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Lung Cancer Medical Documentation Paper

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1. Overview of Lung Cancer

1.1 Definition and Classification

Lung cancer is a malignant tumor characterized by the uncontrolled growth of abnormal cells in one or both lungs. These abnormal cells do not carry out the functions of normal lung cells and do not develop into healthy lung tissue. Instead, they divide rapidly and form tumors that can interfere with the lung's primary function of providing oxygen to the body via the bloodstream. Without treatment, these tumors can spread within the lungs and to other parts of the body, further impairing lung function and overall health.

Lung cancer is broadly classified into two main categories based on the appearance of the cancer cells under a microscope:

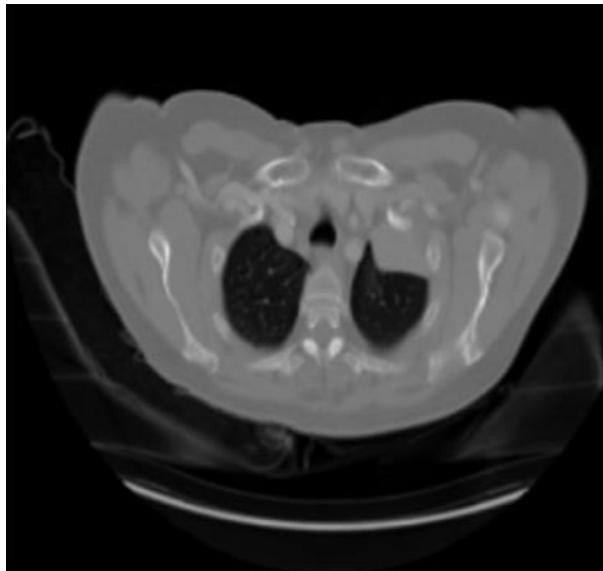
- **Non-Small Cell Lung Cancer (NSCLC):** This is the most common type, accounting for approximately 85% of all lung cancer cases.
- **Small Cell Lung Cancer (SCLC):** Less common and more aggressive, accounting for about 15% of cases.

These classifications are crucial as they guide the therapeutic strategy and have different prognosis and biological behaviors.

1.2 Histological Types: NSCLC vs. SCLC

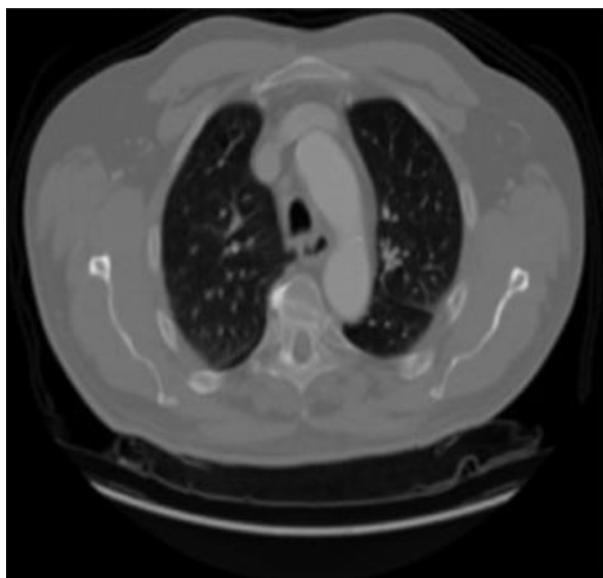
NSCLC comprises several histological subtypes, each with distinct pathological and clinical characteristics:

- **Adenocarcinoma:** The most prevalent subtype of NSCLC, particularly among non-smokers and younger individuals. It originates from glandular epithelial cells and is frequently located in the lung periphery. Adenocarcinomas exhibit significant histological heterogeneity and may present mixed patterns, such as acinar, papillary, solid, or bronchioloalveolar features. The WHO/IASLC classification recognizes several variants, including mucinous, fetal, and signet ring types. [21]



