



[A dissertation submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Dhaka in partial fulfillment of the requirements for the degree of Masters of Pharmacy]

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APPROVAL

This thesis paper, “**An extensive literature review of on breast cancer treatment, diagnosis current status, and future perspective**” submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Masters of Pharmacy and approved as to its style and contents.

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Declaration

I am Md. Shahiduzzaman Miah , hereby declare that, this thesis is done by me under the supervision of Dr. Sharifa Sultana, Associate professor & Associate Head, Department of Pharmacy, Daffodil International University, in impartial fulfillment of the requirements for degree of Masters of Pharmacy. I am also declaring that the results embodied in this project have not been submitted to any other university or institute for the award of any degree.

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“Dedication”

Dedicated To,
My family, my supervisor, my teachers, friends.

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Abstract

Breast cancer is a condition in which the tissues of the breast become excessively enormous. There are various forms of breast cancer. The sort of breast cancer is decided by which cells in the breast become malignant. There are a number of possible origins for breast cancer. Reading the relevant literature is an integral part of this investigation. For this analysis, we go through around 150 publications. The gender gap in the incidence of breast cancer is the focus of my research. Only 12% of women will get breast cancer, whereas 1% of males will. Several aspects of breast cancer and related variables were explored in this article. Breast cancer was shown to be one of the most common and rapidly increasing malignant illnesses among Iranian women during the last four decades. Relevant data for this article was gathered through a search of reputable scientific databases like SID, Google Scholar, and the Comprehensive Portal of Human Sciences using the following keywords: cancer, breast cancer, cell, gene, life quality, women, prevalence, productivity, age, obesity, alcohol, cigarettes, menopause, genetic, Cytokine, and mortality. All facets of a woman's life, both within and outside the home, are negatively impacted by this illness. However, things like having a strong social network and a supportive family amid a health crisis might lessen the impact of the condition. However, risk factors have been discovered despite the fact that the [precise] cause of breast cancer remains unclear. Breast cancer risk factors include age, family history of the disease, alterations in one or both breasts, altered genes, reproductive and menopausal history, inactivity, excess body fat, poor diet, lack of exercise, genetic predisposition, and exposure to radiation in the chest.

Keywords: Cancer, breast cancer, prevalence, treatment, and diagnosis.

CHAPTER ONE

INTRODUCTION

1.1. Introduction

Cancer refers to a group of diseases characterized by abnormal cell growth that has the potential to invade other parts of the body or to spread from its original location. [1] In contrast, benign tumors do not metastasize to other parts of the body. The presence of a lump, abnormal bleeding, a persistent cough, unexplained weight loss, and a change in bowel movements are some of the possible indications and symptoms. [2- 4]. Although these symptoms might point to cancer, there are other possible explanations for why they are occurring. People are affected by more than 100 different kinds of tumors. The use of tobacco products is responsible for around 22 percent of all deaths caused by cancer. Another 10% may be attributed to unhealthy lifestyle factors such as being overweight, eating poorly, not getting enough exercise, or drinking too much alcohol. [5-8] A number of diseases, as well as exposure to ionizing radiation and environmental toxins, are additional causes for worry. Diseases such as *Helicobacter pylori*, hepatitis B, hepatitis C, human papillomavirus infection, Epstein–Barr virus, and human immunodeficiency virus (HIV) are responsible for 15% of all cancers that occur in the developing world. This percentage is higher than in the developed world (HIV). These factors, at least in part, exert their influence via altering the genes contained inside a cell.

Typically, several genetic alterations are necessary before cancer occurs. [9] Approximately 5–10 percent of malignancies are linked to inherited genetic abnormalities. [10] Cancer may be recognized by specific signs and symptoms or screening tests. After this, a medical imaging test and a biopsy are often used to confirm the diagnosis. [11]

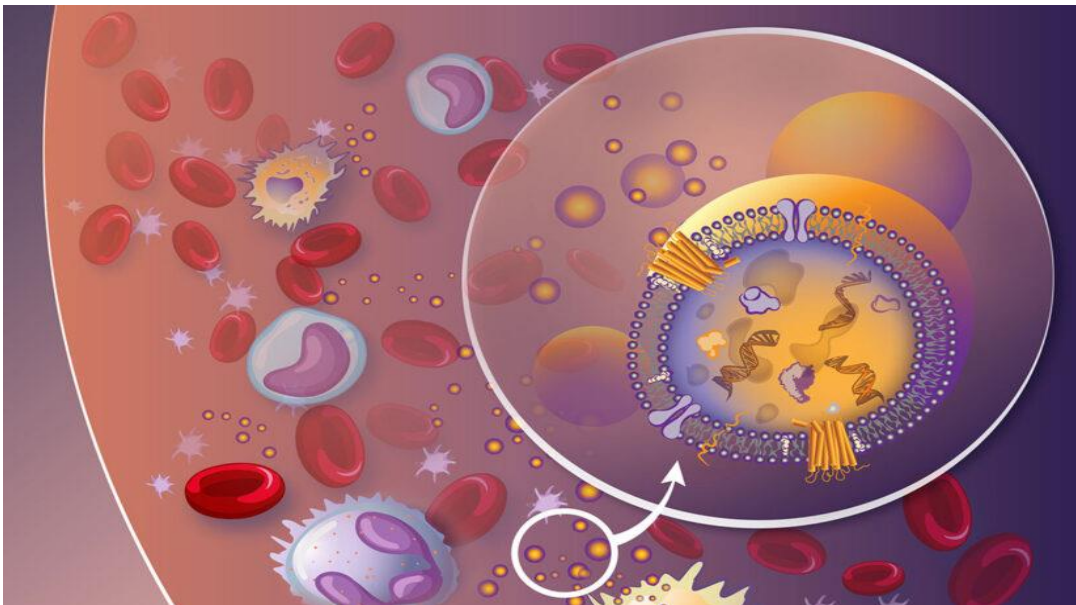


Figure 1.: Cancer metastasis

Anyone can lower your risk of developing certain cancers by not smoking, maintaining a healthy weight, drinking alcohol in moderation, eating plenty of vegetables, fruits, and whole grains, getting vaccinated against certain infectious diseases, reducing the amount of processed meat and red meat you eat, and spending less time in direct sunlight. These are all things that can help you prevent cancer. [12-13] Screening procedures that enable an early diagnosis are beneficial in the treatment of both cervical and colorectal cancers. [14] The question of whether or not breast cancer screening is beneficial has been the subject of some discussion. [14-15] Surgery, radiation therapy, chemotherapy, and targeted therapy are some examples of the various treatment modalities that are frequently combined in the fight against cancer. The alleviation of pain and any and all other symptoms must be a primary focus during treatment. Patients who are in the later stages of their illness reap the greatest benefits from palliative care treatment. The type of cancer a patient has as well as the stage of the disease at the beginning of treatment both play a role in determining how likely they are to survive. The five-year survival rate for children under the age of 15 at the time of diagnosis is typically around 80 percent in countries that are prosperous. [16] When looking at cancer survival rates over a span of five years, the overall survival rate in the United States is 66 percent. Approximately 90.5 million people across the globe were given a cancer diagnosis in the year 2015. [17] The number of people who are newly diagnosed with cancer each year reached 23.6 million in 2019, while the number of people who passed away as a direct result of the disease reached 10 million. These numbers point to increases of 26% and 21%, respectively, over the course of the previous decade. [18] The most common types of cancer in men are lung cancer, colorectal cancer, stomach cancer, and cancer of the prostate. [19] The four types of cancer that affect females the most frequently are breast cancer, colorectal cancer, lung cancer, and cervical cancer. It is estimated that if skin cancers other than melanoma were included in the annual total of newly diagnosed cases of cancer, skin cancer would account for somewhere in the neighborhood of forty percent of instances. [20-21] The types of cancer that are most common in children are acute lymphoblastic leukemia and brain tumors, with the exception of Africa, which has a higher incidence of non-Hodgkin lymphoma. Both of these cancers can be fatal. There were approximately 165,000 new cases of cancer diagnosed in children under the age of 15 in the United States in 2012. The risk of developing cancer dramatically increases as one gets older, and industrialized countries have a significantly higher incidence of many different types of cancer. The rates are climbing due to the fact that

more people are surviving to a ripe old age and also due to changes in lifestyle that are taking place in developing nations. [22] It was estimated that the costs associated with cancer in the year 2010 amounted to a total of 1.16 trillion USD annually.

1.2 History

Since the dawn of human history, cancer has always been a part of it. The Edwin Smith Papyrus, which was written in Egypt about 1600 B.C. and includes the first known written reference to the condition, discusses breast cancer. This papyrus is the oldest known written reference to the disease. Hippocrates, a physician who lived from 460 BC to 370 BC, is credited with being the first person to define many types of cancer. These tumors were referred to by him using the Greek name o Karakinos, which may be translated as either crab or crayfish [24]. It is possible that the origin of this term can be traced back to the appearance of the sliced surface of a solid malignant tumor: "the veins are spread on all sides like the animal the crab has its feet, which is where it gets its name." [C]ause the veins are spread on all sides like the animal the crab has its feet, [C]ause the veins are spread on all sides like [25] According to Galen, "cancer of the breast is so termed because of the supposed similarity to a crab provided by the lateral prolongations of the tumor and the nearby swollen veins." This resemblance was thought to be caused by the presence of distended veins close to the tumor. To put it another way, the look of a crab is created by the lateral prolongations of the tumor as well as the nearby veins that have expanded. [26]: Celsus, a physician who lived between around 25 BC and 50 AD, proposed the use of surgery as a treatment for cancer in the year 738. He converted the Greek term "Karakinos" into the Latin word "cancer," which may alternatively be rendered as "crab." Galen, a physician who flourished during the second century AD, was a staunch opponent of the procedure of surgery and instead supported the use of purgatives. Over the course of the last one thousand years, these recommendations have, for the most part, been adhered to. It wasn't until the 15th, 16th, and 17th centuries that it became standard procedure for medical personnel to dissect dead bodies in order to ascertain the reason of death. Prior to that time, autopsies were the only way to determine the cause of death. [26] Wilhelm Fabry, a professor in Germany, was under the assumption that breast cancer was caused by a milk clot that developed in a mammary duct. Fabry came to this conclusion after years of research. Francois de la Boe Sylvius, a Dutch philosopher and follower of Descartes, believed that all illness was the product of chemical processes and that cancer was caused by acidic lymph fluid. He also believed that chemical processes were the cause of all disease. Sylvius was certain that an acidic lymph fluid was the root of the cancerous condition. Nicolaes Tulp, a contemporaries of his who lived during the same time period, believed that cancer was a toxin that spread slowly and came to the conclusion that it was infectious. He also believed that cancer was caused by an infectious agent. [27] In the year 1761, a doctor by the name of John Hill discovered that tobacco snuff was the factor that led to the development of nose cancer. [28] The following year, in 1775, a British physician by the name of Percivall Pott published a paper in which he stated that chimney sweeps' carcinoma,

also known as cancer of the scrotum, was a condition that was common among chimney sweeps. [29] It wasn't until the 18th century that the microscope was put to widespread use, and it wasn't until then that it was discovered that the so-called "cancer poison" traveled from the primary tumor to other locations via the lymph nodes. This discovery was a significant step in the fight against cancer. An event that occurred between the years 1871 and 1874. He was an English physician by the name of Campbell De Morgan who was the first person to put forward this theory regarding the illness [30].

1.3 Epidemiology

According to current estimates, there will be 18.1 million new cancer diagnoses and 9.6 million cancer-related deaths in the world in 2018. One in every two men and one in every seventeen women will get cancer at some point in their lives, and one in every thirteen men and one in every nine women will die from it. Non-melanoma skin cancers and other non-invasive cancers accounted for roughly 12.7% of all cancer diagnoses in 2008; 7.98 million individuals died from cancer in 2010. [201] Around 16% of fatalities are caused by cancer. Lung cancer (1.76 million fatalities in 2018), colorectal cancer (860,000), stomach cancer (780,000), liver cancer (780,000), and breast cancer (780,000) are the most prevalent types of cancer deaths worldwide (620,000). As a result, invasive cancer is the top cause of death in the developed world and the second-leading cause in the developing world, respectively. In the underdeveloped world, more than half of all instances occur. In 1990, 5.8 million people died from cancer. [30] Longer life spans and lifestyle changes in the developing world are to blame for the rise in deaths. Age is by far the greatest contributor to the development of cancer. A majority of people with aggressive cancer are in their sixties and seventies. "If we lived long enough, sooner or later we all would acquire cancer," says cancer expert Robert A. Weinberg. Several factors, including immunosenescence, mistakes in DNA that accumulate over time, and changes in the endocrine system, have been linked to an increased risk of cancer as we age. [31] Because of the influence of DNA damage and inflammation as well as variables like vascular aging and endocrine alterations on cancer, aging has a mixed impact on cancer. [32] While slow-growing tumors are more frequent, the disease is not always lethal. In Europe and Asia, autopsy studies have shown that up to 36% of individuals die with untreated and seemingly innocuous thyroid cancer, and that up to 80% of males get prostate cancer by the time they reach the age of 80. [33-34] Overdiagnosis of these tumors would have been a waste of time and money, since they do not cause mortality. Leukemia, brain tumors, and lymphomas are the three most frequent pediatric malignancies (12 percent). About 1 in 285 children in the United States is diagnosed with cancer. Children's cancer rates rose by 0.6 percent per year in the United States from 1975 to 2002 and by 1.1 percent per year in Europe from 1978 to 1997. Deaths from juvenile cancer in the United States have fallen by half since 1975. [35]

1.4 Signs and symptoms

Initially, cancer does not cause any symptoms. An increasing or ulcerating tumor causes symptoms and signs. The kind and location of the malignancy determine the results. There are very few symptoms that can be pinpointed. Many of these symptoms are more common in people with underlying health issues. As a "great imitator," cancer might be difficult to detect. [36] Following a diagnosis, some people may experience anxiety or depression. Suicide is more than twice as common among cancer patients. [37]

