

# Non-Small Cell Lung Cancer: An Updated Overview

Mohammad Qasim Minhas

St. Stephen's Episcopal School

## ABSTRACT

Lung cancer is the most common cause of cancer-related deaths worldwide, as 2.1 million people were diagnosed with the disease and 1.8 million passed away from lung cancer worldwide in 2018.<sup>1</sup> The condition is split into two sections: Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC). In this review paper, I discuss key aspects of NSCLC, including risk factors, symptoms, diagnosis, treatment, prevention, and epidemiology. Lastly, I conclude by outlining ongoing research aiming to prevent NSCLC.

## Lung Cancer/NSCLC Definition and History

Lung cancer continues to be the leading cause of cancer-related deaths in the US, with an estimated 235,760 new cases and 131,880 deaths in the US to occur in 2021,<sup>2</sup> with 80-85% of cases being Non-Small Cell Lung Cancer (NSCLC).<sup>3</sup> Cigarette smoking is the primary cause of lung cancer, as it is responsible for 90% of NSCLC cases each year.<sup>4</sup>

NSCLC is one of the two main classifications of lung cancer and is a malignant (cancerous) tumor. Like all cancers, the definition of NSCLC is the uncontrolled replication of abnormal cells in the lungs, which is nearly always the epithelial cells lining the airways of the lungs.<sup>5</sup> For smokers, NSCLC can happen through dysplasia, which is when the cells change their shape due to continuous stress.

There are three types of NSCLC: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma is the most common, representing 40% of all diagnoses. Adenocarcinoma usually originates in the bronchioles, which are located on the ends of the branches in the lungs. It affects both nonsmokers and smokers and spreads relatively slowly, making it more likely to treat before it's too late. Squamous cell carcinoma, which is sometimes referred to as epidermoid carcinoma, makes up 25-30% of all NSCLC diseases. As the name entails, this disease affects the squamous cells - thin, flat cells lining the bronchi. This type of NSCLC is more closely related to smoking than any other type. Large cell carcinoma is very rare, accounting for only

<sup>1</sup> World Health Organization. Cancer Fact Sheet, 2018.

<sup>2</sup> U.S. National Library of Medicine. (n.d.). *Non-small cell lung cancer: Medlineplus Medical Encyclopedia*. MedlinePlus. Retrieved March 10, 2023, from <https://medlineplus.gov/ency/article/007194.htm>

<sup>3</sup> *What is lung cancer?* Types of Lung Cancer. (n.d.). Retrieved March 10, 2023, from <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>

<sup>4</sup> Centers for Disease Control and Prevention. (2022, October 25). *What are the risk factors for lung cancer?* Centers for Disease Control and Prevention. Retrieved March 10, 2023, from [https://www.cdc.gov/cancer/lung/basic\\_info/risk\\_factors.htm](https://www.cdc.gov/cancer/lung/basic_info/risk_factors.htm)

<sup>5</sup> Comparative dosimetry of Radon in mines and homes. (1991). *National Academic Press*, 166–193. <https://doi.org/10.17226/1799>

10% of NSCLC diagnoses. This form of NSCLC is the hardest to treat, as it is very aggressive, and can form anywhere in the lungs.<sup>6</sup>

NSCLC, and lung cancer as a whole, is an important and widespread disease that constitutes a major public health problem today, but this was not always so. As stated in the *Journal of Toxicological Sciences*, lung cancer was an extremely rare disease 150 years ago. In 1878, malignant lung tumors represented a mere 1% of all cancers seen at autopsy in the Institute of Pathology of the University of Dresden in Germany. However, by 1918, the percentage had risen to almost 10%, and by 1927 to more than 14%. In the 1930 edition of the authoritative *Springer Handbook of Special Pathology*, it was noted that malignant lung tumors had begun to increase at the turn of the century and perhaps even more so after World War I.<sup>7</sup>

According to the National Health Service (NHS), about 1 in 3 patients with lung cancer survive at least 1 year after diagnosis, and 1 in 20 patients survive at least 10 years after being diagnosed. However, lung cancer survival rates vary widely, depending on how far the malignant lung cancer cells have spread by the time of diagnosis, which is why early diagnosis is crucial.<sup>6</sup> This paper serves to discuss the key aspects of NSCLC.

## NSCLC Risk Factors

Several risk factors increase one's susceptibility to developing NSCLC. Some risk factors include smoking, air quality, radon, occupational exposure, and family history.<sup>8,9</sup> This section will serve to give an in-depth explanation of each known NSCLC risk factor and its role in developing NSCLC. It is recommended by the American Cancer Society that, if possible, avoid these risk factors to reduce the likelihood of being diagnosed with NSCLC.<sup>10</sup>

### Smoking

Tobacco is an element found in cigarettes and other smoking products containing more than 7,000 poisonous chemicals.<sup>5</sup> It is a well-known risk factor, and by far the most common cause of NSCLC worldwide, as it is estimated that 90% of NSCLC deaths are caused by smoking tobacco products,<sup>5,7</sup> and many others are due to

<sup>6</sup>Herbst, R. S., Sarah Goldberg MD, MPH, & Anne Chiang, MD, PhD. (2022, October 26). *Non-small cell lung cancer*. Yale Medicine. Retrieved March 10, 2023, from <https://www.yalemedicine.org/conditions/non-small-cell-lung-cancer>

<sup>7</sup>Witschi, H. (2001). A short history of lung cancer. *Toxicological Sciences*, 64(1), 4–6. <https://doi.org/10.1093/toxsci/64.1.4>

<sup>8</sup>Mayo Foundation for Medical Education and Research. (2022, March 22). *Lung cancer*. Mayo Clinic. Retrieved March 10, 2023, from <https://www.mayoclinic.org/diseases-conditions/lung-cancer/symptoms-causes/syc-20374620>

<sup>9</sup>Cancer.Net Editorial Board. (2023, January 19). *Lung cancer - non-small cell - risk factors and prevention*. Cancer.Net. Retrieved March 10, 2023, from <https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/risk-factors-and-prevention>

<sup>10</sup>*Lung cancer risk factors*. Smoking & Lung Cancer. (n.d.). Retrieved March 10, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/risk-factors.html>

exposure to secondhand smoke.<sup>11</sup> However, many developed countries have made efforts to help prevent smoking, and their lung cancer incidence and mortality rates have started to slowly decrease.<sup>12</sup>

