with Cancer while Undergoing Cancer Treatment: The MD Anderson practice. Frontiers in Cardio Med. 2018;5:1-5.
51. Pinder MC, Duan Z, Goodwin JS, Hortobagyi GN, Giordano SH. Congestive Heart Failure in Older Women Treated with Adjuvant Anthracycline Chemotherapy for Breast Cancer. J Clini Onco. 2007;25(25):3808-15. PubMed | CrossRef
52. Mitry MA, Edwards JG. Doxorubicin-Induced Heart Failure: Phenotype and Molecular Mechanisms. Int J Cardiol Heart Vasc. 2016;10:17-24.. PubMed | CrossRef
53. Swain SM, Whaley FS, Ewer MS. Congestive Heart Failure in Patients Treated with Doxorubicin: A Retrospective Analysis of Three Trials. Cancer. 2003;97(11):2869-79. PubMed | CrossRef
54. Wolff AC, Blackford AL, Visvanathan K, Rugo HS, Moy B, Goldstein LJ, et al. Risk of Marrow Neoplasms after Adjuvant Breast Cancer Therapy: The National Comprehensive Cancer Network Experience. J Clin Oncol. 2015;33(4):340-8. PubMed | CrossRef
55. Ahmad SS, Reinius MA, Hatcher HM, Ajithkumar TV. Anticancer Chemotherapy in Teenagers and Young Adults: Managing Long Term Side Effects. BMJ. 2016;354:i4567. PubMed | CrossRef
56. Huang WY, Cai YZ, Zhang Y. Natural Phenolic Compounds from Medicinal Herbs and Dietary Plants: Potential Use for Cancer Prevention. Nutr Cancer. 2010;62(1):1-20. PubMed | CrossRef
57. Weinberg SE, Chandel NS. Targeting Mitochondria Metabolism for Cancer Therapy. Nat Chem Biol. 2015;11(1):9-15. PubMed | CrossRef