1.5 Local symptoms

The tumor's bulk or ulceration may cause local symptoms. If a person has lung cancer, their lungs may become narrowed, causing coughing and pneumonia; esophageal cancer can cause a person to choke or have difficulty swallowing; colorectal cancer can cause a person's bowels to become narrowed or blocked, changing their bowel patterns. Lumps in the breasts or the testicles may be indicative of a mass. Symptoms such as spitting up blood (lung cancer), anemia or rectal bleeding (colon cancer), blood in the urine (bladder cancer), or irregular vaginal bleeding might be caused by ulceration (endometrial or cervical cancer). Although advanced cancer might cause regional discomfort, the tumor itself is typically painless. It's possible that some types of cancer may cause fluid to accumulate in the chest or belly. [36]

1.6 Systemic symptoms

In certain cases, the body's reaction to cancer might cause systemic symptoms to appear. Fatigue, unintended weight loss, and changes in the appearance of the skin are all examples of this. [37] In certain malignancies, a chronic inflammatory condition known as cachexia may result in muscle loss and weakness. [38] There are a number of malignancies, including Hodgkin's disease and leukemias, that may induce a persistent fever. [30] The term "paraneoplastic syndromes" refers to conditions in which the cancer's own hormones or other substances are the source of systemic symptoms. Some of the more common paraneoplastic symptoms are hypercalcemia, which may induce mental confusion, constipation and dehydration; and hyponatremia, which can result in nausea, vomiting, migraines, or epilepsy. [39]

1.7 Metastasis

The spread of cancer to other parts of the body is known as metastasis. It is known as a metastatic tumor if it spreads to other parts of the body. Most malignancies have the potential to spread to other parts of the body. In most cases, the cancer has spread to other parts of the body. Late-stage cancer patients often have metastasis, which may spread via the bloodstream, the lymphatic system, or both. The normal phases in metastasis include local invasion, intravasation into the blood or lymph, circulation across the body, extravasation into the new tissue, proliferation and angiogenesis. Different forms of cancer tend to spread to

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specific organs, although the lungs, liver, brain, and bones are the most frequent sites of metastasis. [40]

1.8 Cause of cancer

Mutations, also known as alterations to the DNA in your cells, are considered to be the primary cause of cancer. It is possible to inherit genetic mutations. The effects of environmental factors might also manifest themselves after delivery in certain cases. These exogenous factors, often known as carcinogens, might include the following: carcinogens that are present in the environment, such as ultraviolet and radiation (UV) cigarette smoke, asbestos, alcohol, air pollution, tainted food and drinking water, and other mild chemical carcinogens may all lead to cancer. Biological toxins such as viruses, bacteria, and parasites may cause cancer. According to WHO Trusted Source, smoking, drinking alcohol, having a high body mass index (BMI), eating a diet low in fruits and vegetables, and not getting enough exercise might be responsible for around 33 percent of all deaths caused by cancer. [41-42]

1.9 Diagnosis

The majority of cancers are first identified either because of the manifestation of certain signs or symptoms, or via the use of screening procedures. The only way to arrive at a conclusive diagnosis is for a pathologist to analyze a sample of tissue, which is not possible with any of these methods. Medical tests are performed on patients whose conditions raise concerns about the presence of malignancy. Blood tests, X-rays, computed tomography (CT) scans with contrast, and endoscopies are typical examples of these. The tissue diagnosis obtained from the biopsy provides information on the kind of cell that is replicating itself, as well as its histological grade, genetic abnormalities, and other characteristics. When taken together, these pieces of information are helpful in determining the prognosis and selecting the appropriate course of therapy. There are further tests performed on tissue samples known as cytogenetics and immunohistochemistry. These tests offer information on molecular changes (such as mutations, fusion genes, and numerical chromosomal changes), and as a result, they may also predict the prognosis and the therapy that will be most effective. A diagnosis of cancer may lead individuals to experience emotional distress, however psychosocial therapies like talking therapy may be able to help people cope with this. [43]

1.10 Types of cancer

Even if they have spread to other areas of the body, cancers are given their names based on the part of the body in which they first appear and the sort of cells that compose them. For instance, a cancer that initially develops in the lungs but later spreads to the liver is still referred to as lung cancer. There are also a number of clinical names that are used to refer to various forms of cancer in general, including:

Different types of cancer name

- Breast cancer
- esophageal cancer

- cervical cancer
- appendix cancer
- bladder cancer
- bone cancer
- brain cancer
- Carcinoma
- Sarcoma vessels.
- Lymphoma.
- small intestine cancer
- spleen cancer
- stomach or gastric cancer
- testicular cancer
- thyroid cancer
- uterine cancer
- heart cancer
- gallbladder cancer
- kidney or renal cancer
- leukemia
- liver cancer
- lung cancer
- lymphoma
- mesothelioma
- myeloma
- oral cancers
- ovarian cancer
- pancreatic cancer
- prostate cancer

Details discussion about different types of cancer

1.11 Appendix cancer

Cancer of the vermiform appendix, more often referred to as appendix cancer, is an exceptionally rare form of the disease. The term "gastrointestinal stromal tumors" refers to uncommon tumors that have the potential to become malignant. The appendix carries the risk of developing a primary lymphoma at some point in one's lifetime. Metastases may be caused by cancers such as breast cancer, colon cancer, and malignancies of the female genital tract if they travel to the appendix and cause it to become infected. The results of a recent study indicate that the incidence of primary malignancies in the United States is around 0.12 cases per 1,000,000 individuals per year. [Citation needed] [Citation needed] Carcinoids that did not fulfill the requirements to be classified as malignant were omitted from this study. Carcinoid is found in around one out of every 300–400 appendectomies that are done for acute appendicitis [44].

According to a review of the scientific literature that included 4765 people who had been diagnosed with appendiceal cancer, it was found that the incidences of appendiceal cancer have increased over the past several decades. This trend was found to be true regardless of the type of tumor, the patient's age, gender, or the stage of appendiceal cancer. Metastases were found in around 75% of the appendiceal cases that were included in the research. These metastases had many different forms. There haven't been any clear patterns that can be used to

explain why this expansion is taking place, and there aren't any signs of one emerging either. There has been a rise in the usage of computed tomography imaging in emergency departments since the early 1990s. This has made it feasible for detection to take place before surgery can take place. One of the explanations that has been offered is this one. [45]

1.12 Bladder cancer

There are various subtypes of cancer that begin in the tissues of the urinary bladder, and the term "cancer of the urine bladder" may apply to any one of these multiple subtypes. Symptoms include blood in the urine, discomfort while urinating, and pain in the lower back. Additionally, there may be blood in the urine. This illness may be brought on by the transformation into malignant cells of the epithelial cells that line the bladder. Risk factors for bladder cancer include smoking, having a family history of the illness, having previously had radiation therapy, suffering from recurring bladder infections, and being exposed to certain chemicals. The most common kind of the illness is referred to as transitional cell carcinoma. There are two other kinds of cancer known as squamous cell carcinoma and adenocarcinoma. The diagnosis is often made by the use of a cystoscopy in conjunction with tissue samples. The transurethral resection and medical imaging are the two procedures that are utilized to stage the malignancy. Transurethral resection is the more common of the two. [46-47] The various treatment choices are dependent upon the stage the illness is currently in. It is possible that the treatment will consist of a combination of other methods, such as chemotherapy, radiation therapy, immunotherapy, and surgery. Some of the surgical techniques that may be an option are urinary diversion, bladder removal in part or in its whole, and transurethral resection. In comparison, the survival rate in Canada is 75 percent and the survival rate in Europe is 68 percent after a period of five years, while it is 77 percent in the United States. [48-49] As of the year 2018, bladder cancer has affected around 1.6 million people throughout the world, with 549,000 new cases being diagnosed and 200,000 people losing their lives to the disease. Symptoms often begin to manifest themselves for the first time anywhere between the ages of 65 and 84 on average. The likelihood of the condition affecting a man is much higher than that of a woman. The incidence of bladder cancer was highest in Southern and Western Europe in 2018, followed by the United States of America with rates of 15, 13, and 12 cases per 100,000 persons respectively. The regions of Northern Africa and Western Asia had the highest mortality rate due to bladder cancer, followed by the regions of Southern Europe with the second highest mortality rate. [50]

1.13 Brain cancer

If abnormal cells start to proliferate inside of the brain, this might result in the formation of a brain tumor. There are two major types of tumors that may grow anywhere in the body: malignant tumors and benign (non-

cancerous) tumors. These can be further categorized as primary tumors, which originate within the brain, and secondary tumors, which most commonly have spread from tumors located outside the brain and are referred to as brain metastasis tumors. Primary tumors begin within the brain, whereas secondary tumors spread from tumors located outside the brain. Primary tumors are those that originate inside the brain, while secondary tumors are those that spread from tumors that are situated outside of the brain. Any kind of brain tumor has the potential to produce a broad range of symptoms, which change depending on the size of the tumor and the area of the brain that it is affecting. In the event that symptoms are present, they may consist of things like migraines, seizures, difficulty with eyesight, vomiting, and mental disturbances.

[51]

Other symptoms may include difficulty walking or speaking, difficulty coping with emotions, or even difficulty falling asleep.

The majority of brain tumors have yet to have a definitive etiology identified. Exposure to vinyl chloride, infection with the Epstein–Barr virus, ionizing radiation, and inherited illnesses such as neurofibromatosis, tuberous sclerosis, and von Hippel–Lindau syndrome are all uncommon risk factors that have been linked to ovarian cancer. According to the findings of the research done on the subject, using a mobile phone does not seem to pose any evident health risks. Meningiomas, which are almost always noncancerous, and astrocytomas, which may include glioblastomas, are the two types of primary tumors that are diagnosed most often in people. Malignant medulloblastoma is the form of this illness that is diagnosed in the majority of youngsters. The traditional technique of diagnosis involves a consultation with a medical practitioner, as well as the use of computed tomography (CT) or magnetic resonance imaging (MRI) (MRI). After that, a biopsy is often carried out so that the results may be confirmed. The findings allowed for the tumors to be placed into a number of different severity categories when compared to one another. Surgery, radiation therapy, or chemotherapy, or any combination of these three, could be part of the treatment plan. It is possible that the tumor will return after surgery since the brain is the only organ in the body that cannot be replaced. It is possible that anticonvulsant medication will be necessary in the event that seizures occur. Dexamethasone and furosemide are two examples of potential medications that might help reduce the edema that is present in the region around the tumor. Because the growth of certain tumors is gradual and consistent, it is sufficient to just keep an eye on them; in other cases, they may not even need any further therapy at all. Treatments that take advantage of a person's immune system are the subject of active research at this time. The prognosis for individuals who have been diagnosed with malignant tumors may vary greatly depending on the kind of tumor as well as the degree to which it has already spread at the time of diagnosis. Even though benign tumors only form in one part of the body, depending on how large they are and where they are situated, they may still

constitute a threat to the patient's life. [52] The prognosis for malignant glioblastomas is often fairly bleak, but the prognosis for benign meningiomas is frequently more optimistic. In the United States, after five years, the overall survival percentage for individuals who have been diagnosed with malignant brain cancer is around 33 percent. The occurrence of secondary brain cancers, which are often referred to as metastatic brain tumors, is about four times that of primary brain cancers [53], and lung cancer is the source of over half of all metastases. Primary brain tumors are detected in around 250,000 people annually throughout the globe; however, this represents a far lower percentage of all cancers. Among children under the age of 15 who are diagnosed with cancer, the incidence of brain tumors is only surpassed by the incidence of acute lymphoblastic leukemia in terms of its prevalence. [54] In Australia, the cost of treating brain cancer over the course of a patient's lifetime is estimated to be an average of \$1.9 million, making it the kind of cancer with the biggest economic burden. [55]

1.14 Liver cancer

Hepatocellular carcinoma is a subtype of hepatocellular carcinoma, which affects the liver (also known as primary hepatic cancer or primary hepatic malignancy). Primary liver cancer is cancer that originates in the liver, while secondary liver cancer is cancer that develops elsewhere in the body (meaning cancer which has spread from elsewhere to the liver, known as liver metastasis). There are an excessive number of liver metastases in comparison to the number of liver metastases. Cancer of the liver is increasing at an alarming rate all over the globe. [56-57] It is the sixth most prevalent kind of cancer overall and the fourth most frequent cause of death from cancer everywhere in the globe. [58] In the year 2018, it had an impact on 841,000 people and was responsible for the deaths of 782,000 people all over the globe. The viruses that cause hepatitis B and C are more common in regions of Asia and sub-Saharan Africa that also have higher rates of liver cancer.

Hepatocellular carcinoma, often known as HCC, affects males more frequently than it does women. The highest prevalence of the disease is seen in patients between the ages of 55 and 65. The most prevalent cause of liver cancer is cirrhosis, which may be brought on by hepatitis B, hepatitis C, or alcohol use. Other potential reasons include exposure to aflatoxin, non-alcoholic fatty liver disease, and liver flukes. Both hepatocellular carcinoma (HCC), which accounts for the majority of cases (80%), and intrahepatic cholangiocarcinoma are the most common types. Imaging tests, blood examinations, and tissue samples might all be used to help confirm the diagnosis. Due to the fact that there are so many possible causes of liver cancer, there are also various techniques to prevent getting the condition. In addition, these initiatives include the development of a vaccine and treatment for the hepatitis B virus, as well as decreases in the consumption of alcohol, as well as decreases in the exposure to aflatoxin in agricultural settings, as well as the management of obesity and diabetes. Screening should be done on those who have a previous history of chronic liver disease. Imaging

with ultrasound can be utilized in the screening process for hepatocellular carcinoma in patients who have chronic liver disease and are at an increased risk of developing the illness. The manifestations and warning signs of liver cancer change according to the subtype of cancer that has developed in the patient. It's possible that the symptoms will be vague and all over the place. Cholangiocarcinoma can be identified by its symptoms, which include sweating, jaundice, stomach discomfort, decreased body weight, and an enlarged liver. Abdominal mass, pain, and emesis are two of the most common symptoms of liver cancer. Other symptoms include anemia, back discomfort, jaundice, itching, weight loss, fever, and loss of appetite. [59] There are multiple treatment options available, including radiation therapy, surgery, and targeted therapies. In certain circumstances, the treatment of ablation, the therapy of embolization, or even a liver transplant may be necessary.