CT scan of patient diagnosed with lung Adenocarcinoma. [32]

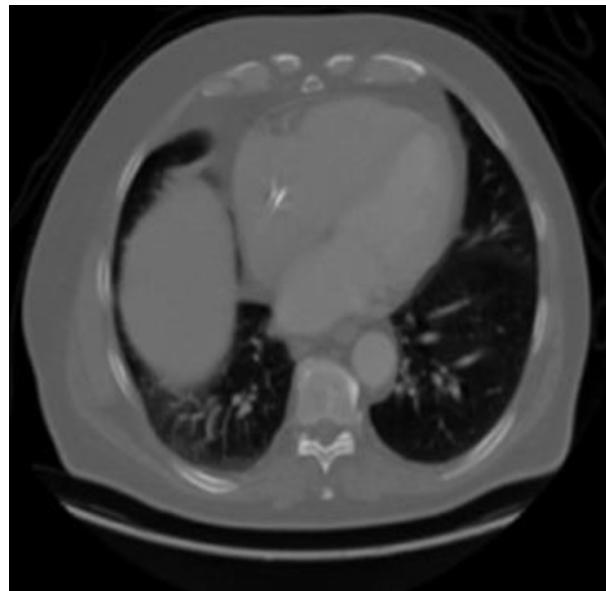
- **Squamous Cell Carcinoma:** Commonly found in the central airways, this subtype arises from squamous epithelial cells and is strongly associated with tobacco smoking. It is characterized histologically by keratinization and intercellular bridges. The incidence of squamous cell carcinoma has declined in recent years due to reduced smoking rates. [21]



CT scan of patient diagnosed with lung Squamous Cell Carcinoma. [32]

- **Large Cell Carcinoma:** A heterogeneous group of poorly differentiated tumors lacking glandular or squamous characteristics. It is often aggressive and located in peripheral lung tissue. The WHO/IASLC classification includes variants such as large cell neuroendocrine carcinoma (LCNEC), basaloid carcinoma, and large cell

carcinoma with rhabdoid phenotype. [21]



CT scan of patient diagnosed with lung Large Cell Carcinoma. [32]

- **Others:** This category encompasses a diverse group of rare or poorly differentiated NSCLC histologies.

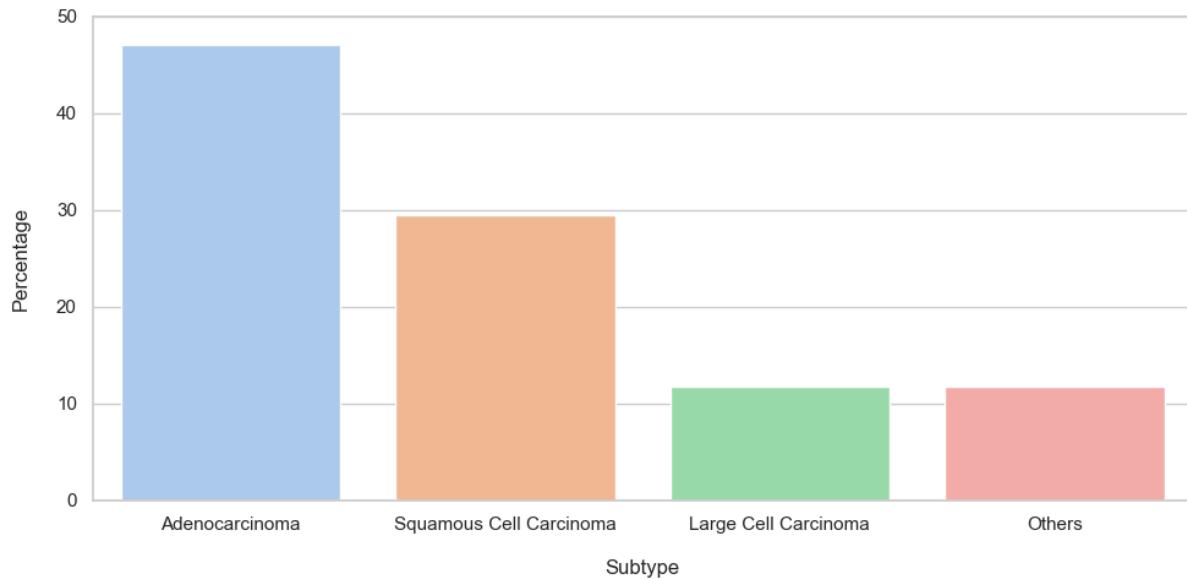
Adenosquamous carcinoma exhibits both glandular (adenocarcinoma) and squamous components, and is typically more aggressive than either component alone.