Smoking items containing tobacco damage the cells that line the lungs, which causes lung cancer. When cigarette smoke is inhaled, which is filled with carcinogens, changes in the lung tissue begin almost immediately.<sup>8</sup> The body may be able to repair these damaged cells at first, but consistent smokers are very likely to develop dysplasia, which is when cells change their appearance due to being under stress, i.e., when the cells in the lungs become abnormally shaped due to stress brought by smoking a tobacco product. As explained by the National Cancer Institute, Dysplasia can be mild, moderate, or severe, depending on how abnormal the cells look under a microscope and how much of the tissue or organ is affected. It is important to know, however, that dysplasia can only sometimes cause cancer.<sup>13,14</sup> Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC) has only a handful of risk factors that are related, but smoking a tobacco product, along with incessantly being around a smoker, is the most significant risk factor for both NSCLC and SCLC.<sup>8</sup>

## Air Quality

Air quality is another significant risk factor accounting for more than 62,000 lung cancer-related deaths worldwide every year.<sup>15</sup> Consistent exposure to polluted air quality caused by factories, vehicles, cooking fumes, or formaldehyde from indoor decoration gradually increases the probability of not just NSCLC, but every form of lung cancer. Outdoor air pollution mostly originates from automobile exhaust, heating systems, and burnt industrial waste. Indoor air pollution, however, consists of cooking fumes, formaldehyde, and benzene from decorative and building materials.<sup>16</sup> Researchers suspect that polluted air can cause oncogenes to be activated, and take over normal functioning genes in the lungs, which, in turn, increases the risk of NSCLC.<sup>17</sup>

## Radon

Increased exposure to radon, a gas formed from soil and rocks is the number one cause of lung cancer in non-smokers. According to the National Cancer Institute, around 15,000 to 22,000 deaths in the US are caused by radon each year. Radon gas usually exists in low levels outdoors and indoors, but can increase through cracks in floors, walls, and foundations. Radon levels can be higher in homes that are well insulated, tightly sealed, and/or built on soil rich in uranium, thorium, and radium. When radon decays, which happens quickly, tiny radioactive particles are released. The cells that line the lungs are damaged when these radioactive particles are inhaled. Long-term exposure to higher levels of radon can lead to NSCLC. The US Environmental Protection

<sup>11</sup> *Lung cancer causes: Lung cancer in Non-Smokers*. Lung Cancer Causes | Lung Cancer in Non-Smokers. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/what-causes.html>

<sup>12</sup> Parascandola, M., & Xiao, L. (2019). Tobacco and the lung cancer epidemic in China. *Translational Lung Cancer Research*, 8(S1). <https://doi.org/10.21037/tlcr.2019.03.12>

<sup>13</sup> Le, T. (2018). *First aid for the Usmlc step 1 2018: A student to Student Guide*. McGraw-Hill.

<sup>14</sup> *NCI Dictionary of Cancer terms*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/dysplasia>

<sup>15</sup> Cohen, A. J. (2003, December 1). *Air pollution and lung cancer: What more do we need to know?* Thorax. Retrieved March 11, 2023, from <https://thorax.bmj.com/content/58/12/1010>

<sup>16</sup> Mao, Y., Yang, D., He, J., & Krasna, M. J. (2016). Epidemiology of Lung Cancer. *Surgical Oncology Clinics of North America*, 25(3), 439–445. <https://doi.org/10.1016/j.soc.2016.02>.

<sup>17</sup> WebMD. (n.d.). *Why a non-smoker can get lung cancer: Radon, secondhand smoke, asbestos, and more*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/lung-cancer/non-smoker-lung-cancer>

Agency (EPA) strongly recommends reducing the amount of radon in households with a level at or above 4 picocuries per liter (pCi/L) of air. Radon is colorless and odorless. Testing the radon levels every 12 months is suggested.<sup>18</sup>

## Occupational Exposure

Exposure to NSCLC carcinogens in a workplace is common in areas like underground mines and construction sites.<sup>19</sup> The most common lung carcinogens in occupational settings are asbestos, radon, arsenic, chromium, silica, beryllium, nickel, cadmium, and diesel exhaust.<sup>11,20</sup> Asbestos is a prominent carcinogen obtained from a workplace and refers to several types of fibrous, naturally occurring silicate minerals; continuous exposure to high levels of asbestos can cause NSCLC and mesothelioma. Concurrent smoking and asbestos exposure are synergistic and increase lung cancer incidence.<sup>17</sup>

## Family History

Although all of the listed NSCLC risk factors can be avoided, a family history of lung cancer is one important risk factor that cannot be avoided. Several studies conducted in the field show that the likelihood of offspring with a parent that has a history of lung cancer is 1.77 times more prone to lung cancer compared to those without a family history of lung cancer.<sup>21</sup> Since those with a family history are more likely to develop NSCLC, it is suggested to do screenings for any abnormality in the lungs once every year. However, it is recommended not to abuse the amount of NSCLC screenings done per year, as the radiation brought from screening too often can also lead to various types of lung cancer.<sup>22</sup>

## Others

Other risk factors for lung cancer include Human Immunodeficiency Virus infection (HIV) and estrogen levels. The question of whether these are authentic lung cancer risk factors is controversial, and further studies are needed to evaluate this conclusively.<sup>17</sup>

## NSCLC Symptoms

Similar to most other cancers, NSCLC has a set of symptoms that, if detected, diagnosed, and treated, could be key to winning the battle against NSCLC before it spreads to other body regions and is too late. This section of the review paper will focus on the symptoms of Non-Small Cell Lung Cancer. The symptoms of NSCLC are

<sup>18</sup> *Radon and cancer*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/substances/radon/radon-fact-sheet>

<sup>19</sup> *Channel features NLR NP Test cap*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/lung/features/risky-jobs-for-your-lungs?amp>

<sup>20</sup> American Cancer Society. (n.d.). *Lung cancer risk factors*. Smoking & Lung Cancer. Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/risk-factors.html>

<sup>21</sup> Kanwal, M., Ding, X.-J., & Cao, Y. (2016). Familial risk for lung cancer. *Oncology Letters*, 13(2), 535–542. <https://doi.org/10.3892/ol.2016.5518>

<sup>22</sup> PF, P. (n.d.). *Assessing the benefits and harms of low-dose computed tomography screening for lung cancer*. Lung cancer management. Retrieved March 11, 2023, from <https://pubmed.ncbi.nlm.nih.gov/26617677/>

common to all lung cancers and include a cough that doesn't go away, coughing up blood, chest pain, trouble breathing, loss of appetite, weight loss, fatigue, trouble swallowing, and swelling in the face or veins.<sup>6</sup>

## NSCLC Diagnosis

Like most other cancers, the prognosis for a patient is better the sooner NSCLC is detected and treated. However, only 16% of patients were diagnosed with NSCLC before it spread to other organs. Moreover, only 9.2% of patients survived 5 years.<sup>23</sup> This section of the paper will give an in-depth explanation of traditional ways of diagnosing Non-Small Cell Lung Cancer.