1.15 Lung cancer

A malignant lung tumor that has uncontrolled cell growth is known as a lung cancer or a lung carcinoma [60, 61]. Since 98–99 percent of all lung cancers are carcinomas, a lung cancer is also known as a lung carcinoma. Lung cancer may originate either from epithelial cells that have undergone a transformation that causes them to become cancerous or from tissues that contain epithelial cells. Other forms of lung cancer, such as the infrequent sarcomas of the lung, are caused by the transformation into cancerous cells of mesenchymal cells that are found in connective tissues (such as nerves, fat, muscle, and bone). In very rare cases, lung cancer may develop from lymphomas or melanomas (derived from lymphoid or melanocyte cell lines). This uncontrolled growth has the potential to spread to other parts of the body either directly or indirectly by way of the lymphatic system or the bloodstream. This process is referred to as metastasis. It is possible for this uncontrolled growth to move to other parts of the body in any of these three ways. [62] The lungs are the site of genesis for the most majority of primary lung malignancies, also known as carcinomas. Small-cell lung carcinoma (SCLC) and non-small-cell lung cancer (NSCLC) are the two subtypes of lung cancer that may occur (NSCLC). The most common symptoms are chest discomfort, coughing that contains blood, loss of weight, and shortness of breath. Coughing is also one of the most common symptoms. Long-term cigarette smoking is responsible for 85 percent of all occurrences of lung cancer. Non-smokers make from ten to fifteen percent of the total number of cases [4]. These conditions often result from a combination of hereditary predisposition and environmental factors, such as exposure to radon gas, asbestos, passive smoking, or other forms of air pollution. [63-65] Chest X-rays and computed tomography are the two methods that may be used to diagnose lung cancer (CT). [66] To ensure accuracy, a sample is collected with the assistance of bronchoscopy or CT and then analyzed to validate the diagnosis. [67] One of the most important aspects of prevention is avoiding exposure to risk factors like smoking and pollution in the air. The state of a person's health is one of the most important determinants of how well they will react to therapy

and how long they will survive with the condition. [68] There is no known treatment or cure for the overwhelming majority of cases. Radiation therapy, chemotherapy drugs, and surgical treatments are the three primary modes of treatment that are most often used. Chemotherapy and radiation are the primary forms of treatment for small cell lung cancer (SCLC), while surgery is reserved for more extreme cases of non-small cell lung cancer (NSCLC). [69] In the year 2020, there will be 2.2 million newly diagnosed instances of lung cancer, and 1.8 million people will lose their lives to the disease. It is the top cause of mortality from cancer in both men and women and is the leading cause of death overall. [70] The average age of a patient diagnosed with Alzheimer's disease is 70 years old. In the majority of countries, only 10 to 20 percent of people survive the first five years of their lives, but the survival rate is 33 percent in Japan, 27 percent in Israel, and 25 percent in South Korea respectively. The developing globe often has less developed countries with more impoverished countries. [71]

1.16 Skin cancer

Cancer that begins in the skin is referred to as skin cancer. It is the most common kind of cancer. These symptoms are caused by cells that have invaded or spread throughout the body and have the ability to migrate to other locations inside the body or grow there. Melanoma, basal cell carcinoma, and squamous cell carcinoma are the three most prevalent forms of skin cancer. Melanoma is the least frequent kind of skin cancer. The first two types of skin cancer are both included in the category of nonmelanoma skin cancer, along with a number of other forms of the illness that are less common (NMSC). It is very unlikely that basal-cell carcinoma would spread to other areas of the body or result in the patient's passing. Either a painful or asymptomatic raised patch of skin that is glossy and has little blood vessels running across it or a raised area of skin that is ulcerous is possible manifestations of this condition. When compared to other forms of skin cancer, squamous cell carcinoma has a higher risk of metastasizing. Even though it has the potential to grow into an ulcer, it is often dry and crusty in most instances. Second, compared to other forms of skin cancer, melanomas have a greater propensity to spread rapidly. One of the most popular methods to determine whether or not a mole on your skin is abnormal is to look for changes in the appearance of any moles that are already there. More than ninety percent of cases may be attributed to the sun's ultraviolet (UV) rays. Because of this, it is currently believed that there is an increased risk of developing all three types of skin cancer. The ozone layer is depleting, which has led to an increase in people's likelihood of being exposed to harmful UV rays. [72] A tanning booth is another another ubiquitous source of ultraviolet light. It is extremely dangerous for infants to be subjected to melanomas and basal cell tumors throughout their formative years. When it comes to squamous-cell skin cancer, the total amount of exposure, independent of when it takes place, is more significant than any one specific exposure period. It is believed that moles are the cause of between 20 and 30 percent of all cases of melanomas. People with fair skin are

more likely to acquire skin cancer than those with darker complexion. People whose immune systems are already compromised due to factors such as taking medication or having HIV/AIDS are also at risk. A biopsy is performed in order to arrive at a diagnosis. It would seem that minimizing one's exposure to ultraviolet radiation and wearing sunscreen are the two most effective ways to prevent melanoma and squamous cell skin cancer. It is unknown whether or not using sunscreen lowers the chance of developing basal cell carcinoma. The vast majority of skin malignancies other than melanomas are amenable to curative treatment. As a kind of treatment, surgery is used much more often than other options such as radiation therapy or topical medications like fluorouracil. Melanoma treatment options include, but are not limited to, surgery, chemotherapy, radiation treatment, and targeted therapy. Palliative care is a kind of therapy that may be helpful to patients whose cancer has already spread to other areas of their body. Melanoma is one of the most frequent malignancies that may be effectively treated, with a survival rate that is over 86 percent in the United Kingdom and over 90 percent in the United States. [73-74] At least forty percent of all cancer cases are attributable to some kind of skin cancer, making it the most common form of the disease. The most common kind of skin cancer, known as nonmelanoma skin cancer, affects between 2 and 3 million people each year. [75-76] On the other hand, this is just an estimate since there is not enough precise data. In the nonmelanoma skin cancer group, about 80 percent of cases are caused by basal cells and 20 percent are caused by squamous cells. In the United States, squamous cell carcinoma and basal cell carcinoma are very uncommon causes of death. They were responsible for a fraction of one-tenth of one percent of all cancer-related deaths in the United States. According to the World Health Organization, there were 232,000 newly diagnosed cases of melanoma and 55,000 deaths caused by the disease in 2012. In Australia, New Zealand, and South Africa, the incidence of melanoma is highest among white people. [77] The incidence rates of the three principal types of skin cancer have risen significantly over the last 20 to 40 years, especially in regions with a mostly white population. [78]

1.17 Uterine cancer

Uterine cancer and womb cancer are both terms that refer to malignant growths that develop in the uterine tissues. Uterine cancer may take two different forms. Endometrial carcinoma and uterine sarcoma are both forms of cancer that may begin in the uterus and can progress to other parts of the body. [79-80] Endometrial carcinoma is the root cause of ninety percent of all cases of uterine cancer that occur in the United States. Endometrial cancer symptoms include irregular periods or pelvic pain. Uterine sarcoma may present itself with abnormal vaginal bleeding or the appearance of a tumor in the uterus as one of its symptoms. Women who are obese, have metabolic syndrome or diabetes type 2, are using estrogen-only pills, have used tamoxifen in the past, are in the later stages of menopause, or have a family history of ovarian cancer are more likely to develop the disease. Other risk factors include having a family history of

the disease. [81] Uterine sarcoma is more likely to develop if the patient has a history of pelvic radiation therapy. Endometrial biopsies are routinely used to diagnose endometrial cancer. Women may be diagnosed with uterine sarcoma based on the findings of medical imaging, their symptoms, and the results of a pelvic exam. Treatment for uterine sarcoma is often more challenging than treatment for endometrial cancer. There are a number of different treatment options available, including surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapy. Over eighty percent of women who are diagnosed with breast cancer go on to survive at least five years after receiving their diagnosis. In 2015, the disease affected 3.8 million women all over the globe and was responsible for the deaths of 90,000.00 persons. [82-83] Cancer of the endometrium is quite frequent, in contrast to uterine sarcomas, which are extremely unusual. The number of newly diagnosed cases of uterine cancer in the United States accounts for 3.5 percent of all cases. The majority of victims are females, and the ages of those victims range from 45 to 74, with 63 being the median age.

1.18 Colon cancer

The development of cancer in the colon or rectum is referred to as colorectal cancer, often referred to as bowel cancer, colon cancer, or rectal adenocarcinoma (parts of the large intestine). [84] There are a number of potential indications and symptoms, including blood in the stool, a change in bowel movements, weight loss, and extreme tiredness. A very small fraction of cases of colorectal cancer may be attributed to underlying genetic disorders as the root cause. A poor diet, being overweight, engaging in unhealthy behaviors like smoking, and not getting enough exercise are all risk factors. Alcohol, processed meat, and red meat are all recognized as potential health hazards. Another factor to consider is having an inflammatory bowel condition, such as Crohn's disease or ulcerative colitis. These rare forms of colorectal cancer include familial adenomatous polyposis and hereditary non-polyposis colon cancer. Together, they make up less than five percent of all cases of colorectal cancer. In most cases, when it initially manifests itself, it is a benign growth known as a polyp; but, as time passes, it transforms into something more deadly. The removal of a tissue sample from the colon during a sigmoidoscopy or colonoscopy may be an important part of the diagnostic process for bowel cancer. After then, diagnostic imaging is done to determine whether or not the sickness has spread. Screening for colorectal cancer is a good method for preventing the illness and reducing death rates associated with it. Screening should begin anywhere between the ages of 50 and 75 and may be performed using a number of different methods. If a colonoscopy reveals that a patient has little polyps, the doctor may be able to remove them. A biopsy may be performed in order to establish whether or not a large polyp or tumor is cancerous. Aspirin and other non-steroidal anti-inflammatory medications, such as ibuprofen, may help lower the risk. However, due to the possibility of unfavorable side effects, it is not recommended

that these be used on a widespread scale in the current context. [85] Surgery, radiation therapy, chemotherapy, and targeted therapy are some of the potential treatment options for colorectal cancer. In some cases, colon cancer can be cured through surgical removal of the tumor. However, in most cases, colon cancer that has spread to other parts of the body is not curable and must instead be managed to improve the patient's quality of life and alleviate symptoms. Roughly sixty-five percent of Americans reach the age of sixty-five or older. [7] The extent to which the disease has progressed, the possibility that all of the cancer can be surgically removed, and the patient's general health are all factors that influence the likelihood of survival. The third most common form of cancer worldwide, colorectal disease is responsible for approximately ten percent of all newly diagnosed cases each year. In 2018, there were 1.09 million newly diagnosed cases of the illness, and 551,000 people lost their lives as a result of it. [86] The incidence rate is highest in countries with high levels of wealth in more than two thirds of cases. Women are affected by it at a significantly lower rate than men. [87-89]

1.19 Breast cancer

The term "breast cancer" refers to malignant tumors that originate in the breast tissue. The most frequent signs and symptoms of breast cancer include lumps in the breasts, changes in the contour of the breasts, dimpling of the skin, fluid leaking from the nipple, an inverted nipple, and a patch of skin that is red or scaly. Those who have the disease in their bones, lymph nodes, or skin may have symptoms such as pain in the bones, swollen lymph nodes, or shortness of breath. It is essential to be aware of the fact that factors that increase one's likelihood of developing breast cancer include being overweight and inactive, as well as drinking alcohol, undergoing hormone replacement therapy after the menopause, being exposed to ionizing radiation, beginning menstruation at a younger age, and having children later in life or not at all. [90-91] It is estimated that between 5 and 10 percent of cases are the result of inherited genetic predispositions. Some of these predispositions include BRCA1 and BRCA2, among others. The lining of milk ducts and the lobules that provide milk to these ducts are the most common places where breast cancer may begin. Both ductal and lobular carcinomas are distinct forms of cancer that begin in the ducts of the digestive system. Ductal carcinomas are more common than lobular carcinomas. More than 18 distinct subtypes of breast cancer have been identified. Existing lesions, such as ductal carcinoma in situ, have the potential to give rise to the development of cancer. In order to conclusively diagnose breast cancer, a biopsy is need to be performed. After the initial diagnosis has been made, more testing has to be done in order to determine whether or not the breast cancer

has spread to other parts of the body and which treatments have the best chance of being effective. Both the benefits and the drawbacks of breast cancer screening have been called into question. It is not clear if mammography screening is useful or detrimental, according to a research that was conducted by Cochrane in 2013. The reason for this is because a large majority of women who test positive truly do not have the condition. [92] In 2009, the United States Preventive Services Task Force carried out a research and discovered indications of benefit in females between the ages of 40 and 70 [93-94]. The organization now recommends screening tests take place once every two years for women aged 50 to 74. [95] In women who are at a high risk of developing breast cancer, the use of raloxifene or tamoxifen may be helpful in preventing the disease. Another preventative measure is the surgical removal of both breasts in high-risk women who are candidates for the procedure. Cancer patients who have been given a diagnosis of the illness have a variety of treatment choices to choose from, including surgical, radiation, chemotherapeutic, hormonal, and targeted therapy. Different types of breast surgeries, such as mastectomy and breast-conserving surgery, are examples of surgical operations. [96] Reconstructive breast surgery may take place either at the time of the first operation or at a later period. Patients whose cancer has spread to other parts of the body often get treatments that concentrate primarily on improving the patients' quality of life and level of comfort. [97] There is a possibility that the results of breast cancer will differ depending on the kind of cancer, the severity of the sickness, and the age of the patient. [98] It is anticipated that between 80 and 90 percent of patients in both England and the United States will still be alive after five years. [99-100] The five-year survival rates are lower in countries with lower levels of income. The most frequent kind of cancer seen in females everywhere in the globe is breast cancer, which accounts for twenty-five percent of all instances. [101] The disease was responsible for 2 million new cases and 627,000 deaths in 2018. [102] The prevalence of this condition is higher in females than in males, and it is more prevalent in developed countries. [103]

1.20 Signs and symptoms Breast cancer

It's typical for breast cancer to show up as a lump that's distinct from other breast tissue. Most instances are identified by a person's fingers feeling for such a bump. [104] A mammography, on the other hand, is used to identify the early breast tumors. [105-106] Breast cancer may also be diagnosed by the presence of lumps in lymph nodes in the armpits.[107] Besides a lump, additional signs of breast cancer include thickening that is distinct from the surrounding breast tissue, a nipple that is inverted, skin puckering or dimpling, drainage