Sarcomatoid carcinomas are poorly differentiated tumors that show sarcoma-like features and include pleomorphic carcinoma, spindle cell carcinoma, and giant cell carcinoma. These are rare and generally associated with a poor prognosis.

Salivary gland-type tumors, such as mucoepidermoid carcinoma and adenoid cystic carcinoma, are histologically similar to tumors of the salivary glands and are extremely rare in the lungs.

Carcinoid tumors are neuroendocrine in origin and tend to be less aggressive, although atypical variants can exhibit more malignant behavior.

Finally, some tumors remain *unclassified* due to ambiguous histological features or inadequate sampling, and are grouped as NSCLC not otherwise specified (NOS). [41]



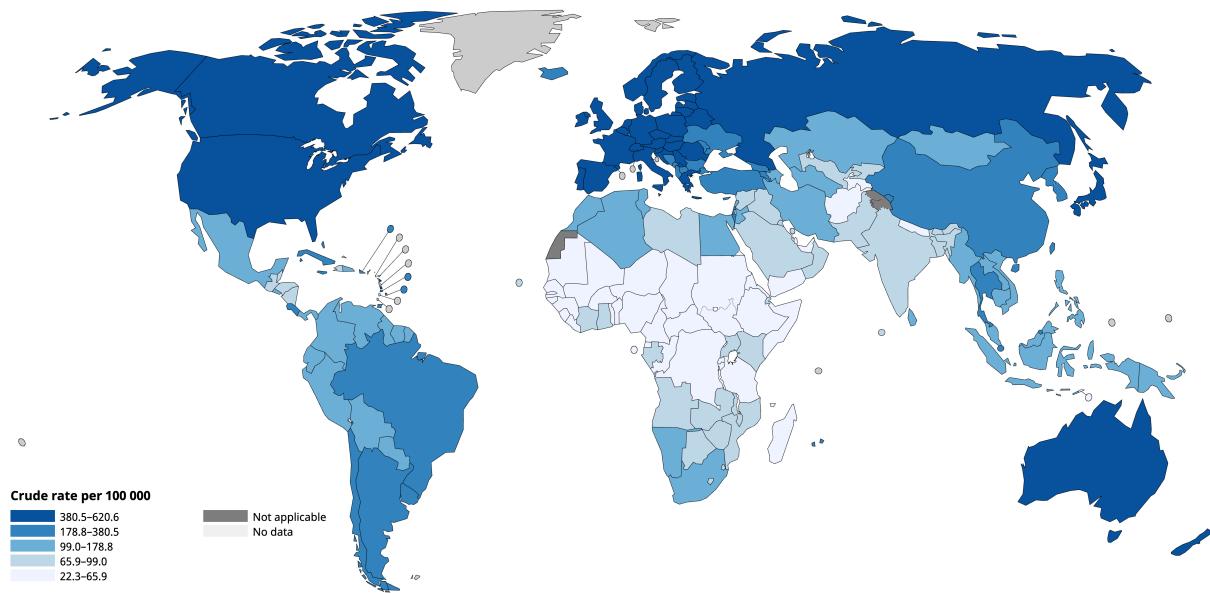
Distribution of NSCLC histological subtypes. Data source: [21].