## Radiographic Screening

Radiographic screening to detect NSCLC is one of the most effective and crucial methods of diagnosing lung cancer. This is backed up by a study done in Japan, which proved that traditional clinic-based x-ray screening alone reduces lung cancer mortality rates.<sup>23</sup> The main type of x-ray used to detect NSCLC is Low Dose Helical Computed Tomography (LDCT). Lung cancer screening is recommended for older adults who have been smoking regularly.<sup>24</sup>

Low Dose Helical Computed Tomography (LDCT) is an x-ray that, as the name entails, uses a low dose of radiation to produce a detailed image of the lungs, along with any abnormalities.<sup>25</sup> LDCT is better than traditional x-ray machines in two areas: its ability to produce more detailed images to detect defects that otherwise may go unnoticed and its ability to use 90% less radiation than other CT scans.<sup>26</sup> Those who are at risk may scan for NSCLC multiple times over time, but the radiation from an x-ray itself can also cause cancer,<sup>27</sup> which is why a low dose of radiation, which is what LDCT uses, is important. However, LDCT can sometimes identify abnormalities that are not cancer, which could start rounds of more invasive biopsies that are meant for NSCLC, including surgery, to remove the anomaly, which adds to the risks of complications.<sup>28</sup> False positives

<sup>23</sup> Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). (n.d.). *SEER Cancer Statistics Review, 1975-2016*. SEER. Retrieved March 11, 2023, from [https://seer.cancer.gov/csr/1975\\_2016/](https://seer.cancer.gov/csr/1975_2016/)

<sup>24</sup> Sobue, T., Moriyama, N., Kaneko, M., Kusumoto, M., Kobayashi, T., Tsuchiya, R., Kakinuma, R., Ohmatsu, H., Nagai, K., Nishiyama, H., Matsui, E., & Eguchi, K. (2002). Screening for lung cancer with low-dose helical computed tomography: Anti-Lung Cancer Association Project. *Journal of Clinical Oncology*, 20(4), 911–920. <https://doi.org/10.1200/jco.2002.20.4.911>

<sup>25</sup> Mayo Foundation for Medical Education and Research. (2022, February 11). *Lung cancer screening*. Mayo Clinic. Retrieved March 11, 2023, from <https://www.mayoclinic.org/tests-procedures/lung-cancer-screening/about/pac-20385024>

<sup>26</sup> *Low-dose CT Scan*. Cancer Treatment Centers of America. (2022, May 6). Retrieved March 11, 2023, from <https://www.cancercenter.com/cancer-types/lung-cancer/diagnosis-and-detection/low-dose-ct-scan>

<sup>27</sup> *Risk factors: Radiation*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/radiation>

<sup>28</sup> Nooreldeen, R., & Bach, H. (2021). Current and future development in lung cancer diagnosis. *International Journal of Molecular Sciences*, 22(16), 8661. <https://doi.org/10.3390/ijms22168661>

are common for LDCT, as the false positive rates were an astonishing 96.4% according to the National Lung Screening Trial.<sup>29,30</sup>

## NSCLC Treatment

Although many strategies can be implemented into daily lives to reduce the risk, it is still always possible to be diagnosed with NSCLC. When this occurs, there are many treatment methods used to try to stop the spread of NSCLC or lessen the pain brought by it. Mortality rates of lung cancer peaked at 159,292 in 2005 and have since decreased by about 6.5% in 2016 with the arrival of many modern treatments to fight against it.<sup>31</sup> The type of treatment that a patient will get depends on the tumor's type and stage, the size of the tumor, and how the patient can tolerate it.<sup>32</sup> All of the factors help consider the type of treatment that will have the best effect on getting rid of the tumor. Common lung cancer treatments include surgery, chemotherapy, radiotherapy, and targeted therapy.<sup>33</sup> However, the final decision for which treatment method will be used is made by the patient.

### Surgery

Surgery is a common option for NSCLC patients, but the type of surgery is dependent on the stage and location of the tumor, along with any other medical condition the patient may have. An attempt to cure lung cancer with surgery will include removing the tumor and some surrounding tissues from the lung and is considered one of the best options for treatment. Surgery can be used to remove both benign and malignant tumors.<sup>34</sup> There are two common approaches used when removing a part of the lung.

The first approach is thoracotomy.<sup>35</sup> Thoracotomy is performed under mild anesthesia, and before starting surgery, an epidural catheter may be inserted in the mid-back of the patient for pain management. For

<sup>29</sup> Denise R Aberle, Christine D Berg, William C Black, Timothy R Church, Richard M Fagerstrom, Barbara Galen, Ilana F Gareen, Constantine Gatsonis, Jonathan Goldin, John K Gohagan, Bruce Hillman, Carl Jaffe, Barnett S Kramer, David Lynch, Pamela M Marcus, Mi. (2011). The National Lung Screening Trial: Overview and study design. *Radiology*, 258(1), 243–253. <https://doi.org/10.1148/radiol.10091808>

<sup>30</sup> Denise R Aberle, Amanda M Adams, Christine D Berg, William C Black, Jonathan D Clapp, Richard M Fagerstrom, Ilana F Gareen, Constantine Gatsonis, Pamela M Marcus, JoRean D Sicks. (2011). Reduced lung-cancer mortality with low-dose computed tomographic screening. *New England Journal of Medicine*, 365(5), 395–409. <https://doi.org/10.1056/nejmoa1102873>

<sup>31</sup> Association, A. L. (n.d.). *Lung cancer fact sheet*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/resource-library/lung-cancer-fact-sheet>

<sup>32</sup> *Non-small cell lung cancer treatment by stage*. Non-small Cell Lung Cancer Treatment by Stage. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/by-stage.html>

<sup>33</sup> Centers for Disease Control and Prevention. (2022, October 25). *How is lung cancer diagnosed and treated?* Centers for Disease Control and Prevention. Retrieved March 11, 2023, from [https://www.cdc.gov/cancer/lung/basic\\_info/diagnosis\\_treatment.htm](https://www.cdc.gov/cancer/lung/basic_info/diagnosis_treatment.htm)

<sup>34</sup> *Non-small cell lung cancer surgery: Lung cancer surgery*. Non-small Cell Lung Cancer Surgery | Lung Cancer Surgery. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/surgery.html>

<sup>35</sup> Association, A. L. (n.d.). *Lung cancer surgery*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/treatment/types-of-treatment/lung-cancer-surgery>



both lungs to be properly inflated, a breathing tube is placed in the trachea once the patient is unconscious. The patient is then positioned to the side. An approximate 6-inch incision is made below the tip of the shoulder blade, generally between the 5<sup>th</sup> and 6<sup>th</sup> ribs. Typically, doctors will insert a chest tube on the side of the thoracotomy used to drain the excess fluid and air leaking into the chest. This chest tube stays in the patient's body for days. The doctors conducting the surgery then move on to incise and remove the tumor. Side effects brought by thoracotomy include infection, bleeding, persistent air leakage from the lungs, and pain. Life-threatening injuries from thoracotomy are rare.<sup>36</sup>