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from the nipple, continuous discomfort in the breast or armpit, and swelling behind the armpit or around the collarbone. Pain (mastodynia) is not a reliable indicator of breast cancer, but it might be a sign of other health conditions in the breast. [108]Paget's disease of the breast is another indication of breast cancer that is often overlooked. Eczema-like symptoms might be seen on the skin of the nipple; for example, redness, discoloration, or slight peeling. Itching, tingling, heightened sensitivity, burning and discomfort are all possible symptoms of Paget's disease of the breast as it progresses. Nipple discharge may also occur. A lump in the breast is seen in around half of Paget's disease patients. [109-110]It is an uncommon (less than 5% of breast cancer cases) and aggressive kind of breast cancer that is defined by the red, swollen regions on the breast's upper surface. Inflammatory breast cancer's visible symptoms are caused by cancer cells obstructing lymph vessels. In younger women, obese women, and African American women, this kind of breast cancer is more prevalent. Due to the lack of a lump, the diagnosis of inflammatory breast cancer may be delayed. [111]It is possible that a hard, moveable non-cancerous lump that first looks to be a fibroadenoma is really a phyllodes tumor. This kind of tumor is produced in the stroma (connective tissue) of the breast and includes both glandular and stromal tissue. It is not common practice to stage phyllodes tumors; instead, their microscopic appearance is used to classify them as benign, borderline, or malignant. [112]Metastatic tumors are secondary cancers that originate from the main tumor and spread to other parts of the body. Metastatic breast cancer may produce a wide range of symptoms, depending on where the disease has spread. Metastasis may occur in the bone, liver, lung, and brain. [113] As stage 4 malignancies are generally terminal, they are referred to as such. [114]Bone and joint pain, jaundice, and neurological symptoms are among the most common signs of stage 4 cancer. For this reason, symptoms such as these are referred to be non-specific symptoms.[115] Peripancreatic lymph nodes, which cause biliary obstruction and make diagnosis more difficult, are a rare place where breast cancer may spread. [116]Most signs of breast problems, including most lumps, do not indicate an underlying cancerous condition. " More prevalent breast problem symptoms include mastitis and fibroadenoma than malignant lumps, which account for less than 20 percent of all breast lumps. [117-118]

1.21 Diagnosis

For the majority of breast cancers, a biopsy of the afflicted region is all that is needed to confirm the presence of the disease. Additionally, certain breast cancers need specialist laboratory testing. Mammography and physical breast examination by a healthcare professional may give an estimated possibility that a lump is cancerous and also identify certain other abnormalities, such as a simple cyst, as the two most often utilized screening modalities.[119] Fine needle aspiration, or fine needle aspiration and cytology, or FNAC, is a technique in which a healthcare professional removes a sample of the fluid in the lump for microscopic study.

A healthcare provider's office or clinic might be used to do a needle aspiration. A local anesthetic may be used to numb the breast tissue to avoid discomfort during the surgery, however it may not be required if the lump is not under the surface of the breast. Even if the mass is found to be malignant despite the presence of clear fluid, the bloody fluid may still be submitted for examination under a microscope to look for cancerous cells. Breast cancer may be accurately diagnosed using a combination of physical examination, mammography, and FNAC. Core biopsy or vacuum-assisted breast biopsy [120] are further biopsy techniques that remove a part of the breast mass, whereas excisional biopsy removes the tumor in its whole. As the final diagnostic and main therapeutic approach, an excisional biopsy is often justified by the findings of a physical examination by a healthcare professional, a mammogram, and any further tests that may be conducted under specific conditions (such as imaging by ultrasound or MRI)[121]

1.22 Classification of Breast cancer

Histopathology. The histological appearance of breast cancer is used to classify it. In the majority of cases, malignancies of the ductal or lobular epithelium are the source of breast cancers. Precancerous cells, such as those seen in the mammary gland, develop unnoticed and uninvaded inside their own tissues, creating what is known as a carcinoma in situ. When compared to the primary tissue compartment, invasive cancer is able to spread throughout the body.

Grade. A breast cancer cell's appearance is graded by comparing it to the appearance of normal breast tissue. They become differentiated, which means they take on a particular shape or form to represent their role as part of the organ they belong to. Cancerous cells are unable to distinguish between normal and malignant stem cells. The cells that ordinarily form the milk ducts line up in an unorganized manner in cancer patients. As a result, unchecked cell division occurs. The nuclei of cells change in shape. Cancerous breast cancer cells may be categorized as well differentiated (low grade), medium-differentiated (intermediate grade), or poorly differentiated (high grade). Because of their poor differentiation, poorly differentiated tumors have a worse prognosis.

Stage. Breast cancer is staged according to the TNM method, which takes into account three factors: tumor size (T), whether or not lymph nodes in the armpits have been affected (N), and whether or not the disease has migrated to other organs (M) (i.e. spread to a more distant part of the body). The worse the prognosis, the higher the stage number, and the more widespread the cancer is.

In order of precedence, there are the following stages:

- ✓ Both DCIS and LCIS are pre-cancerous or marker conditions, which means they are in the early stages of cancer development (LCIS).

- ✓ Breast or lymph node lymph nodes are the site of stages 1–3.
- ✓ As it has migrated outside of the breast and its local lymph nodes, cancer that is in the fourth stage is considered "metastatic" and has a worse prognosis.

Receptor status: The cytoplasm, nucleus, and surface of breast cancer cells all have receptors. The cell changes as a result of chemical messengers such as hormones binding to receptors. ER, PR, and HER2 are three key receptors that breast cancer cells may or may not contain. To combat the growth-promoting effects of estrogen, cancer cells with ER+ status may be treated with medications that inhibit such effects (e.g. tamoxifen), and as a result, they have a better prognosis. HER2+ breast cancers tend to be more deadly if left untreated [122] than HER2-type tumors. The monoclonal antibody trastuzumab (in conjunction with standard treatment) has improved the prognosis dramatically for patients with HER2+ cancer cells. When no estrogen, progesterone, or HER2 receptors can be found in a cell, that cell is referred to be "triple-negative," however it may nonetheless have receptors for androgens and prolactins.

DNA assays: Breast cancer cells and normal cells have been compared using a variety of DNA testing methods, including DNA microarrays. To identify breast cancer, researchers utilize the precise alterations in the tumour's DNA. This information may then be used to choose the most successful therapy for that particular DNA type. [123-124]

1.23 Prevention

Lifestyle

The risk of breast cancer may be reduced in women by eating healthily, abstaining from alcohol, increasing physical activity, and exclusively breastfeeding. These alterations might prevent 38% of US breast cancers, 42% of UK cases, 28% of Brazilian cases, and 20% of Chinese cases. Postmenopausal women may get the advantages of moderate exercise, such as brisk walking, regardless of their age. [125] About 14 percent of breast cancer cases may be attributed to high levels of physical exercise. [126] Obesity reduction and improved cardiovascular health are possible side effects of these and other obesity-related prevention strategies. [33] In 2016, the American Cancer Society and the American Society of Clinical Oncology recommended that individuals consume a diet rich in fruits, vegetables, whole grains, and legumes to prevent cancer. [127] Breast cancer risk may be reduced by 10% if you consume a lot of citrus fruit. [128] Polyunsaturated fatty acids from marine sources seem to lower the risk. [129] Soy-based diets are thought to lower risk. [130]

1.24 Pre-emptive surgery

Preliminary bilateral mastectomy (also known as "risk lowering mastectomy") may be considered for women with BRCA1 or BRCA2 mutations who have an increased likelihood of breast cancer diagnosis. [131-132] There is insufficient evidence to warrant this operation in any but the most vulnerable women. [133] Following genetic counseling, BRCA testing is suggested for people with a high familial risk. It's not a good idea to do it every day. [134] Due to the wide range of BRCA gene mutations, from innocuous polymorphisms to clearly harmful frameshift mutations, this is the case. [134] Most of the gene alterations that may be identified have no known impact. Testing in a person with an average level of risk is more likely to produce one of these ambiguous and pointless outcomes. Contralateral risk-reducing mastectomy (CRRM) may lower the risk of cancer in a person's second breast, but it is not certain whether removing a person's second breast after being diagnosed with breast cancer increases their chance of survival.

1.25 Medications

Thromboembolism and endometrial cancer risk are increased by selective estrogen receptor modulators, which lower breast cancer risk. [135] Overall, the chance of mortality does not change. [135-136] As a result, they are not advised for the prevention of breast cancer in women with an average risk, but are indicated for those with a high risk and who are over 35. [137] After completing a course of therapy with these drugs, breast cancer risk is reduced for at least five years.

[138] Tamoxifen and other selective estrogen receptor modulators may be less effective in reducing breast

cancer risk than aromatase inhibitors (such as exemestane and anastrozole), but they are not related with an increased risk of endometrial cancer and thromboembolism. [139-140]

1.26 Management

Breast cancer care is influenced by a number of variables, including the disease's stage and the patient's age. When the cancer is more advanced or there is a greater danger of recurrence after therapy, more aggressive treatments are used. In most cases, breast cancer is surgically removed and then treated with chemotherapy or radiation treatment. In this case, it's best to use a multidisciplinary approach. Several years of hormone-blocking treatment are often used to treat tumors that express hormone receptors. Certain instances of metastatic and other advanced stages of breast cancer may be treated with monoclonal antibodies or other immune-modulating medicines. Even yet, further research is needed to determine the effectiveness of this therapy option. [141]

Surgery

During surgery, the tumor and portions of the surrounding tissue are physically removed. During surgery, one or more lymph nodes may be biopsied; sentinel lymph node biopsy is becoming more common.

The following are common procedures:

- A mastectomy is the surgical removal of both breasts.
- A quadrantectomy is the removal of one-quarter of the breast.
- Surgically removing a tiny portion of breast tissue.

To enhance the look of the treated area after the tumor has been removed, breast reconstruction surgery, a sort of cosmetic surgery, might be done. Women may also opt to have a flat chest or utilize breast prosthesis to make it seem as though they have breasts beneath their clothes. After a mastectomy, a nipple prosthesis may be used at any time.

Medication

Adjuvant treatment refers to the use of medications after and in addition to surgery. Neoadjuvant therapy refers to treatments administered before surgery, such as chemotherapy. The combination of aspirin and other cancer therapies has been shown to lower mortality in women with breast cancer. [142-144] Breast cancer patients are being treated with hormone-blocking drugs (HRT), chemotherapy, and monoclonal antibodies (mAbs).

Chemotherapy

Stages 2–4 breast cancer is the most common usage of chemotherapy, and ER-negative breast cancers benefit the most from it. Combinations of chemotherapy drugs are commonly given for intervals of three to six months. Cyclophosphamide and doxorubicin are often used in the "AC" regimen. A taxane medicine like docetaxel may be added to the regimen, in which case the treatment is referred to as "CAT." Cyclophosphamide, methotrexate, and fluorouracil are additional popular treatments (or "CMF"). Most chemotherapy drugs target cancer cells that are rapidly growing and/or rapidly reproducing, either by causing DNA damage during replication or by other means. However, the drugs may potentially produce major negative effects by damaging fast-growing normal cells. Doxorubicin's most lethal side effect, for example, is heart muscle damage.

Monoclonal antibodies

One monoclonal anti-HER2 antibody, trastuzumab, has raised the 5-year survival rate for HER2- positive stage 1–3 breast cancer patients from roughly 87% to 89%. (overall survival 95 percent).[151] As many as 25 to 30 percent of breast tumors overexpress the HER2 gene or its protein product,[152] which has been linked to an increased risk of recurrence and poorer prognosis. Trastuzumab, on the other hand, is a costly and potentially dangerous drug (approximately 2 percent of people who receive it develop significant heart damage). [153] HER2 dimerization is prevented by the antibody pertuzumab, which is used in combination with trastuzumab and chemotherapy when the illness is severe. [154-155]

Radiation

Once the tumor has been surgically removed, radiotherapy is used to eliminate any tiny tumor cells that may have evaded the surgeons. As a kind of intraoperative radiation, it may also have a positive impact on the tumor microenvironment. [156-157] Brachytherapy and external beam radiotherapy are both methods of delivering radiation therapy (internal radiotherapy). Traditionally, radiation for breast cancer is administered after surgery. Radiation may also be used during a breast cancer procedure. When given at the right dosage, radiation may lower the probability of recurrence by 50–66 percent (a half- to a third-reduction in risk)[158] and is thus regarded vital in the treatment of breast cancer when just the lump is removed (Lumpectomy or Wide local excision). Partial irradiation in the early stages of breast cancer is less effective than full irradiation, and it may induce more severe adverse effects. [159]

Follow-up care

'Follow-up care', or frequent laboratory testing in asymptomatic persons, may be quite thorough in order to identify any metastases in the early stages of the disease. According to a recent study, routine physical exams and annual mammography follow-up programs are just as beneficial as more comprehensive

programs that include laboratory testing in detecting recurrence early, ensuring overall survival, and improving quality of life for survivors. [160]Short-term gains in functional ability, psychosocial adjustment, and social involvement in breast cancer patients may be achieved via multidisciplinary rehabilitation programs that include exercise, education, and psychological support.[161]Objective of my studies

CHAPTER TWO

AIM AND OBJECTIVE OF THIS STUDY

My aim of this study is

- To see the ratio of Breast cancer in males and females.
- To find out the cause of Breast cancer.
- To see therapeutic option for breast cancer.
- To open a new area of higher studies.

CHAPTER THREE

MATERIALS AND METHOD

3.0. working procedure

I have collected literature review/ research and Newspaper which was published in different time for the cancer. In this case, around 40 articles for this study have been include.

For this collecting the paper, I have used google scholar/ PubMed database and various website. All collected information are between 1990-2020. After collecting information, I want to try, discuss about and correlated with my investigation.

Figure 2. . Website and search engine

CHAPTER FOUR

RESULT AND DISCUSSION

3.1 Breast Cancer ratio among male and Female

Breast Cancer ratio among male and Female: According to our studies, 6% male, and 94% could be affected by breast cancer in each year.