SCLC, in contrast, tends to grow rapidly and spread early to distant body sites. It is strongly associated with cigarette smoking and is often diagnosed at an advanced stage.

1.3 Epidemiology and Global Burden

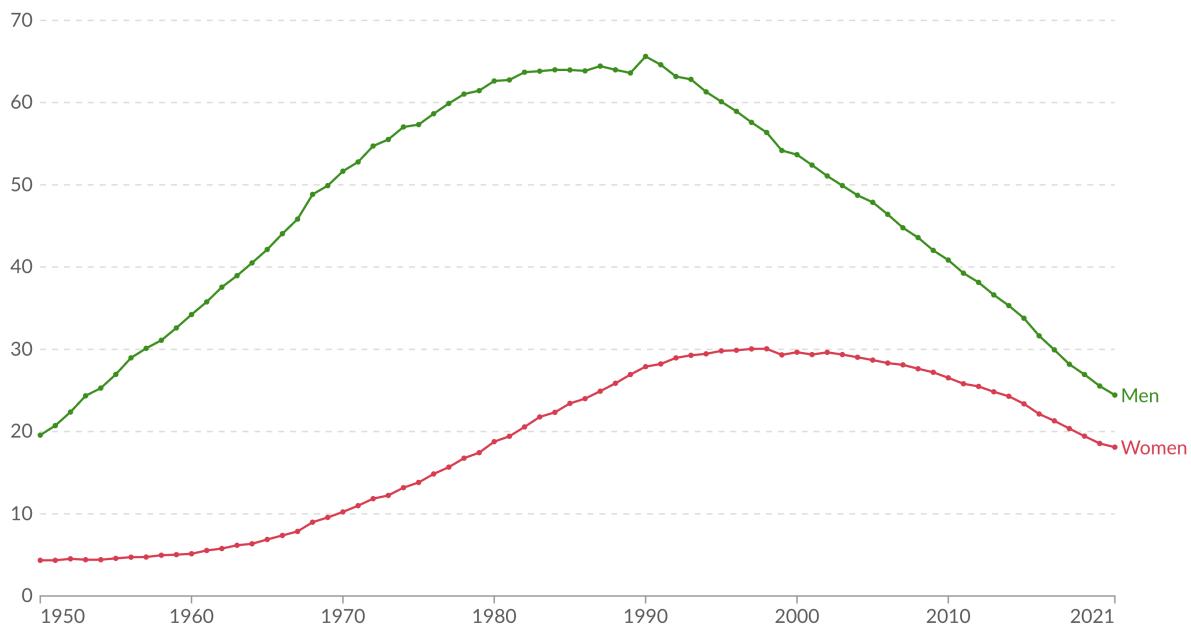
Lung cancer remains one of the leading causes of cancer-related deaths worldwide. According to the World Health Organization (WHO), lung cancer causes approximately 1.8 million deaths annually, making it the most lethal form of cancer. [47]

- **Incidence:** Varies globally, significantly depending by region, often reflecting differences in tobacco use, environmental exposure, and socioeconomic status. High-income countries generally show declining trends in incidence due to successful tobacco control efforts, while many low and middle-income countries are seeing rising rates due to increased smoking prevalence and industrial pollution.



Lung cancer estimated incidence crude rate (per 100,000 people). [47]