The second method used to remove the tumor in the lung is minimally invasive thoracic surgery. As the name entails, this method is less intrusive, as it does not require the ribs to be spread apart. Instead, this method is executed through small incisions. Minimally invasive thoracoscopic surgery can be performed in two ways that are equally as popular; Video-Assisted Thoracoscopic Surgery (VATS), and robotic-assisted surgery. When using VATS in minimally invasive thoracic surgery, the patient is put out of consciousness using general anesthesia and placed on the side, and then 1 or more centimeter-wide incisions between the ribs follow. The VATS device, a thoracoscope, is inserted between a small cut between the ribs. A camera is fitted to the end of the tube, which lets the surgeon see the chest cavity without having to fully open up the chest. The surgeon(s) then proceed(s) to cut and remove the tumor from the lung. At the end of the surgery, doctors will place a chest tube into the patient to drain excess fluid leaking into the chest to help reinflate the lungs. Robotic-assisted surgery utilizes the same procedures as VATS, but instead of the VATS device being inserted into the small incisions, wristed robotic instruments are inserted.<sup>37</sup>

## Chemotherapy

Chemotherapy is when a patient is given one or more anti-cancer drugs to shrink or eliminate the lung tumor which can be pills that are swallowed or medicines injected into the veins.<sup>34,38</sup> Chemotherapy is used when the patient's tumor has spread to other regions in the body (a malignant tumor) or has the potential to do so. There are several ways in which chemotherapy can be performed, but two techniques are more commonly used compared to others.

The first technique is intravenous chemotherapy (chemotherapy given through injections). Intravenous chemotherapy involves medicine being injected usually through the patient's arm or hand. Another common practice is oral chemotherapy (chemotherapy given through pills). This consists in taking orally taking a course of medicine from home, and having regular checkups with a doctor. As well as eliminating cancerous cells in the lungs, chemotherapy may also damage some healthy cells, including blood cells and skin cells. This can set off a variety of side effects. Some include hair loss, fatigue, feeling and being sick, increased vulnerability to infections, a sore mouth, dry and itchy skin, and diarrhea/constipation. However, no side effects have a lasting effect, as they can be prevented via treatment.<sup>39</sup>

<sup>36</sup> Association, A. L. (n.d.). *Thoracotomy*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-procedures-and-tests/thoracotomy>

<sup>37</sup> Association, A. L. (n.d.). *Minimally Invasive Thoracic Surgery*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-procedures-and-tests/minimally-invasive-thoracic-surgery>

<sup>38</sup> Alfarouk, K. O., Stock, C.-M., Taylor, S., Walsh, M., Muddathir, A. K., Verduzco, D., Bashir, A. H. H., Mohammed, O. Y., Elhassan, G. O., Harguindey, S., Reshkin, S. J., Ibrahim, M. E., & Rauch, C. (2015, July 15). *Resistance to cancer chemotherapy: Failure in drug response from ADME to P-Gp - Cancer Cell International*. BioMed Central. Retrieved March 11, 2023, from <https://doi.org/10.1186/s12935-015-0221-1>

<sup>39</sup> NHS. (n.d.). *Chemotherapy*. NHS choices. Retrieved March 11, 2023, from <https://www.nhs.uk/conditions/chemotherapy/>

## Targeted Therapy

Targeted therapy uses drugs as pills or injections designed to kill cancer cells while, unlike other treatment methods, not harming healthy cells. Chemotherapy also uses pills and injections to eliminate cancerous cells, but drugs used in targeted therapy work differently from traditional chemotherapy drugs.<sup>40</sup>

Targeted drugs take advantage of changes that differentiate cancer cells from normal cells, thus making targeted therapy drugs different from chemotherapy drugs in two ways. Targeted therapy prevents the uncontrolled division of cancerous cells while traditional chemotherapy kills already existing cancer cells. Additionally, healthy cells are generally left unaffected by targeted therapy due to its “targeted” action. On the other hand, chemotherapy kills all cells, including normal ones, since it is cytotoxic to most cells.<sup>41</sup>

Many types of cancer can be treated using targeted therapy. There are many types of targeted therapy, but there are 4 types that are the most popular. The first widely used type of targeted therapy is angiogenesis inhibitors. By blocking blood vessels and proteins that help nourish the cancer cells, Angiogenesis works to starve and kill cancerous cells. Another widely used targeted therapy is monoclonal antibodies. These deliver molecules with or without drugs into or onto cancer cells to destroy them. The third type of targeted therapy is proteasome inhibitors. Proteasome inhibitors work by eliminating cancer cells by disrupting their normal functions, which in turn gets rid of the tumor itself. Signal transduction inhibitors are the fourth most renowned type of targeted therapy. These change the actions of the cancerous cells by disrupting the cancerous cell’s signals.<sup>41</sup>

Many side effects may be experienced during and/or after a patient has undergone targeted therapy. Targeted therapy side effects include skin problems, high blood pressure, bleeding/blood clotting problems, slow wound healing, autoimmune reactions, swelling, and nausea. However, not all of the side effects will occur, and a few targeted therapy patients reported no side effects.<sup>41</sup>

## NSCLC Prevention

Along with there being many risk factors, many methods can be implemented to reduce the risk of being diagnosed with NSCLC. Some prevention strategies include staying away from smoking, avoiding secondhand smoke, regularly testing the radon gas levels in households, researching family lung cancer history, avoiding hazardous substances, and reducing the risk of HIV infection.<sup>42</sup>

## Circumvent Smoking

Avoiding cigarettes is the single most beneficial way to reduce the risk of being diagnosed with NSCLC. According to the Centers for Disease Control and Prevention (CDC) and Healthline, men who smoke are 25 times

<sup>40</sup> *Targeted cancer therapy: Targeted drug therapy for cancer.* Targeted Cancer Therapy | Targeted Drug Therapy for Cancer. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy/what-is.html>

<sup>41</sup> *Targeted drug therapy side effects: American cancer society.* Targeted Drug Therapy Side Effects | American Cancer Society. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy/side-effects.html>

<sup>42</sup> Hersh, E. (2021, March 12). *Lung cancer prevention: 10 Ways to Lower Your Risk.* Healthline. Retrieved March 11, 2023, from <https://www.healthline.com/health/lung-cancer/lung-cancer-prevention>



more likely to develop lung cancer, and women who constantly smoke are 25.7 times more likely.<sup>43,43</sup> A non-smoker must stay away from smoking, as certain chemicals such as nicotine can cause an addiction to products such as cigarettes.<sup>44</sup>