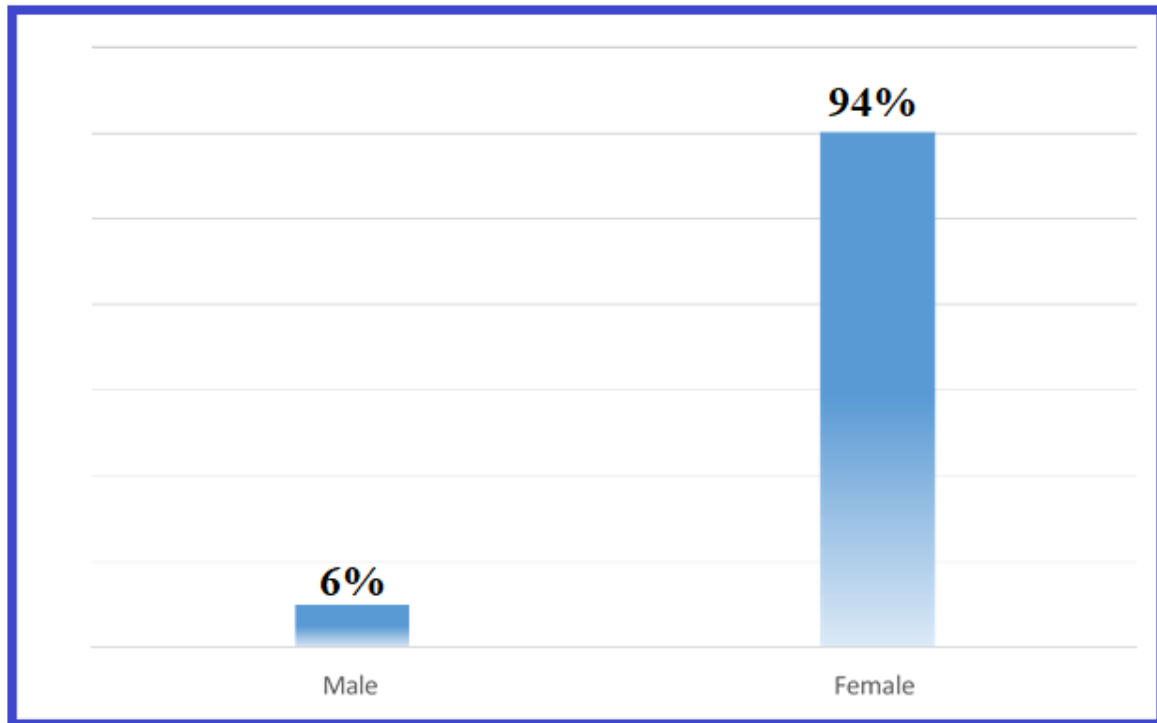


Figure 3. Breast Cancer affected number displayed in graph.

Breast cancer is the most frequent cancer in women worldwide, apart from nonmelanoma skin cancer. According to this assessment, in 2017, more than 250 000 new instances of breast cancer were identified in the United States, and 12 percent of all women in the United States will be diagnosed with breast cancer over their lives [187]. Male breast cancer affects one in every 100,000 men in Europe, and men account for fewer than 1% of all breast cancer patients. Male breast cancer rates vary significantly across nations, with 5% and 15% yearly incidence rates in Uganda and Zambia, respectively [188].

3.2 Causes Of Breast Cancer

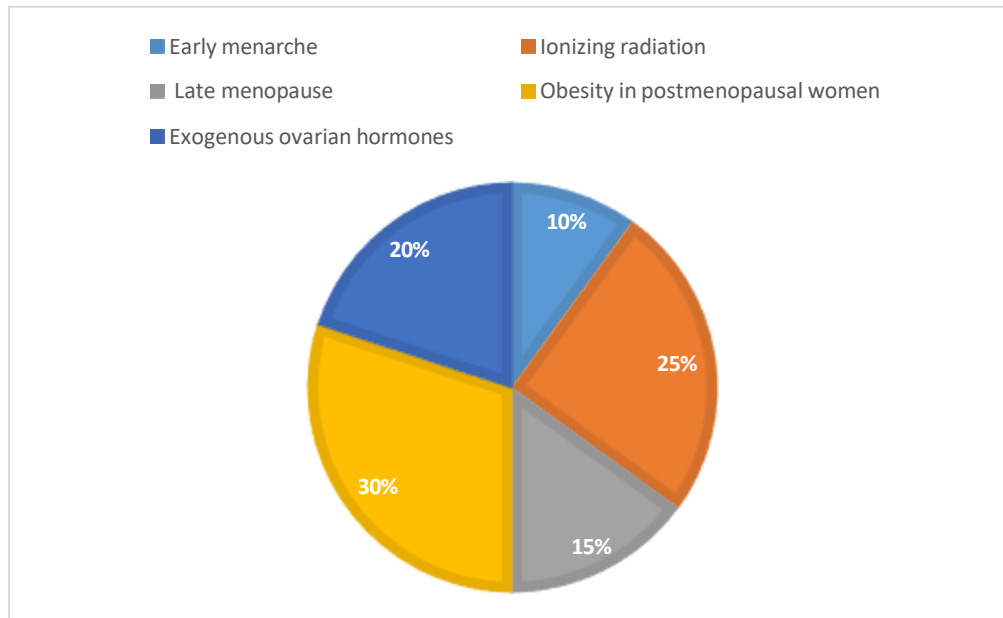


Figure 4. Different Causes of Breast Cancer with percentage

Breast cancer is the leading cause of mortality among women throughout the globe. Rates vary around fivefold worldwide, but they are rising in areas where the illness was formerly uncommon. Estrogens are connected to several known risk factors. In this review, I saw that 30% of people have Breast cancer for Obesity in postmenopausal. 25% of people have Breast cancer for Ionizing radiation. 20% of people have Breast cancer from Exogenous ovarian hormones. 15% of people have Breast cancer for Late menopause. 10% of people have Breast cancer from Early menarche. [189-190]

3.3 Hormone Levels and Breast Cancer Risk

Few studies have evaluated breast cancer risk based on blood hormone levels. Study outcomes vary because it's challenging to measure hormone levels in postmenopausal women. Blood estradiol levels were linked to the disease in a follow-up analysis of 130 women with breast cancer. The follow-up research on osteoporotic fractures indicated a high association between hormone levels and breast cancer risk among women not using postmenopausal hormones. Comparing extreme estrone quartiles, women in the highest quartile had an RR of 3.2 (95 percent CI 1.4– 7.0). [191]Guernsey has 61 breast cancer diagnoses. Guernsey women with breast cancer had greater baseline hormone levels than those without. [192]Other prospective studies concur with this link. The number of cases is limited or has failed to identify a statistical correlation but is consistent with a statistically meaningful relationship between increased risk and greater hormone levels. Greater serum estradiol levels were associated with a higher breast cancer risk. Some but not all prospective studies have linked androgens to an increased risk of breast cancer. Two major future trials had mixed results. [193] Although the study of 81 cases showed a statistically significant positive relationship between testosterone levels and risk when adjusted only for age, once other hormones such as estradiol and percent sex hormone-binding globulin-bound estradiol are controlled for, the results showed no statistically significant dose-response relationship, and the RR, comparing highest versus lowest quartile of serum testosterone, was not significant (RR 4.1). [194] In little research with 24 instances, total estradiol had no impact. The statistically substantial beneficial connection between testosterone levels and breast cancer risk disappeared when controlled estradiol levels were. These findings imply testosterone may have an indirect influence via estrogens rather than being a risk factor. This theory needs more data. [195]Growing data suggest a link between blood estrogen levels and breast cancer risk, with a fourfold rise between extreme quartiles of estradiol. This link is higher than that between cholesterol levels and heart disease, indicating estrogen levels may serve as a clinical predictor of breast cancer risk if laboratory procedures to test estrogens are standardized and the optimal estrogen fraction to predict risk is discovered. [196]

3.4 Mechanisms by Which Hormones Can Influence Breast Cancer Risk

Cell proliferation is how DNA damage (genetic mistakes) accumulates, and breast cancer risk rises (69,70). Breast proliferative activity is highest in premenopausal women during the luteal phase. Progesterone is a significant mitogen in premenopausal breast epithelium [197]. This approach supports a study of surgically postmenopausal Cynomolgus macaques administered with conjugated equine estrogen or conjugated equine estrogen + medroxyprogesterone acetate. The combination treatment increased breast cell proliferation more than conjugated equine estrogen alone. In vitro, estrogens enhance breast cell growth, whereas progestins hinder it. Uncertainty remains about the impact of progestins and whether their usage pattern (continuous vs. interrupted) affects DNA damage and breast cancer development. [198] Cell proliferation is decreased in postmenopause. Unopposed estrogen after menopause may increase breast cancer risk by 2.1% per year compared to non-users. Progestins will enhance cell proliferation and breast cancer, they said. Changes in mammographic patterns with different hormone replacement regimens corroborate this link. Combination of estrogen+progestins increased mammographic density more than estrogens alone. [199] Studies of hormonal carcinogenesis reveal estrogens cause nongenotoxic cell growth and genotoxic effects. Epidemiologic studies indicate a higher link between current usage of replacement hormones (mostly unopposed estrogen) and breast cancer risk than prior use. This shows that replacement hormones promote cancer development rather than being genotoxic. In a combined reanalysis of epidemiologic data, women who ceased using hormones more than five years ago were not at elevated risk compared with never users, no matter how long they had used replacement hormones. The role of estrogen plus progestins in breast cancer risk among former users has not been examined since this regimen is new. [200]

CHAPTER FIVE

CONCLUSION

5.0 Conclusion:

Incidence rates of breast cancer continue to increase slowly in the United States, largely driven by the occurrence of localized and HR-positive disease. This trend reflects in part an increased prevalence of excess body weight and declines in the fertility rate. Nevertheless, breast cancer mortality continues to decline, albeit at a slower pace than during the 1990s and 2000s. Black women have a 40% higher breast cancer mortality than White women despite lower incidence. Further, this disparity that has remained unabated for a decade, even as awareness has grown within the oncology community. Driving this trend, Black women have the lowest survival of any racial and ethnic group for every molecular subtype and stage of disease (except stage I), with 8% lower survival than White women in absolute terms for HR-positive/HER2-negative disease and HR-negative/HER2-positive disease and a 13% gap for stage III disease (64% vs. 77%). These inequalities could be mitigated by expanding access to high-quality prevention, early detection, and treatment services to all women through nationwide Medicaid expansion and forging partnerships between community stakeholders, advocacy organizations, and health systems to address detection and treatment inequalities.

CHAPTER SIX

REFERENCES

Reference

1. "Cancer". World Health Organization. 12 September 2018. Retrieved 19 December 2018.
2. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB (September 2008). "Cancer is a preventable disease that requires major lifestyle changes". *Pharmaceutical Research*. 25 (9): 2097–116. doi:10.1007/s11095-008-9661-9. PMC 2515569. PMID 18626751.
3. "Targeted Cancer Therapies". cancer.gov. National Cancer Institute. 26 February 2018. Retrieved 28 March 2018.
4. "SEER Stat Fact Sheets: All Cancer Sites". National Cancer Institute. Archived from the original on 26 September 2010. Retrieved 18 June 2014.
5. Kocarnik, JM; others (2022). "Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019. A Systematic Analysis for the Global Burden of Disease Study 2019". *JAMA Oncology*. 8 (3): 420–444. doi:10.1001/jamaoncol.2021.6987. PMC 8719276. PMID 34967848.
6. "Defining Cancer". National Cancer Institute. 17 September 2007. Retrieved 28 March 2018.
7. "Obesity and Cancer Risk". National Cancer Institute. 3 January 2012. Archived from the original on 4 July 2015. Retrieved 4 July 2015.
8. Jayasekara H, MacInnis RJ, Room R, English DR (May 2016). "Long-Term Alcohol Consumption and Breast, Upper Aero-Digestive Tract and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis". *Alcohol and Alcoholism*. 51 (3): 315–30. doi:10.1093/alcalc/agv110. PMID 26400678.
9. World Cancer Report 2014. World Health Organization. 2014. pp. Chapter 1.1. ISBN 978-92-832-0429-9. Archived from the original on 12 July 2017.
10. "Heredity and Cancer". American Cancer Society. Archived from the original on 2 August 2013. Retrieved 22 July 2013.
11. "How is cancer diagnosed?". American Cancer Society. 29 January 2013. Archived from the original on 14 July 2014. Retrieved 10 June 2014.
12. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV,

- Gapstur S, Patel AV, Andrews K, Gansler T (2012). "American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity". *CA: A Cancer Journal for Clinicians*. 62 (1): 30–67. doi:10.3322/caac.20140. PMID 22237782. S2CID 2067308.
13. Parkin DM, Boyd L, Walker LC (December 2011). "16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010". *British Journal of Cancer*. 105 (Suppl 2): S77–81. doi:10.1038/bjc.2011.489. PMC 3252065. PMID 22158327.
14. *World Cancer Report 2014*. World Health Organization. 2014. pp. Chapter 4.7. ISBN 978-92-832-0429-9. Archived from the original on 12 July 2017.
15. Gøtzsche PC, Jørgensen KJ (June 2013). "Screening for breast cancer with mammography". *The Cochrane Database of Systematic Reviews*. 6 (6): CD001877. doi:10.1002/14651858.CD001877.pub5. PMC 6464778. PMID 23737396.
16. *World Cancer Report 2014*. World Health Organization. 2014. pp. Chapter 1.3. ISBN 978-92-832-0429-9. Archived from the original on 12 July 2017.
17. Disease and Injury Incidence and Prevalence Collaborators (8 October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015". *The Lancet*. 388 (10053): 1545–1602. doi:10.1016/S0140-6736(16)31678-6. PMC 5055577. PMID 27733282.
18. Sciacovelli M, Schmidt C, Maher ER, Frezza C (2020). "Metabolic Drivers in Hereditary Cancer Syndromes". *Annual Review of Cancer Biology*. 4: 77–97. doi:10.1146/annurev-cancerbio-030419-033612.
19. *World Cancer Report 2014*. World Health Organization. 2014. pp. Chapter 1.1. ISBN 978-92-832-0429-9.
20. Dubas LE, Ingraffea A (February 2013). "Nonmelanoma skin cancer". *Facial Plastic Surgery Clinics of North America*. 21 (1): 43–53. doi:10.1016/j.fsc.2012.10.003. PMID 23369588.
21. Cakir BÖ, Adamson P, Cingi C (November 2012). "Epidemiology and economic burden of nonmelanoma skin cancer". *Facial Plastic Surgery Clinics of North America*. 20 (4): 419–22. doi:10.1016/j.fsc.2012.07.004. PMID 23084294.
22. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D (February 2011). "Global cancer statistics". *CA: A Cancer Journal for Clinicians*. 61 (2): 69–90. doi:10.3322/caac.20107. PMID 21296855. S2CID

30500384.