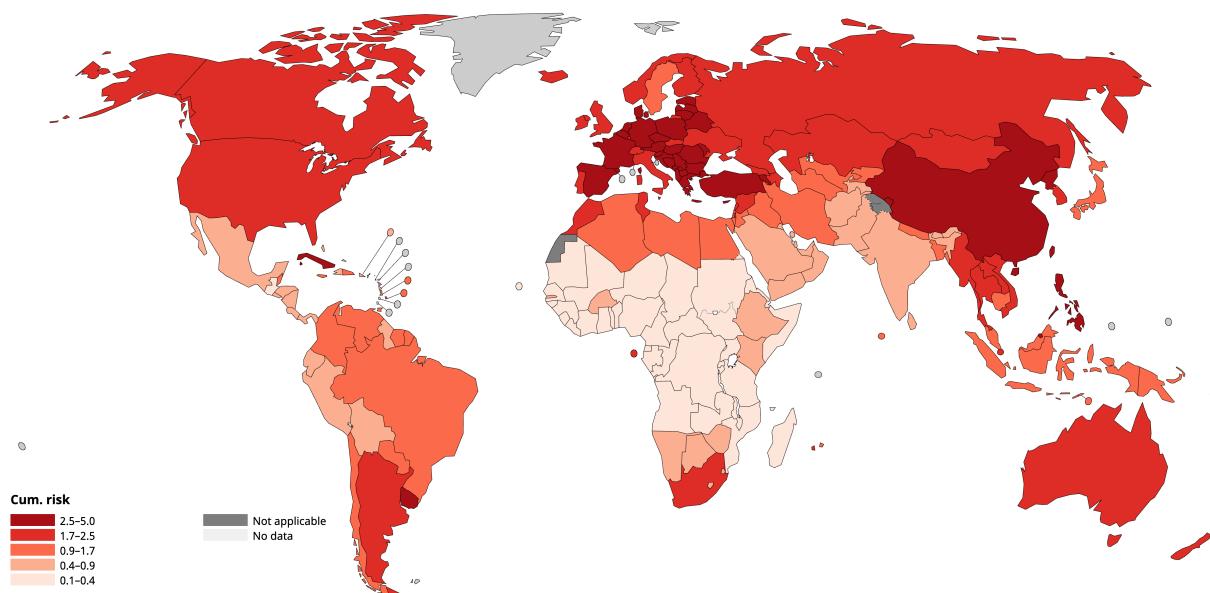
- **Gender Distribution:** Historically more prevalent in men, but the gap is narrowing due to increased smoking rates among women over time. Biological differences, including hormonal and genetic factors, may also contribute to distinct patterns of disease development and progression between sexes.



Lung cancer death rates (per 100,000 people). [25, 47]

- **Survival Rates:** The 5-year survival rate remains low (around 20%) [21], especially for cases diagnosed at a late stage. Mortality closely mirrors incidence rates, with lung cancer accounting for nearly one in five cancer deaths. Non-small cell lung

cancer (NSCLC), the most common type, generally has better outcomes than small cell lung cancer (SCLC), especially when diagnosed early.



Lung cancer estimated mortality cumulative risk (per 100,000 people). [47]

The global burden of lung cancer is not only reflected in mortality rates but also in the economic and social costs of treatment and loss of productivity. Prevention and early detection remain critical in reducing this burden.

2. Etiological Risk Factors

Lung cancer is the leading cause of global cancer incidence and mortality. Tobacco smoking is the greatest preventable cause of death worldwide, accounting for up to 90% of lung cancer cases, and continued consumption is projected to increase global cancer incidence, particularly in developing nations such as China, Russia, and India. Second-hand smoke among children and spouses has likewise been implicated. Radon from natural underground uranium decay is the second leading cause of lung cancer in the developed world. Occupational hazards such as asbestos and environmental exposures such as air pollution, arsenic, and HIV and Tb infection have all been implicated in lung carcinogenesis, while cannabis smoking, electronic cigarettes, heated tobacco products, and COVID-19 have been hypothesized to increase risk. [39]