In addition, those who quit smoking after continuously using cigarettes will start receiving health benefits almost immediately; 20 minutes after a smoker quits, their heart rate and blood pressure drop. A few days later, the carbon monoxide levels in the blood drop back to normal. 2 to 3 weeks after quitting, oxygen circulation improves and the lung function increases, therefore expanding stamina. After 1 to 12 months, tiny hair particles called cilia used to keep mucus out of the lungs regain normal function, eliminating the smoker's cough and shortness of breath. The risk of heart disease drops adequately 1 to 2 years after quitting. In 5 to 10 years, the risk of cancers of the mouth, throat, and larynx is halved. Finally, after around 15 years of quitting smoking, the risk of being diagnosed with lung cancer or heart disease is close to that of a nonsmoker.<sup>45</sup>

While quitting smoking isn't an easy task, it is possible. Methods such as finding nicotine substitutes like nicotine gum, avoiding alcohol and other triggers, and communicating with nonsmoking friends are some useful strategies that can be used to end the smoking addiction.<sup>46</sup>

## Avoiding Secondhand Smoke

Secondhand smoke is smoke from others' tobacco products such as a cigarette and cigars, as well as the smoke that others exhale.<sup>47</sup> 70 chemicals in secondhand smoke cause lung cancer and many more are toxic. Secondhand smoke is almost as dangerous as smoking; the CDC claims that more than 7,300 deaths in the USA are linked to secondhand smoke. Although laws have been implemented in many areas to reduce exposure to secondhand smoke in public, it is important to stay away from settings containing tobacco smoke.<sup>46</sup>

## Regularly Testing for Radon

Typically, radon gas is everywhere, but at low levels. Houses that are well-insulated and/or built on soil built uranium, thorium, and radium are more likely to have radon levels higher than the normal radon level (4 picocuries per liter [pCi/L]).<sup>48</sup> The US Environmental Protection Agency (EPA) claims that 1 in 15 houses have radon levels higher than 4 picocuries per liter (pCi/L).<sup>49</sup> Radon does not have properties that can be observed by the naked eye, so testing for radon gas is the only way to detect if the radon levels are higher than the healthy levels and take action if needed. The EPA suggests that home radon levels are tested every 1 to 2 years.<sup>50</sup>

<sup>43</sup> Centers for Disease Control and Prevention. (2021, October 29). *Health effects of cigarette smoking*. Centers for Disease Control and Prevention. Retrieved March 11, 2023, from [https://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/health\\_effects/effects\\_cig\\_smoking/index.htm](https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm)

<sup>44</sup> NIDA. 2021, April 12. Is nicotine addictive? Retrieved March 11, 2023, from <https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/nicotine-addictive>

<sup>45</sup> *Health benefits of quitting smoking over time*. American Cancer Society. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/healthy/stay-away-from-tobacco/benefits-of-quitting-smoking-over-time.html>

<sup>46</sup> WebMD. (n.d.). *13 best quit-smoking tips ever*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/smoking-cessation/ss/slideshow-13-best-quit-smoking-tips-ever>

<sup>47</sup> *Risk factors: Radiation*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/radiation>

<sup>48</sup> "Radon and Cancer." *National Cancer Institute*. Web. 21 July 2021.

<sup>49</sup> Kanwal, M., Ding, X.-J., & Cao, Y. (2016). Familial risk for lung cancer. *Oncology Letters*, 13(2), 535–542. <https://doi.org/10.3892/ol.2016.5518>

## Knowing Family NSCLC History

It is crucial to be aware of whether an immediate family member has a history of NSCLC.<sup>43</sup> This information can facilitate a quick diagnosis, which according to the NHS, is crucial and might be the single factor between life and death.<sup>50</sup> It is recommended to screen for NSCLC regularly if a family member has a history of lung cancer, as those with a family history, are about 1.77 times more likely to develop lung cancer.<sup>22</sup> Both genetic and environmental factors play a role in the increased risk.<sup>43</sup>

## Reducing the Risk of HIV Infection

Lung cancer is emerging to be the leading cause of death in people infected with the Human Immunodeficiency Virus (HIV). Although the question of whether HIV is or isn't linked to cancer is controversial, studies show that being infected with it may double the likelihood of being diagnosed with lung cancer. The increased risk of lung cancer in HIV-infected persons is related to high rates of smoking and may also be associated with HIV-specific etiologies including immunodeficiency and inflammatory processes.<sup>51</sup> To prevent HIV, it is recommended to not abuse alcohol or drugs. Moreover, it is best to perform HIV tests regularly and get vaccinated.<sup>52</sup>

## Others

A 2019 study published in the journal *Nutrients* reported that a healthy diet helped reduce the chances of lung cancer; a daily increase of 100 grams of vegetables reduced the risk by 3% in smokers (but not former smokers or never-smokers). Similarly, a daily increase in fruits decreases the likelihood of lung cancer by 5% in former smokers and smokers.<sup>53</sup>

Furthermore, according to a 2016 review in the *American Journal of Epidemiology*, heavy alcohol is associated with adenocarcinoma.<sup>54</sup> Consuming more than seven hard-liquor drinks per day is related to an 11% increased risk of lung cancer compared to non-drinkers.<sup>55</sup>

Moreover, it is recommended to exercise regularly to reduce the risk of lung cancer. Even moderate amounts of exercise can aid in lung cancer prevention. According to a 2011 review from the City of Hope National Medical Center in California, routine physical activity can reduce lung cancer risk by 20% to 30% in women and 20% to 50% in men.<sup>56</sup> The benefits of exercising are in tandem with the intensity and duration of

<sup>50</sup>NHS. (n.d.). *Overview: Lung Cancer*. NHS choices. Retrieved March 11, 2023, from <https://www.nhs.uk/conditions/lung-cancer/>

<sup>51</sup> Sigel, K., Makinson, A., & Thaler, J. (2017). Lung cancer in persons with HIV. *Current Opinion in HIV and AIDS*, 12(1), 31–38. <https://doi.org/10.1097/coh.0000000000000326>

<sup>52</sup> *HIV prevention*. HIV prevention | Office on Women's Health. (n.d.). Retrieved March 11, 2023, from <https://www.womenshealth.gov/hiv-and-aids/hiv-prevention>

<sup>53</sup> Wang, C., Yang, T., Guo, X.-fei, & Li, D. (2019). The associations of fruit and vegetable intake with lung cancer risk in participants with different smoking status: A meta-analysis of prospective cohort studies. *Nutrients*, 11(8), 1791. <https://doi.org/10.3390/nu11081791>

<sup>54</sup> Troche, J. R., Mayne, S. T., Freedman, N. D., Shebl, F. M., & Abnet, C. C. (2015). The association between alcohol consumption and lung carcinoma by histological subtype. *American Journal of Epidemiology*, 183(2), 110–121. <https://doi.org/10.1093/aje/kwv170>