23. World Cancer Report 2014. World Health Organization. 2014. pp. Chapter 6.7. ISBN 978-92-832-0429-9. Archived from the original on 12 July 2017.
24. Hajdu SI (March 2011). "A note from history: landmarks in history of cancer, part 1". *Cancer*. 117 (5): 1097–102. doi:10.1002/cncr.25553. PMID 20960499. S2CID 39667103.
25. Paul of Aegina, 7th century AD, quoted in Moss, Ralph W. (2004). "Galen on Cancer". *CancerDecisions*. Archived from the original on 16 July 2011. Referenced from Michael Shimkin, *Contrary to Nature*, Washington, DC: Superintendent of Document, DHEW Publication No. (NIH) 79–720, p. 35.
26. Majno G, Joris I (12 August 2004). *Cells, Tissues, and Disease : Principles of General Pathology: Principles of General Pathology*. Oxford University Press. ISBN 978-0-19- 974892-1. Retrieved 11 September 2013.
27. Hajdu SI (June 2011). "A note from history: landmarks in history of cancer, part 2". *Cancer*. 117 (12): 2811–20. doi:10.1002/cncr.25825. PMID 21656759. S2CID 28148111.
28. Yalom, Marilyn (1998). *A history of the breast* (1 ed.). New York: Ballantine Books. ISBN 978-0-679-43459-7.
29. Hajdu SI (February 2012). "A note from history: landmarks in history of cancer, part 3". *Cancer*. 118 (4): 1155–68. doi:10.1002/cncr.26320. PMID 21751192. S2CID 38892895.
30. Grange JM, Stanford JL, Stanford CA (June 2002). "Campbell De Morgan's 'Observations on cancer', and their relevance today". *Journal of the Royal Society of Medicine*. 95 (6): 296–99. doi:10.1258/jrsm.95.6.296. PMC 1279913. PMID 12042378.
31. Anisimov VN, Sikora E, Pawelec G (August 2009). "Relationships between cancer and aging: a multilevel approach". *Biogerontology*. 10 (4): 323–38. doi:10.1007/s10522-008-9209-8. PMID 19156531. S2CID 17412298.
32. de Magalhães JP (May 2013). "How ageing processes influence cancer". *Nature Reviews. Cancer*. 13 (5): 357–65. doi:10.1038/nrc3497. PMID 23612461. S2CID 5726826.
33. Schottenfeld D, Fraumeni JF (24 August 2006). *Cancer Epidemiology and Prevention*. Oxford University Press. p. 977. ISBN 978-0-19-974797-9.
34. Bostwick DG, Eble JN (2007). *Urological Surgical Pathology*. St. Louis: Mosby. p. 468. ISBN 978-0-323-01970-5.
35. Kaatsch P (June 2010). "Epidemiology of childhood cancer". *Cancer Treatment Reviews*. 36 (4):

277–85. doi:10.1016/j.ctrv.2010.02.003. PMID 20231056.

36. Anguiano L, Mayer DK, Piven ML, Rosenstein D (July–August 2012). "A literature review of suicide in cancer patients". *Cancer Nursing*. 35 (4): E14–26. doi:10.1097/NCC.0b013e31822fc76c. PMID 21946906. S2CID 45874503.
37. ^ O'Dell M, Stubblefield M (2009). *Cancer rehabilitation principles and practice*. New York: Demos Medical. p. 983. ISBN 978-1-933864-33-4.
38. ^ Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. (May 2011). "Definition and classification of cancer cachexia: an international consensus". *The Lancet. Oncology*. 12 (5): 489–95. doi:10.1016/S1470-2045(10)70218-7. PMID 21296615.
39. ^ Dimitriadis GK, Angelousi A, Weickert MO, Randeve HS, Kaltsas G, Grossman A (June 2017). "Paraneoplastic endocrine syndromes". *Endocrine-Related Cancer*. 24 (6): R173– R190. doi:10.1530/ERC-17-0036. PMID 28341725.
40. ^ Jump up to: a b c d "Metastatic Cancer: Questions and Answers". National Cancer Institute. 12 May 2015. Retrieved 28 March 2018.
41. Cohen S, Murphy ML, Prather AA (January 2019). "Ten Surprising Facts About Stressful Life Events and Disease Risk". *Annual Review of Psychology*. 70: 577–597. doi:10.1146/annurev-psych-010418-102857. PMC 6996482. PMID 29949726. the strongest conclusion derived from decades of research on stressors and cancer is that stressful events may be associated with decreased cancer survival but are probably not associated with disease incidence (Chida et al. 2008).
42. Heikkilä K, Nyberg ST, Theorell T, Fransson EI, Alfredsson L, Bjorner JB, et al. (February 2013). "Work stress and risk of cancer: meta-analysis of 5700 incident cancer events in 116,000 European men and women". *BMJ*. 346: f165. doi:10.1136/bmj.f165. PMC 3567204. PMID 23393080.
43. Galway K, Black A, Cantwell M, Cardwell CR, Mills M, Donnelly M (November 2012). "Psychosocial interventions to improve quality of life and emotional wellbeing for recently diagnosed cancer patients". *The Cochrane Database of Systematic Reviews*. 11: CD007064. doi:10.1002/14651858.cd007064.pub2. PMC 6457819. PMID 23152241
44. Bailey and Love's *Short Practice of Surgery* (27th ed.). p. 1315.
45. Selim, Jocelyn (Fall 2009), "The Fairest of All", CR, Philadelphia: American Association for Cancer Research, vol. 4, no. 4, archived from the original on April 19, 2010, retrieved January 22, 2011

46. he original on 14 July 2017. Retrieved 18 July 2017.
47. "EAU Guidelines: Non-muscle-invasive Bladder Cancer". Uroweb.
48. "Bladder Cancer - Stages and Grades". Cancer.Net. 25 June 2012.
49. "Bladder cancer". World Cancer Research Fund. 24 April 2018.
50. "Survival statistics for bladder cancer - Canadian Cancer Society". www.cancer.ca.
51. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. (GBD 2015 Mortality and Causes of Death Collaborators) (October 2016). "Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet*. 388 (10053): 1459–1544. doi:10.1016/S0140-6736(16)31012-1. PMC 5388903. PMID 27733281.
52. Longo DL (2012). "369 Seizures and Epilepsy". *Harrison's principles of internal medicine* (18th ed.). McGraw-Hill. p. 3258. ISBN 978-0-07-174887-2.
53. "Benign brain tumour (non-cancerous)". nhs.uk. 20 October 2017. Retrieved 29 July 2019.
54. Merrell RT (December 2012). "Brain tumors". *Disease-a-Month*. 58 (12): 678–89. doi:10.1016/j.disamonth.2012.08.009. PMID 23149521.
55. *World Cancer Report 2014*. World Health Organization. 2014. pp. Chapter 1.3. ISBN 978-9283204299.
56. Mantovani, Alessandro; Targher, Giovanni (July 2017). "Type 2 diabetes mellitus and risk of hepatocellular carcinoma: spotlight on nonalcoholic fatty liver disease". *Annals of Translational Medicine*. 5 (13): 270. doi:10.21037/atm.2017.04.41. ISSN 2305-5839. PMC 5515814. PMID 28758096.
57. Akinyemiju, Tomi; Abera, Semaw; Ahmed, Muktar; Alam, Noore; Alemayohu, Mulubirhan Assefa; Allen, Christine; Al-Raddadi, Rajaa; Alvis-Guzman, Nelson; Amoako, Yaw; Artaman, Al; Ayele, Tadesse Awoke (2017-12-01). "The Burden of Primary Liver Cancer and Underlying Etiologies From 1990 to 2015 at the Global, Regional, and National Level". *JAMA Oncology*. 3 (12): 1683–1691. doi:10.1001/jamaoncol.2017.3055. hdl:10037/11672. ISSN 2374-2437. PMC 5824275. PMID 28983565.
58. Cholangiocarcinoma at eMedicine

59. "Liver tumors in Children". Boston Children's Hospital. Archived from the original on 2011-06-04.
60. White V, Ruperelia P (2020). "28.Respiratory disease". In Feather A, Randall D, Waterhouse M (eds.). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier. pp. 975–982. ISBN 978-0-7020-7870-5.
61. "Non-Small Cell Lung Cancer Treatment – Patient Version (PDQ®)". NCI. 12 May 2015. Archived from the original on 29 February 2016. Retrieved 5 March 2016.
62. Falk S, Williams C (2010). "Chapter 1". Lung Cancer – the facts (3rd ed.). Oxford University Press. pp. 3–4. ISBN 978-0-19-956933-5.
63. Thun MJ, Hannan LM, Adams-Campbell LL, Boffetta P, Buring JE, Feskanich D, et al. (September 2008). "Lung cancer occurrence in never-smokers: an analysis of 13 cohorts and 22 cancer registry studies". PLOS Medicine. 5 (9): e185. doi:10.1371/journal.pmed.0050185. PMC 2531137. PMID 18788891.
64. Carmona RH (27 June 2006). The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. Publications and Reports of the Surgeon General. U.S. Department of Health and Human Services. Archived from the original on 15 February 2017. Secondhand smoke exposure causes disease and premature death in children and adults who do not smoke. Retrieved 2014-06-16
65. "Tobacco Smoke and Involuntary Smoking" (PDF). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. WHO International Agency for Research on Cancer. 83. 2004. Archived (PDF) from the original on 13 August 2015. There is sufficient evidence that involuntary smoking (exposure to secondhand or 'environmental' tobacco smoke) causes lung cancer in humans. ... Involuntary smoking (exposure to secondhand or 'environmental' tobacco smoke) is carcinogenic to humans (Group 1).
66. "Lung Carcinoma: Tumors of the Lungs". Merck Manual Professional Edition, Online edition. July 2020. Retrieved 21 July 2021.
67. Collins LG, Haines C, Perkel R, Enck RE (January 2007). "Lung cancer: diagnosis and management". American Family Physician. 75 (1): 56–63. PMID 17225705. Archived from the original on 29 September 2007.
68. "Lung Cancer Prevention–Patient Version (PDQ®)". NCI. 4 November 2015. Archived from the original on 9 March 2016. Retrieved 5 March 2016.
69. Chapman S, Robinson G, Stradling J, West S, Wrightson J (2014). "Chapter 31". Oxford

- Handbook of Respiratory Medicine (3rd ed.). Oxford University Press. p. 284. ISBN 978- 0-19-870386-0.
70. Romaszko AM, Doboszyńska A (May 2018). "Multiple primary lung cancer: A literature review". *Advances in Clinical and Experimental Medicine*. 27 (5): 725–730. doi:10.17219/acem/68631. PMID 29790681. S2CID 46897665.
 71. Majumder S (2009). *Stem cells and cancer* (Online-Ausg. ed.). New York: Springer. p. 193. ISBN 978-0-387-89611-3. Archived from the original on 18 October 2015.
 72. doi:10.1097/00001622-200309000-00008. PMID 12960522. S2CID 33259363.
 73. "SEER Stat Fact Sheets: Melanoma of the Skin". NCI. Archived from the original on 6 July 2014. Retrieved 18 June 2014.
 74. "Release: Cancer Survival Rates, Cancer Survival in England, Patients Diagnosed 2005– 2009 and Followed up to 2010". Office for National Statistics. 15 November 2011. Archived from the original on 17 October 2014. Retrieved 30 June 2014.
 75. Dubas LE, Ingraffea A (February 2013). "Nonmelanoma skin cancer". *Facial Plastic Surgery Clinics of North America*. 21 (1): 43–53. doi:10.1016/j.fsc.2012.10.003. PMID 23369588.
 76. "How common is skin cancer?". World Health Organization. Archived from the original on 27 September 2010. Retrieved 30 June 2014.
 77. Harris RE (2013). *Epidemiology of Chronic Disease*. Jones & Bartlett Publishers. p. 271. ISBN 9780763780470.
 78. Swetter SM (30 August 2010). "Malignant Melanoma". *eMedicine Dermatology*. Archived from the original on 7 October 2010.
 79. "Cancer – Signs and symptoms". NHS Choices. Archived from the original on 8 June 2014. Retrieved 10 June 2014.
 80. "Cancer". World Health Organization. 12 September 2018. Retrieved 19 December 2018.
 81. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB (September 2008). "Cancer is a preventable disease that requires major lifestyle changes". *Pharmaceutical Research*. 25 (9): 2097–116. doi:10.1007/s11095-008-9661-9. PMC 2515569. PMID 18626751.
 82. "Targeted Cancer Therapies". cancer.gov. National Cancer Institute. 26 February 2018. Retrieved 28 March 2018.
 83. "SEER Stat Fact Sheets: All Cancer Sites". National Cancer Institute. Archived from the original

- on 26 September 2010. Retrieved 18 June 2014.
84. "Colon Cancer Treatment (PDQ®)". NCI. May 12, 2014. Archived from the original on July 5, 2014. Retrieved June 29, 2014.
 85. "SEER Stat Fact Sheets: Colon and Rectum Cancer". NCI. Archived from the original on June 24, 2014. Retrieved June 18, 2014.
 86. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, et al. (GBD 2015 Disease and Injury Incidence and Prevalence Collaborators) (October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet*. 388 (10053): 1545–1602. doi:10.1016/S0140-6736(16)31678-6. PMC 5055577. PMID 27733282.
 87. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (November 2018). "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries". *CA: A Cancer Journal for Clinicians*. 68 (6): 394–424. doi:10.3322/caac.21492. PMID 30207593. S2CID 52188256.
 88. Thorat MA, Cuzick J (December 2013). "Role of aspirin in cancer prevention". *Current Oncology Reports*. 15 (6): 533–540. doi:10.1007/s11912-013-0351-3. PMID 24114189. S2CID 40187047.
 89. "Routine aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer: recommendation statement". *American Family Physician*. 76 (1): 109–113. July 2007. PMID 17668849. Archived from the original on July 14, 2014.
 90. "Breast Cancer Treatment (PDQ®)". NCI. 23 May 2014. Archived from the original on 5 July 2014. Retrieved 29 June 2014.
 91. *World Cancer Report 2014*. World Health Organization. 2014. pp. Chapter 5.2. ISBN 978-92-832-0429-9.
 92. Saunders C, Jassal S (2009). *Breast cancer* (1. ed.). Oxford: Oxford University Press. p. Chapter 13. ISBN 978-0-19-955869-8. Archived from the original on 25 October 2015.
 93. Gøtzsche PC, Jørgensen KJ (June 2013). "Screening for breast cancer with mammography". *The Cochrane Database of Systematic Reviews*. 6 (6): CD001877. doi:10.1002/14651858.CD001877.pub5. PMC 6464778. PMID 23737396.

94. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan B, Nygren P, Humphrey L (November 2009). "Screening for Breast Cancer: Systematic Evidence Review Update for the US Preventive Services Task Force [Internet]". U.S. Preventive Services Task Force Evidence Syntheses. Rockville, MD: Agency for Healthcare Research and Quality. PMID 20722173. Report No.: 10-05142-EF-1.
95. Siu AL (February 2016). "Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement". *Annals of Internal Medicine*. 164 (4): 279–96. doi:10.7326/M15-2886. PMID 26757170.
96. "Five Things Physicians and Patients Should Question". Choosing Wisely: an initiative of the ABIM Foundation. American College of Surgeons. September 2013. Archived from the original on 27 October 2013. Retrieved 2 January 2013.
97. "Breast Cancer Treatment (PDQ®)". NCI. 26 June 2014. Archived from the original on 5 July 2014. Retrieved 29 June 2014.
98. "World Cancer Report" (PDF). International Agency for Research on Cancer. 2008. Archived from the original (PDF) on 20 July 2011. Retrieved 26 February 2011.
99. World Cancer Report 2014. World Health Organization. 2014. pp. Chapter 1.1. ISBN 978-92-832-0429-9.
100. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (November 2018). "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries". *CA: A Cancer Journal for Clinicians*. 68 (6): 394–424. doi:10.3322/caac.21492. PMID 30207593. S2CID 52188256.
101. "Male Breast Cancer Treatment". National Cancer Institute. 2014. Archived from the original on 4 July 2014. Retrieved 29 June 2014.
102. Merck Manual of Diagnosis and Therapy (February 2003). "Breast Disorders: Breast Cancer". Archived from the original on 2 October 2011. Retrieved 5 February 2008.
103. American Cancer Society (2007). "Cancer Facts & Figures 2007" (PDF). Archived from the original (PDF) on 10 April 2007. Retrieved 26 April 2007.
104. Merck Manual of Diagnosis and Therapy (February 2003). "Breast Disorders: Breast Cancer". Archived from the original on 2 October 2011. Retrieved 5 February 2008.
105. American Cancer Society (2007). "Cancer Facts & Figures 2007" (PDF). Archived from the original (PDF) on 10 April 2007. Retrieved 26 April 2007.

106. Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, et al. (January 2007). "Mammographic density and the risk and detection of breast cancer". *The New England Journal of Medicine*. 356 (3): 227–36. doi:10.1056/NEJMoa062790. PMID 17229950.
107. Watson M (2008). "Assessment of suspected cancer". *InnoAiT*. 1 (2): 94–107. doi:10.1093/innovait/inn001. S2CID 71908359.
108. "Breast Cancer Evaluation". *eMedicine*. 23 August 2006. Archived from the original on 12 February 2008. Retrieved 5 February 2008.
109. Ashikari R, Park K, Huvos AG, Urban JA (September 1970). "Paget's disease of the breast". *Cancer*. 26 (3): 680–5. doi:10.1002/1097-0142(197009)26:3<680::aid-cncr2820260329>3.0.co;2-p. PMID 4318756.
110. Kollmorgen DR, Varanasi JS, Edge SB, Carson WE (August 1998). "Paget's disease of the breast: a 33-year experience". *Journal of the American College of Surgeons*. 187 (2): 171–7. doi:10.1016/S1072-7515(98)00143-4. PMID 9704964.
111. Kleer CG, van Golen KL, Merajver SD (1 December 2000). "Molecular biology of breast cancer metastasis. Inflammatory breast cancer: clinical syndrome and molecular determinants". *Breast Cancer Research*. 2 (6): 423–9. doi:10.1186/bcr89. PMC 138665. PMID 11250736.
112. answers.com. "Oncology Encyclopedia: Cystosarcoma Phyllodes". *Answers.com*. Archived from the original on 8 September 2010. Retrieved 10 August 2010.
113. Lacroix M (December 2006). "Significance, detection and markers of disseminated breast cancer cells". *Endocrine-Related Cancer*. 13 (4): 1033–67. doi:10.1677/ERC-06-0001. PMID 17158753.

114. "Stage 4 :: The National Breast Cancer Foundation".
www.nationalbreastcancer.org.
115. National Cancer Institute (1 September 2004). "Metastatic Cancer: Questions and Answers". Archived from the original on 27 August 2008. Retrieved 6 February 2008.
116. Perera N, Fernando N, Perera R (March 2020). "Metastatic breast cancer spread to peripancreatic lymph nodes causing biliary obstruction". *The Breast Journal*. 26 (3): 511–13. doi:10.1111/tbj.13531. PMID 31538691.
117. *Interpreting Signs and Symptoms*. Lippincott Williams & Wilkins. 2007. pp. 99–. ISBN 978-1-58255-668-0.
118. Merck Manual of Diagnosis and Therapy (February 2003). "Breast Disorders: Overview of Breast Disorders". Archived from the original on 3 October 2011. Retrieved 5 February 2008.
119. Saslow D, Hannan J, Osuch J, Alciati MH, Baines C, Barton M, et al. (2004). "Clinical breast examination: practical recommendations for optimizing performance and reporting". *CA: A Cancer Journal for Clinicians*. 54 (6): 327–44. doi:10.3322/canjclin.54.6.327. PMID 15537576.
120. Yu YH, Liang C, Yuan XZ (April 2010). "Diagnostic value of vacuum-assisted breast biopsy for breast carcinoma: a meta-analysis and systematic review". *Breast Cancer Research and Treatment*. 120 (2): 469–79. doi:10.1007/s10549-010-0750-1. PMID 20130983. S2CID 22685290.
121. Ferguson MJ (June 2020). "Multifocal invasive mucinous carcinoma of the breast". *Journal of Medical Radiation Sciences*. 67 (2): 155–158. doi:10.1002/jmrs.379. PMC 7276192. PMID 31975569.
122. Kumar V, Abul Abbas (2010). *Robbins and Cotran Pathologic Basis of Disease*. Philadelphia: Saunders, an imprint of Elsevier inc. p. 1090. ISBN 978-1-4160-3121-5.
123. Sotiriou C, Pusztai L (February 2009). "Gene-expression signatures in breast cancer". *The New England Journal of Medicine*. 360 (8): 790–800. doi:10.1056/NEJMra0801289. PMID 19228622.
124. Romond EH, Perez EA, Bryant J, Suman VJ, Geyer CE, Davidson NE, et al. (October 2005). "Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer". *The New England Journal of Medicine*. 353 (16): 1673–84.
125. "Lifestyle-related Breast Cancer Risk Factors". www.cancer.org. Retrieved 18 April 2018.
126. Eliassen AH, Hankinson SE, Rosner B, Holmes MD, Willett WC (October 2010). "Physical activity and risk of breast cancer among postmenopausal women". *Archives of Internal Medicine*. 170

(19): 1758–64. doi:10.1001/archinternmed.2010.363. PMC 3142573. PMID 20975025.

127. Kyu HH, Bachman VF, Alexander LT, Mumford JE, Afshin A, Estep K, et al. (August 2016). "Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013". *BMJ*. 354: i3857. doi:10.1136/bmj.i3857. PMC 4979358. PMID 27510511.
128. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, et al. (January 2016). "American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline". *CA: A Cancer Journal for Clinicians*. 66 (1): 43–73. doi:10.3322/caac.21319. PMID 26641959.
129. Song JK, Bae JM (March 2013). "Citrus fruit intake and breast cancer risk: a quantitative systematic review". *Journal of Breast Cancer*. 16 (1): 72–6. doi:10.4048/jbc.2013.16.1.72. PMC 3625773. PMID 23593085.
130. Zheng JS, Hu XJ, Zhao YM, Yang J, Li D (June 2013). "Intake of fish and marine n-3 polyunsaturated fatty acids and risk of breast cancer: meta-analysis of data from 21 independent prospective cohort studies". *BMJ*. 346: f3706. doi:10.1136/bmj.f3706. PMID 23814120.
131. Wu AH, Yu MC, Tseng CC, Pike MC (January 2008). "Epidemiology of soy exposures and breast cancer risk". *British Journal of Cancer*. 98 (1): 9–14. doi:10.1038/sj.bjc.6604145. PMC 2359677. PMID 18182974.
132. Hartmann LC, Schaid DJ, Woods JE, Crotty TP, Myers JL, Arnold PG, et al. (January 1999). "Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer". *The New England Journal of Medicine*. 340 (2): 77–84. doi:10.1056/NEJM199901143400201. PMID 9887158.
133. Meijers-Heijboer H, van Geel B, van Putten WL, Henzen-Logmans SC, Seynaeve C, Menke-Pluymers MB, et al. (July 2001). "Breast cancer after prophylactic bilateral mastectomy in women with a BRCA1 or BRCA2 mutation" (PDF). *The New England Journal of Medicine*. 345 (3): 159–64. doi:10.1056/NEJM200107193450301. PMID 11463009.
134. Carbine NE, Lostumbo L, Wallace J, Ko H (April 2018). "Risk-reducing mastectomy for the prevention of primary breast cancer". *The Cochrane Database of Systematic Reviews*. 4: CD002748.

doi:10.1002/14651858.cd002748.pub4. PMC 6494635. PMID 29620792.

135. Moyer VA (February 2014). "Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement". *Annals of Internal Medicine*. 160 (4): 271–81. doi:10.7326/M13-2747. PMID 24366376.
136. Nelson HD, Smith ME, Griffin JC, Fu R (April 2013). "Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. Preventive Services Task Force". *Annals of Internal Medicine*. 158 (8): 604–14. doi:10.7326/0003-4819-158-8-201304160-00005. PMID 23588749.
137. Cuzick J, Sestak I, Bonanni B, Costantino JP, Cummings S, DeCensi A, et al. (May 2013). "Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data". *Lancet*. 381 (9880): 1827–34. doi:10.1016/S0140-6736(13)60140-3. PMC 3671272. PMID 23639488.
138. Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, Caughey AB, et al. (September 2019). "Medication Use to Reduce Risk of Breast Cancer: US Preventive Services Task Force Recommendation Statement". *JAMA*. 322 (9): 857–867. doi:10.1001/jama.2019.11885. PMID 31479144.
139. Cuzick J, Sestak I, Bonanni B, Costantino JP, Cummings S, DeCensi A, et al. (May 2013). "Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data". *Lancet*. 381 (9880): 1827–34. doi:10.1016/S0140-6736(13)60140-3. PMC 3671272. PMID 23639488.
140. Mocellin S, Goodwin A, Pasquali S (April 2019). "Risk-reducing medications for primary breast cancer: a network meta-analysis". *The Cochrane Database of Systematic Reviews*. 4: CD012191. doi:10.1002/14651858.cd012191.pub2. PMC 6487387. PMID 31032883.
141. Khalil DN, Smith EL, Brentjens RJ, Wolchok JD (May 2016). "The future of cancer treatment: immunomodulation, CARs and combination immunotherapy". *Nature Reviews. Clinical Oncology*. 13 (5): 273–90. doi:10.1038/nrclinonc.2016.25. PMC 5551685. PMID 26977780.
142. Leite AM, Macedo AV, Jorge AJ, Martins WA (August 2018). "Antiplatelet Therapy in Breast Cancer Patients Using Hormonal Therapy: Myths, Evidence and Potentialities – Systematic Review". *Arquivos Brasileiros de Cardiologia*. 111 (2): 205–

212. doi:10.5935/abc.20180138. PMC 6122903. PMID 30183988.
143. Holmes MD, Chen WY, Li L, Hertzmark E, Spiegelman D, Hankinson SE (March 2010). "Aspirin intake and survival after breast cancer". *Journal of Clinical Oncology*. 28 (9): 1467–72. doi:10.1200/JCO.2009.22.7918. PMC 2849768. PMID 20159825.
144. Bao T, Rudek MA (2011). "The Clinical Pharmacology of Anastrozole". *European Oncology & Haematology*. 7 (2): 106–8. doi:10.17925/EOH.2011.07.02.106. S2CID 1802863.
145. Burstein HJ, Temin S, Anderson H, Buchholz TA, Davidson NE, Gelmon KE, et al. (July 2014). "Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: american society of clinical oncology clinical practice guideline focused update". *Journal of Clinical Oncology*. 32 (21): 2255–69. doi:10.1200/JCO.2013.54.2258. PMC 4876310. PMID 24868023.
146. Romero SA, Young K, Hickey M, Su HI (21 December 2020). "Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen". *Cochrane Database Syst Rev*. 12 (2): CD007245. doi:10.1002/14651858.CD007245.pub4. PMC 8092675. PMID 33348436.
147. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) (October 2015). "Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials". *Lancet*. 386 (10001): 1341–1352. doi:10.1016/S0140-6736(15)61074-1. PMID 26211827.
148. Petit T, Dufour P, Tannock I (June 2011). "A critical evaluation of the role of aromatase inhibitors as adjuvant therapy for postmenopausal women with breast cancer". *Endocrine-Related Cancer*. 18 (3): R79-89. doi:10.1530/ERC-10-0162. PMID 21502311.
149. "Treatment of metastatic breast cancer". www.uptodate.com. Archived from the original on 4 September 2017. Retrieved 4 September 2017.
150. "Combination of Ribociclib and Letrozole Is a Home Run in Advanced Breast Cancer – The ASCO Post". ascopost.com. Retrieved 31 January 2019.
151. Jahanzeb M (August 2008). "Adjuvant trastuzumab therapy for HER2-positive breast cancer". *Clinical Breast Cancer*. 8 (4): 324–33. doi:10.3816/CBC.2008.n.037. PMID 18757259.
152. "Entrez Gene: ERBB2 v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)". Archived from the original on 26 October 2009.

Retrieved 17 November 2015.