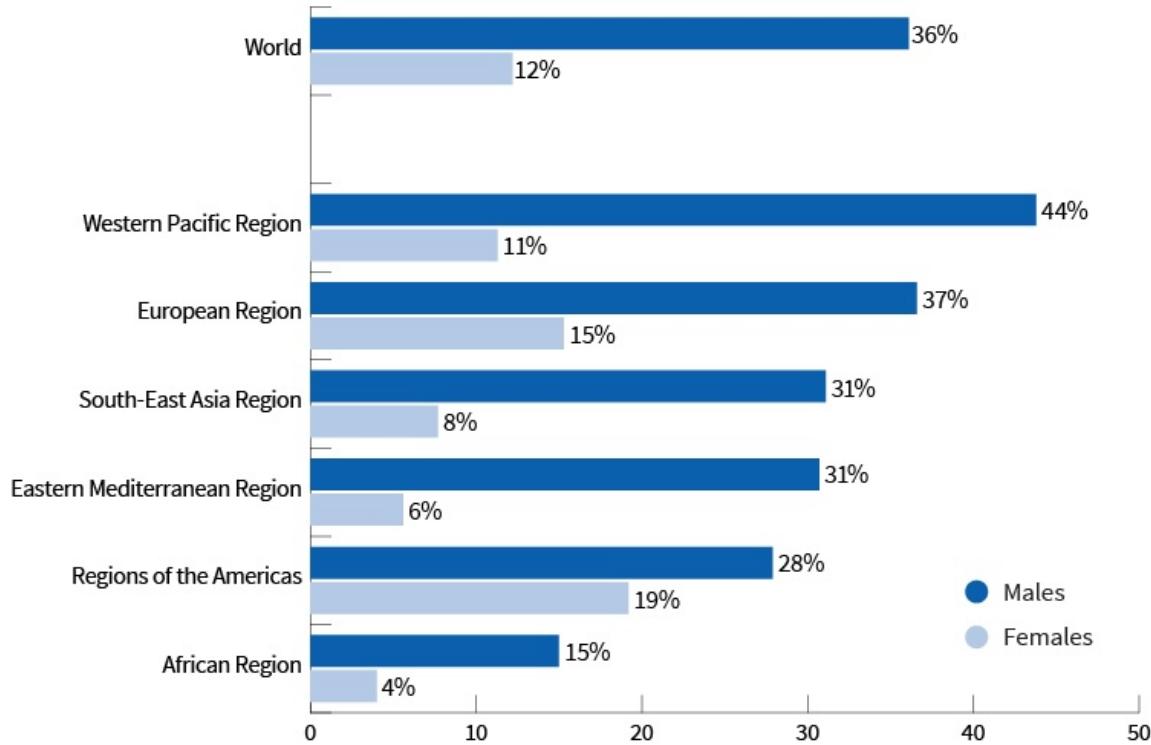
Risk factors for lung cancer. [14]

2.1 Tobacco Use and Exposure

While, at the beginning of the twentieth century, lung cancer was a rare disease, it was diagnosed progressively more often over the next 50 years, and various suggestions were made during this period that cigarette smoking might be the cause, deriving mainly from the simple fact that the incidence and cigarette consumption were increasing concomitantly.[27]

Tobacco smoke is a complex chemical mixture, containing several thousand compounds,

including at least 60 known carcinogens. It is reported that there are an estimated 1.1 billion smokers globally, 1.8 million deaths from lung cancer each year, and about 80–90% of those deaths are attributable to tobacco smoke exposure. [30]