<sup>55</sup> Lynne Eldridge, M. D. (n.d.). *10 tips for preventing lung cancer*. Verywell Health. Retrieved March 11, 2023, from <https://www.verywellhealth.com/tips-for-lung-cancer-prevention-2249286>

<sup>56</sup> Emaus, A., & Thune, I. (2010). Physical activity and lung cancer prevention. *Physical Activity and Cancer*, 101–133. [https://doi.org/10.1007/978-3-642-04231-7\\_5](https://doi.org/10.1007/978-3-642-04231-7_5)

the exercise per week and extend to both smokers and non-smokers. It's believed that exercise reduces the risk of lung cancer due to improved lung function, reduced concentration of carcinogens in the lungs, stronger immune function, reduced inflammation, and the enhanced ability of the body to rebuild damaged DNA in lung cells.<sup>56</sup>

## NSCLC Epidemiology

Although new laws in developed countries have placed laws to limit and prevent smoking, which is the main cause of NSCLC, studies show that those in developed countries have the highest incidence and mortality rates of NSCLC. However, more research in underdeveloped areas on this subject is needed, as many of those countries lack a centralized reporting system, and many lung cancer-related deaths in underdeveloped regions have most likely gone unreported.<sup>57</sup>

Black men have a 20% higher incidence rate of lung cancer compared to white men, although the incidence rates for both have been declining over the past years.<sup>58</sup> On the other hand, the ethnicities with the lowest incidence rates are Pacific Islanders, Hispanic women, and Asian Americans.<sup>59</sup>

Like many other cancers, NSCLC is most likely to develop as one gets older, and data can prove this, as NSCLC rates are low for everyone aged 40 and under,<sup>60</sup> and 90% of diagnoses are for those aged 55 years and older. The age group of 65-84 years remains the group with the highest diagnosis rate, with the median age being 71 years.<sup>61</sup>

Although smoking rates will most likely play a detrimental role in future NSCLC rates, nonsmoking women have a 19% incidence rate for NSCLC, while only 9% of nonsmoking men are diagnosed with NSCLC.<sup>62</sup>

## Current Research

NSCLC has no cure/vaccine that can either make those who take it immune to NSCLC or always completely eradicate it at any stage. Since NSCLC is a widespread and deadly disease, many scientists are working tirelessly to make a cure for it, and although none have been officially released to the public, a few are undergoing testing and have the potential to be the anticipated cure. This section of the review paper will highlight a few of them.

<sup>57</sup> Duma, N., Santana-Davila, R., & Molina, J. R. (2019). Non-small cell lung cancer: Epidemiology, screening, diagnosis, and treatment. *Mayo Clinic Proceedings*, 94(8), 1623–1640. <https://doi.org/10.1016/j.mayocp.2019.01.013>

<sup>58</sup> Jemal, A., R. Siegel, J. Xu, and E. Ward. "Cancer Statistics, 2010." *CA: A Cancer Journal for Clinicians* 60.5 (2010): 277-300. Print.

<sup>59</sup> Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians*, 68(1), 7–30. <https://doi.org/10.3322/caac.21442>

<sup>60</sup> Kratzke, R., & Franklin, M. J. (2017). Lung Cancer Epidemiology. *Encyclopedia of Cancer*, 2100–2104. [https://doi.org/10.1007/978-3-642-16483-5\\_6893](https://doi.org/10.1007/978-3-642-16483-5_6893)

<sup>61</sup> Kohler, B. A., Ward, E., McCarthy, B. J., Schymura, M. J., Ries, L. A., Ehemann, C., Jemal, A., Anderson, R. N., Ajani, U. A., & Edwards, B. K. (2011). Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. *JNCI Journal of the National Cancer Institute*, 103(9), 714–736. <https://doi.org/10.1093/jnci/djr077>

<sup>62</sup> Wakelee, H. A., Chang, E. T., Gomez, S. L., Keegan, T. H., Feskanich, D., Clarke, C. A., Holmberg, L., Yong, L. C., Kolonel, L. N., Gould, M. K., & West, D. W. (2007). Lung cancer incidence in never smokers. *Journal of Clinical Oncology*, 25(5), 472–478. <https://doi.org/10.1200/jco.2006.07.2983>

## GVAX®

GVAX is a cell-based vaccine for NSCLC and prostate cancer. Cell-based vaccines are made by using inactivated vaccine cells, copying their genetic information (which is similar to the rest of the cancer cells still in the patient's body), and triggering an immune response that makes the immune system recognize the cancer cells as hostile and start attacking it.<sup>64</sup>

The Phase I trial for GVAX was promising: 34 patients with NSCLC were administered the vaccine for three weeks until either there was no supply left or the patient was removed from the study. After the trial had ended, 5 patients showed no change in disease progression, 1 patient had a mixed response, and 2 patients that had undergone surgery prior to the start of the trial showed no evidence of NSCLC after 42 months. The only side effect noticed in some patients was skin reactions around the vaccination.<sup>64</sup>

With Phase I's satisfactory results, Phase II trials were initiated. Here, 10 patients with stage I/II NSCLC, and 33 patients with stage III/IV NSCLC were administered the vaccine. The patients were given a biweekly dose for 6 weeks. Monthly treatment for 6 months followed afterward. The results of the trial showed that 3 patients with late-stage NSCLC, which is extremely hard to treat, had complete regression of the tumor.<sup>63</sup>

Despite GVAX's promising results for being the future NSCLC vaccine, it did not produce sufficient results for its effectiveness against prostate cancer, so enthusiasm for conducting phase III trials of the GVAX vaccine is limited.

## Discussion

This paper provides a systematic review of common risk factors behind NSCLC and the corresponding preventive methods, symptoms, treatments, epidemiology, and current research that has the potential to be groundbreaking in the field of NSCLC prevention. Although the incidence of lung cancer has decreased over the past several decades, lung cancer is the most frequently diagnosed cancer and additional preventative methods are still needed.

## Acknowledgments

I would like to thank my advisor for the valuable insight provided to me on this topic.

## Bibliography

World Health Organization. Cancer Fact Sheet, 2018.