153. "Herceptin (trastuzumab) Adjuvant HER2+ Breast Cancer Therapy Pivotal Studies and Efficacy Data". Herceptin.com. Archived from the original on 6 April 2010. Retrieved 8 May 2010.
154. "New ASCO Guidelines on Treating Advanced-Stage HER2-Positive Breast Cancer". Breastcancer.org. 4 October 2016. Retrieved 31 January 2019.
155. Slamon DJ, Leyland-Jones B, Shak S, Fuchs H, Paton V, Bajamonde A, et al. (March 2001). "Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2". *The New England Journal of Medicine*. 344 (11): 783–92. doi:10.1056/NEJM200103153441101. PMID 11248153.
156. Massarut S, Baldassare G, Belletti B, Reccanello S, D'Andrea S, Ezio C, Perin T, Roncadin M, Vaidya JS (2006). "Intraoperative radiotherapy impairs breast cancer cell motility induced by surgical wound fluid". *J Clin Oncol*. 24 (18S): 10611. doi:10.1200/jco.2006.24.18_suppl.10611. Archived from the original on 12 January 2012. Retrieved 9 June 2010.
157. Belletti B, Vaidya JS, D'Andrea S, Entschladen F, Roncadin M, Lovat F, et al. (March 2008). "Targeted intraoperative radiotherapy impairs the stimulation of breast cancer cell proliferation and invasion caused by surgical wounding". *Clinical Cancer Research*. 14 (5): 1325–32. doi:10.1158/1078-0432.CCR-07-4453. PMID 18316551.
158. "Radiation Therapy". Breastcancer.org. Archived from the original on 17 November 2015. Retrieved 17 November 2015.
159. Hickey BE, Lehman M (30 August 2021). "Partial breast irradiation versus whole breast radiotherapy for early breast cancer". *The Cochrane Database of Systematic Reviews*. 2021 (8): CD007077. doi:10.1002/14651858.CD007077.pub4. PMC 8406917. PMID 34459500.
160. Moschetti I, Cinquini M, Lambertini M, Levaggi A, Liberati A (May 2016). "Follow-up strategies for women treated for early breast cancer". *The Cochrane Database of Systematic Reviews*. 2016 (5): CD001768. doi:10.1002/14651858.cd001768.pub3. PMC 7073405. PMID 27230946.
161. Khan F, Amatya B, Ng L, Demetrios M, Zhang NY, Turner-Stokes L (December 2012). "Multidisciplinary rehabilitation for follow-up of women treated for breast cancer". *The Cochrane Database of Systematic Reviews*. 12 (3): CD009553. doi:10.1002/14651858.cd009553.pub2. PMC 8078577. PMID 23235677.

162. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ (November 2015). "Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline" (PDF). *J. Clin. Endocrinol. Metab.* 100 (11): 3975– 4011. doi:10.1210/jc.2015-2236. PMID 26444994.
163. Santen RJ, Allred DC, Ardoin SP, Archer DF, Boyd N, Braunstein GD, Burger HG, Colditz GA, Davis SR, Gambacciani M, Gower BA, Henderson VW, Jarjour WN, Karas RH, Kleerekoper M, Lobo RA, Manson JE, Marsden J, Martin KA, Martin L, Pinkerton JV, Rubinow DR, Teede H, Thiboutot DM, Utian WH (July 2010). "Postmenopausal hormone therapy: an Endocrine Society scientific statement". *J. Clin. Endocrinol. Metab.* 95 (7 Suppl 1): s1–s66. doi:10.1210/jc.2009-2509. PMC 6287288. PMID 20566620.
164. Shuster, Lynne T.; Rhodes, Deborah J.; Gostout, Bobbie S.; Grossardt, Brandon R.; Rocca, Walter A. (2010). "Premature menopause or early menopause: Long-term health consequences". *Maturitas.* 65 (2): 161–166. doi:10.1016/j.maturitas.2009.08.003. ISSN 0378-5122. PMC 2815011. PMID 19733988.
165. Eden KJ, Wylie KR (1 July 2009). "Quality of sexual life and menopause". *Women's Health.* 6 (4): 385–396. doi:10.2217/WHE.09.24. PMID 19586430.
166. Ziaei S., Moghasemi M., Faghihzadeh S. (2010). "Comparative effects of conventional hormone replacement therapy and tibolone on climacteric symptoms and sexual dysfunction in postmenopausal women". *Climacteric.* 13 (3): 147–156. doi:10.1016/j.maturitas.2006.04.014. PMID 16730929.
167. Manson, JE; Aragaki, AK; Rossouw, JE; Anderson, GL; Prentice, RL; LaCroix, AZ; Chlebowski, RT; Howard, BV; Thomson, CA; Margolis, KL; Lewis, CE; Stefanick, ML; Jackson, RD; Johnson, KC; Martin, LW; Shumaker, SA; Espeland, MA; Wactawski- Wende, J; WHI, Investigators. (12 September 2017). "Menopausal Hormone Therapy and Long-term All-Cause and Cause-Specific Mortality: The Women's Health Initiative Randomized Trials". *JAMA.* 318 (10): 927–938. doi:10.1001/jama.2017.11217. PMC 5728370. PMID 28898378.
168. Langer, RD; Hodis, HN; Lobo, RA; Allison, MA (February 2021). "Hormone replacement therapy - where are we now?". *Climacteric : The Journal of the International Menopause Society.* 24 (1): 3–10. doi:10.1080/13697137.2020.1851183. PMID 33403881.

S2CID 230783545.

169. Løkkegaard, E; Nielsen, LH; Keiding, N (August 2017). "Risk of Stroke With Various Types of Menopausal Hormone Therapies: A National Cohort Study". *Stroke*. 48 (8): 2266–2269. doi:10.1161/STROKEAHA.117.017132. PMID 28626058. S2CID 207579406.
170. Files, JA; Ko, MG; Pruthi, S (July 2011). "Bioidentical hormone therapy". *Mayo Clinic Proceedings*. 86 (7): 673–80, quiz 680. doi:10.4065/mcp.2010.0714. PMC 3127562. PMID 21531972.
171. Zeng, Z; Jiang, X; Li, X; Wells, A; Luo, Y; Neapolitan, R (2018). "Conjugated equine estrogen and medroxyprogesterone acetate are associated with decreased risk of breast cancer relative to bioidentical hormone therapy and controls". *PLOS ONE*. 13 (5): e0197064. Bibcode:2018PLoSO..1397064Z. doi:10.1371/journal.pone.0197064. PMC 5955567. PMID 29768475.
172. Fournier, A. S.; Berrino, F.; Clavel-Chapelon, F. O. (2007). "Unequal risks for breast cancer associated with different hormone replacement therapies: Results from the E3N cohort study". *Breast Cancer Research and Treatment*. 107 (1): 103–111. doi:10.1007/s10549-007-9523-x. PMC 2211383. PMID 17333341.
173. Beral, V; Reeves, G; Bull, D; Green, J; Million Women Study, Collaborators. (16 February 2011). "Breast cancer risk in relation to the interval between menopause and starting hormone therapy". *Journal of the National Cancer Institute*. 103 (4): 296–305. doi:10.1093/jnci/djq527. PMC 3039726. PMID 21278356. {{cite journal}}: |first5= has generic name (help)
174. Letendre, I.; Lopes, P. (2012). "Ménopause et risques carcinologiques". *Journal de Gynécologie Obstétrique et Biologie de la Reproduction*. 41 (7): F33–F37. doi:10.1016/j.jgyn.2012.09.006. PMID 23062839.
175. Chlebowski, RT; Anderson, GL; Aragaki, AK; Manson, JE; Stefanick, ML; Pan, K; Barrington, W; Kuller, LH; Simon, MS; Lane, D; Johnson, KC; Rohan, TE; Gass, MLS; Cauley, JA; Paskett, ED; Sattari, M; Prentice, RL (28 July 2020). "Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long- term Follow-up of the Women's Health Initiative Randomized Clinical Trials". *JAMA*. 324 (4): 369–380. doi:10.1001/jama.2020.9482. PMC 7388026. PMID 32721007.
176. Anderson, G. L.; Limacher, M.; Assaf, A. R.; Bassford, T.; Beresford, S. A.; Black, H.;

- Bonds, D.; Brunner, R.; Brzyski, R.; Caan, B.; Chlebowski, R.; Curb, D.; Gass, M.; Hays, J.; Heiss, G.; Hendrix, S.; Howard, B. V.; Hsia, J.; Hubbell, A.; Jackson, R.; Johnson, K. C.; Judd, H.; Kotchen, J. M.; Kuller, L.; Lacroix, A. Z.; Lane, D.; Langer, R. D.; Lasser, N.; Lewis, C. E.; Manson, J. (2004). "Effects of Conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy: The Women's Health Initiative Randomized Controlled Trial". *JAMA: The Journal of the American Medical Association*. 291 (14): 1701–1712. doi:10.1001/jama.291.14.1701. PMID 15082697.
177. Stefanick ML; Anderson GL; Margolis KL; et al. (2006). "Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy". *JAMA*. 295 (14): 1647–57. doi:10.1001/jama.295.14.1647. PMID 16609086.
178. "Association between hormone replacement therapy use and breast cancer risk varies by race/ethnicity, body mass index, and breast density". *JNCI Journal of the National Cancer Institute*. 105 (18). 2013. doi:10.1093/jnci/djt264. ISSN 0027-8874.
179. In turn citing: Hou, N.; Hong, S.; Wang, W.; Olopade, O. I.; Dignam, J. J.; Huo, D. (2013). "Hormone Replacement Therapy and Breast Cancer: Heterogeneous Risks by Race, Weight, and Breast Density". *JNCI Journal of the National Cancer Institute*. 105 (18): 1365–1372. doi:10.1093/jnci/djt207. ISSN 0027-8874. PMC 3776262. PMID 24003037.
180. Kuhl, H.; Schneider, H. P. G. (2013). "Progesterone – promoter or inhibitor of breast cancer". *Climacteric*. 16 Suppl 1: 54–68. doi:10.3109/13697137.2013.768806. PMID 23336704. S2CID 20808536.
181. Azam, S; Lange, T; Huynh, S; Aro, AR; von Euler-Chelpin, M; Vejborg, I; Tjønneland, A; Lynge, E; Andersen, ZJ (June 2018). "Hormone replacement therapy, mammographic density, and breast cancer risk: a cohort study". *Cancer Causes & Control*. 29 (6): 495–505. doi:10.1007/s10552-018-1033-0. PMC 5938298. PMID 29671181.
182. Stute, P; Wildt, L; Neulen, J (April 2018). "The impact of micronized progesterone on breast cancer risk: a systematic review". *Climacteric : The Journal of the International Menopause Society*. 21 (2): 111–122. doi:10.1080/13697137.2017.1421925. PMID 29384406. S2CID 3642971.
183. Panay, N; Medical Advisory Council of the British Menopause, Society. (June 2019).

- "BMS - Consensus statement: Bioidentical HRT". *Post Reproductive Health*. 25 (2): 61–63. doi:10.1177/2053369119841844. PMID 31192760. S2CID 189816648.
184. Management of the menopause after breast cancer Archived 2016-04-07 at archive.today, from The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement C-Gyn 15. 1st Endorsed: February 2003. Current: November 2011. Review: November 2014
185. Gordhandas, S; Norquist, BM; Pennington, KP; Yung, RL; Laya, MB; Swisher, EM (April 2019). "Hormone replacement therapy after risk reducing salpingo- oophorectomy in patients with BRCA1 or BRCA2 mutations; a systematic review of risks and benefits". *Gynecologic Oncology*. 153 (1): 192–200. doi:10.1016/j.ygyno.2018.12.014. PMID 30661763. S2CID 58593390.
186. Heinig, M; Schwarz, S; Haug, U (16 February 2021). "Self-selection for mammography screening according to use of hormone replacement therapy: A systematic literature review". *Cancer Epidemiology*. 71 (Pt A): 101812. doi:10.1016/j.canep.2020.101812. PMID 33608235. S2CID 231970420.
187. Waks, A. G., & Winer, E. P. (2019). Breast cancer treatment: a review. *Jama*, 321(3), 288-300.
188. Fentiman, I. S., Fourquet, A., & Hortobagyi, G. N. (2006). Male breast cancer. *The Lancet*, 367(9510), 595-604.
189. MacMahon, B. (2006). Epidemiology and the causes of breast cancer. *International journal of cancer*, 118(10), 2373-2378.
190. Key, T. J., Verkasalo, P. K., & Banks, E. (2001). Epidemiology of breast cancer. *The lancet oncology*, 2(3), 133-140.
191. Hankinson SE, Manson JE, London SJ, Willett WC, Speizer FE. Laboratory reproducibility of endogenous hormone levels in postmenopausal women. *Cancer Epidemiol Biomarkers Prev* 1994;3:51–6.
192. Toniolo PG, Levitz M, Zeleniuch-Jacquotte A, Banerjee S, Koenig KL, Shore RE, et al. A prospective study of endogenous estrogens and breast cancer in postmenopausal women. *J Natl Cancer Inst* 1995;87:190–7.
193. Cauley J, Lucas F, Kuller L, Stone K, Cummings SR. Is bone mineral density a biological marker of a woman's cumulative exposure to estrogen? Presented at a meeting of the American Epidemiological Society, Rochester, MN, March 13 and 14, 1997.

194. Thomas HV, Key TJ, Allen DS, Moore JW, Dowsett M, Fentiman IS, et al. A prospective study of endogenous serum hormone concentrations and breast cancer risk in postmenopausal women on the island of Guernsey. *Br J Cancer* 1997;76:401–5.
195. Helzlsouer KJ, Alberg AJ, Bush TL, Longcope C, Gordon GB, Comstock GW. A prospective study of endogenous hormones and breast cancer. *Cancer Detect Prev* 1994;18:79–85.
196. Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, Sciajno R, et al. Serum sex hormone levels after menopause and subsequent breast cancer. *J Natl Cancer Inst* 1996;88:291–6.
197. Clarke C, Sutherland R. Progestin regulation of cellular proliferation. update 1993. In: Horwitz K, editor. *Endocrine reviews. Monograph 1. Endocrine aspects of cancer*. Bethesda (MD): Endocr Soc, 1993: 132–5.
198. Wren B. Hormonal replacement therapy and breast cancer. *Eur Menopause J* 1995;2:13–9.
199. Myers JS, Connor RE. Cell proliferation in fibrocystic disease and postmenopause breast ducts measured by thymidine labeling. *Cancer* 1982;50: 746–51.
200. Yager JD, Liehr JG. Molecular mechanisms of estrogen carcinogenesis. *Annu Rev Pharmacol Toxicol* 1996;36:203–32.