U.S. National Library of Medicine. (n.d.). *Non-small cell lung cancer: Medlineplus Medical Encyclopedia*. MedlinePlus. Retrieved March 10, 2023, from <https://medlineplus.gov/ency/article/007194.htm>

*What is lung cancer?* Types of Lung Cancer. (n.d.). Retrieved March 10, 2023, from <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>

Centers for Disease Control and Prevention. (2022, October 25). *What are the risk factors for lung cancer?*

Centers for Disease Control and Prevention. Retrieved March 10, 2023, from [https://www.cdc.gov/cancer/lung/basic\\_info/risk\\_factors.htm](https://www.cdc.gov/cancer/lung/basic_info/risk_factors.htm)

<sup>63</sup> Ramlogan-Steel, C. A., Steel, J. C., & Morris, J. C. (2013, December 26). *Lung cancer vaccines: Current status and future prospects*. Translational Lung Cancer Research. Retrieved March 11, 2023, from <https://tlcr.amegroups.com/article/view/1850/2726>

- Comparative dosimetry of Radon in mines and homes. (1991). *National Academic Press*, 166–193.  
<https://doi.org/10.17226/1799>
- Herbst, R. S., Sarah Goldberg MD, MPH, & Anne Chiang, MD, PhD. (2022, October 26). *Non-small cell lung cancer*. Yale Medicine. Retrieved March 10, 2023, from <https://www.yalemedicine.org/conditions/non-small-cell-lung-cancer>
- Witschi, H. (2001). A short history of lung cancer. *Toxicological Sciences*, 64(1), 4–6.  
<https://doi.org/10.1093/toxsci/64.1.4>
- Mayo Foundation for Medical Education and Research. (2022, March 22). *Lung cancer*. Mayo Clinic. Retrieved March 10, 2023, from <https://www.mayoclinic.org/diseases-conditions/lung-cancer/symptoms-causes/syc-20374620>
- Cancer.Net Editorial Board. (2023, January 19). *Lung cancer - non-small cell - risk factors and prevention*. Cancer.Net. Retrieved March 10, 2023, from <https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/risk-factors-and-prevention>
- Lung cancer risk factors*. Smoking & Lung Cancer. (n.d.). Retrieved March 10, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/risk-factors.html>
- Lung cancer causes: Lung cancer in Non-Smokers*. Lung Cancer Causes | Lung Cancer in Non-Smokers. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/what-causes.html>
- Parascandola, M., & Xiao, L. (2019). Tobacco and the lung cancer epidemic in China. *Translational Lung Cancer Research*, 8(S1). <https://doi.org/10.21037/tlcr.2019.03.12>
- Le, T. (2018). *First aid for the USMLE step 1 2018: A student to Student Guide*. McGraw-Hill.
- NCI Dictionary of Cancer terms*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/dysplasia>
- Cohen, A. J. (2003, December 1). *Air pollution and lung cancer: What more do we need to know?* Thorax. Retrieved March 11, 2023, from <https://thorax.bmj.com/content/58/12/1010>
- Mao, Y., Yang, D., He, J., & Krasna, M. J. (2016). Epidemiology of Lung Cancer. *Surgical Oncology Clinics of North America*, 25(3), 439–445. <https://doi.org/10.1016/j.soc.2016.02.001>
- WebMD. (n.d.). *Why a non-smoker can get lung cancer: Radon, secondhand smoke, asbestos, and more*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/lung-cancer/non-smoker-lung-cancer>
- Radon and cancer*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/substances/radon/radon-fact-sheet>
- Channel features NLR NP Test cap*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/lung/features/risky-jobs-for-your-lungs?amp>
- American Cancer Society. (n.d.). *Lung cancer risk factors*. Smoking & Lung Cancer. Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/risk-factors.html>
- Kanwal, M., Ding, X.-J., & Cao, Y. (2016). Familial risk for lung cancer. *Oncology Letters*, 13(2), 535–542. <https://doi.org/10.3892/ol.2016.5518>
- PF;, P. (n.d.). *Assessing the benefits and harms of low-dose computed tomography screening for lung cancer*. Lung cancer management. Retrieved March 11, 2023, from <https://pubmed.ncbi.nlm.nih.gov/26617677/>
- Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). (n.d.). *SEER Cancer Statistics Review, 1975-2016*. SEER. Retrieved March 11, 2023, from [https://seer.cancer.gov/csr/1975\\_2016/](https://seer.cancer.gov/csr/1975_2016/)
- Sobue, T., Moriyama, N., Kaneko, M., Kusumoto, M., Kobayashi, T., Tsuchiya, R., Kakinuma, R., Ohmatsu, H., Nagai, K., Nishiyama, H., Matsui, E., & Eguchi, K. (2002). Screening for lung cancer with low-dose helical computed tomography: Anti-Lung Cancer Association Project. *Journal of Clinical Oncology*, 20(4), 911–920. <https://doi.org/10.1200/jco.2002.20.4.911>



- Mayo Foundation for Medical Education and Research. (2022, February 11). *Lung cancer screening*. Mayo Clinic. Retrieved March 11, 2023, from <https://www.mayoclinic.org/tests-procedures/lung-cancer-screening/about/pac-20385024>
- Low-dose CT Scan*. Cancer Treatment Centers of America. (2022, May 6). Retrieved March 11, 2023, from <https://www.cancercenter.com/cancer-types/lung-cancer/diagnosis-and-detection/low-dose-ct-scan>
- Risk factors: Radiation*. National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/radiation>
- Nooreldeen, R., & Bach, H. (2021). Current and future development in lung cancer diagnosis. *International Journal of Molecular Sciences*, 22(16), 8661. <https://doi.org/10.3390/ijms22168661>
- Denise R Aberle, Christine D Berg, William C Black, Timothy R Church, Richard M Fagerstrom, Barbara Galen, Ilana F Gareen, Constantine Gatsonis, Jonathan Goldin, John K Gohagan, Bruce Hillman, Carl Jaffe, Barnett S Kramer, David Lynch, Pamela M Marcus, Mi. (2011). The National Lung Screening Trial: Overview and study design. *Radiology*, 258(1), 243–253. <https://doi.org/10.1148/radiol.10091808>
- Denise R Aberle, Amanda M Adams, Christine D Berg, William C Black, Jonathan D Clapp, Richard M Fagerstrom, Ilana F Gareen, Constantine Gatsonis, Pamela M Marcus, JoRean D Sicks. (2011). Reduced lung-cancer mortality with low-dose computed tomographic screening. *New England Journal of Medicine*, 365(5), 395–409. <https://doi.org/10.1056/nejmoa1102873>
- Association, A. L. (n.d.). *Lung cancer fact sheet*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/resource-library/lung-cancer-fact-sheet>
- Non-small cell lung cancer treatment by stage*. Non-small Cell Lung Cancer Treatment by Stage. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/by-stage.html>
- Centers for Disease Control and Prevention. (2022, October 25). *How is lung cancer diagnosed and treated?* Centers for Disease Control and Prevention. Retrieved March 11, 2023, from [https://www.cdc.gov/cancer/lung/basic\\_info/diagnosis\\_treatment.htm](https://www.cdc.gov/cancer/lung/basic_info/diagnosis_treatment.htm)
- Non-small cell lung cancer surgery: Lung cancer surgery*. Non-small Cell Lung Cancer Surgery | Lung Cancer Surgery. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/surgery.html>
- Association, A. L. (n.d.). *Lung cancer surgery*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/treatment/types-of-treatment/lung-cancer-surgery>
- Association, A. L. (n.d.). *Thoracotomy*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-procedures-and-tests/thoracotomy>
- Association, A. L. (n.d.). *Minimally Invasive Thoracic Surgery*. American Lung Association. Retrieved March 11, 2023, from <https://www.lung.org/lung-health-diseases/lung-procedures-and-tests/minimally-invasive-thoracic-surgery>
- Alfarouk, K. O., Stock, C.-M., Taylor, S., Walsh, M., Muddathir, A. K., Verduzco, D., Bashir, A. H. H., Mohammed, O. Y., Elhassan, G. O., Harguindey, S., Reshkin, S. J., Ibrahim, M. E., & Rauch, C. (2015, July 15). *Resistance to cancer chemotherapy: Failure in drug response from ADME to P-Gp - Cancer Cell International*. BioMed Central. Retrieved March 11, 2023, from <https://doi.org/10.1186/s12935-015-0221-1>
- NHS. (n.d.). *Chemotherapy*. NHS choices. Retrieved March 11, 2023, from <https://www.nhs.uk/conditions/chemotherapy/>
- Targeted cancer therapy: Targeted drug therapy for cancer*. Targeted Cancer Therapy | Targeted Drug Therapy for Cancer. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy/what-is.html>



- Targeted drug therapy side effects: American cancer society.* Targeted Drug Therapy Side Effects | American Cancer Society. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy/side-effects.html>
- Hersh, E. (2021, March 12). *Lung cancer prevention: 10 Ways to Lower Your Risk*. Healthline. Retrieved March 11, 2023, from <https://www.healthline.com/health/lung-cancer/lung-cancer-prevention>
- Centers for Disease Control and Prevention. (2021, October 29). *Health effects of cigarette smoking*. Centers for Disease Control and Prevention. Retrieved March 11, 2023, from [https://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/health\\_effects/effects\\_cig\\_smoking/index.htm](https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm)
- NIDA. 2021, April 12. Is nicotine addictive? Retrieved March 11, 2023, from <https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/nicotine-addictive>
- Health benefits of quitting smoking over time.* American Cancer Society. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.org/healthy/stay-away-from-tobacco/benefits-of-quitting-smoking-over-time.html>
- WebMD. (n.d.). *13 best quit-smoking tips ever*. WebMD. Retrieved March 11, 2023, from <https://www.webmd.com/smoking-cessation/ss/slideshow-13-best-quit-smoking-tips-ever>
- Risk factors: Radiation.* National Cancer Institute. (n.d.). Retrieved March 11, 2023, from <https://www.cancer.gov/about-cancer/causes-prevention/risk/radiation>
- "Radon and Cancer." *National Cancer Institute*. Web. 21 July 2021.
- Kanwal, M., Ding, X.-J., & Cao, Y. (2016). Familial risk for lung cancer. *Oncology Letters*, *13*(2), 535–542. <https://doi.org/10.3892/ol.2016.5518>
- NHS. (n.d.). *Overview: Lung Cancer*. NHS choices. Retrieved March 11, 2023, from <https://www.nhs.uk/conditions/lung-cancer/>
- Sigel, K., Makinson, A., & Thaler, J. (2017). Lung cancer in persons with HIV. *Current Opinion in HIV and AIDS*, *12*(1), 31–38. <https://doi.org/10.1097/coh.0000000000000326>
- HIV prevention.* HIV prevention | Office on Women's Health. (n.d.). Retrieved March 11, 2023, from <https://www.womenshealth.gov/hiv-and-aids/hiv-prevention>
- Wang, C., Yang, T., Guo, X.-fei, & Li, D. (2019). The associations of fruit and vegetable intake with lung cancer risk in participants with different smoking status: A meta-analysis of prospective cohort studies. *Nutrients*, *11*(8), 1791. <https://doi.org/10.3390/nu11081791>
- Troche, J. R., Mayne, S. T., Freedman, N. D., Shebl, F. M., & Abnet, C. C. (2015). The association between alcohol consumption and lung carcinoma by histological subtype. *American Journal of Epidemiology*, *183*(2), 110–121. <https://doi.org/10.1093/aje/kwv170>
- Lynne Eldridge, M. D. (n.d.). *10 tips for preventing lung cancer*. Verywell Health. Retrieved March 11, 2023, from <https://www.verywellhealth.com/tips-for-lung-cancer-prevention-2249286>
- Emaus, A., & Thune, I. (2010). Physical activity and lung cancer prevention. *Physical Activity and Cancer*, 101–133. [https://doi.org/10.1007/978-3-642-04231-7\\_5](https://doi.org/10.1007/978-3-642-04231-7_5)
- Duma, N., Santana-Davila, R., & Molina, J. R. (2019). Non-small cell lung cancer: Epidemiology, screening, diagnosis, and treatment. *Mayo Clinic Proceedings*, *94*(8), 1623–1640. <https://doi.org/10.1016/j.mayocp.2019.01.013>
- Jemal, A., R. Siegel, J. Xu, and E. Ward. "Cancer Statistics, 2010." *CA: A Cancer Journal for Clinicians* 60.5 (2010): 277-300. Print.
- Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians*, *68*(1), 7–30. <https://doi.org/10.3322/caac.21442>
- Kratzke, R., & Franklin, M. J. (2017). Lung Cancer Epidemiology. *Encyclopedia of Cancer*, 2100–2104. [https://doi.org/10.1007/978-3-642-16483-5\\_6893](https://doi.org/10.1007/978-3-642-16483-5_6893)
- Kohler, B. A., Ward, E., McCarthy, B. J., Schymura, M. J., Ries, L. A., Ehemann, C., Jemal, A., Anderson, R. N., Ajani, U. A., & Edwards, B. K. (2011). Annual report to the nation on the status of cancer, 1975–2007,

featuring tumors of the brain and other nervous system. *JNCI Journal of the National Cancer Institute*, 103(9), 714–736. <https://doi.org/10.1093/jnci/djr077>

Wakelee, H. A., Chang, E. T., Gomez, S. L., Keegan, T. H., Feskanich, D., Clarke, C. A., Holmberg, L., Yong, L. C., Kolonel, L. N., Gould, M. K., & West, D. W. (2007). Lung cancer incidence in never smokers. *Journal of Clinical Oncology*, 25(5), 472–478. <https://doi.org/10.1200/jco.2006.07.2983>

Ramlogan-Steel, C. A., Steel, J. C., & Morris, J. C. (2013, December 26). *Lung cancer vaccines: Current status and future prospects*. Translational Lung Cancer Research. Retrieved March 11, 2023, from <https://tlcr.amegroups.com/article/view/1850/2726>