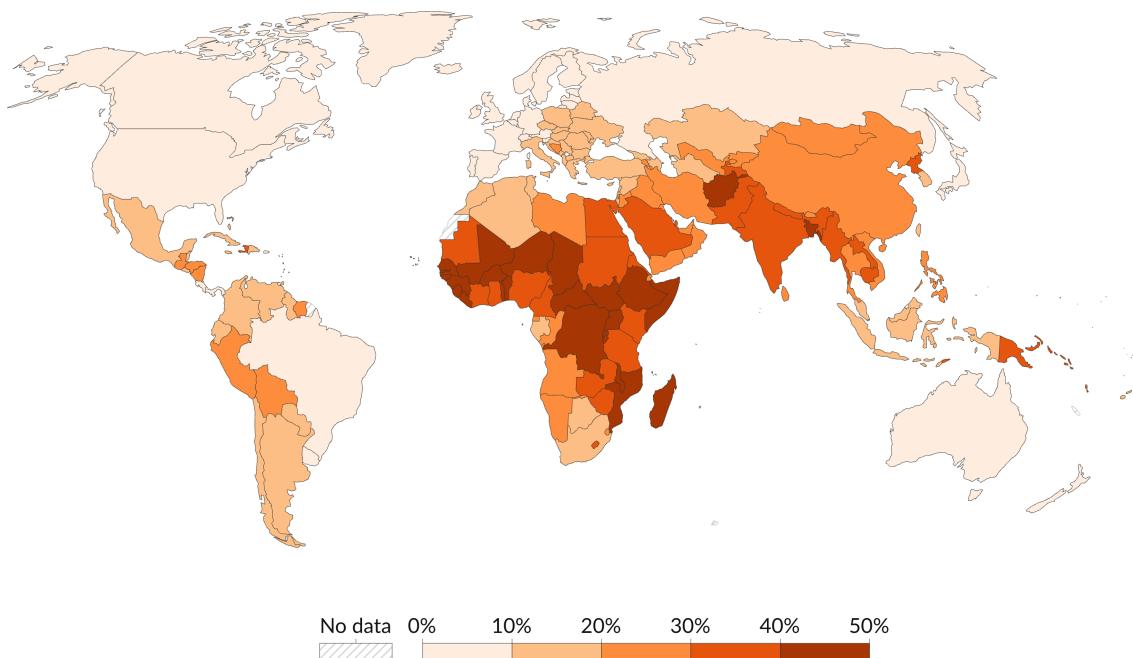


Deaths from Cancer Caused from Using Tobacco, Worldwide in 2019. [31]

There are several ways in which smoking promotes cancer. The primary method is harming our cells' DNA. Our cells' growth and behavior are governed by their DNA. Benzoapyrene and nitrosamines, two carcinogenic substances found in tobacco smoke, are the main source of DNA damage because they are metabolically converted into reactive intermediates in the body. By directly binding to DNA, these intermediates create chemical lesions known as DNA adducts, which alter the structure of DNA and obstruct proper transcription and replication. High amounts of reactive oxygen species (ROS) produced by tobacco smoking also cause oxidative stress, which harms DNA bases. Tobacco smoke not only directly damages DNA but also disrupts essential DNA repair processes such as base excision repair and nucleotide excision repair, which permits mutations to accumulate. Tobacco smoke also causes epigenetic modifications, like aberrant DNA methylation, which inhibit tumor suppressor genes and accelerate the development of cancer. All of these processes work together to explain the molecular link between cigarette smoke and lung cancer.

2.2 Environmental and Air Pollutants

Environmental and air pollutants significantly influence lung cancer risk through both direct carcinogenic effects and chronic inflammatory mechanisms. The relationship varies by pollutant type, exposure duration, and geographic context, with outdoor and indoor sources contributing differently across income levels.



The estimated share of lung cancer deaths attributed to the risk factor air pollution, 2021. [23]

- **Outdoor Air Pollution:** Particulate matter is a major driver, with studies showing a $10 \mu\text{g}/\text{m}^3$ increase in PM2.5 correlates with an 8% rise in lung cancer mortality [28] and long-term exposure increases lung adenocarcinoma risk, particularly in urbanized areas. Nitrogen dioxide (NO₂) and ozone (O₃) also contribute, with NO₂ linked to a 3% higher incidence per 1% concentration increase. Geographically, middle-income countries see a 0.28% lung cancer risk increase per 1% rise in outdoor pollution, while high-income countries face a 0.51% increase. [17]
- **Indoor Air Pollution:** Sources like cooking fumes, coal burning, and radon disproportionately affect high-income countries: a 1% increase in indoor pollution raises lung cancer risk by 0.37% in these regions. [18]

Lung cancer incidence might be significantly decreased by mitigating air pollution through stronger emission restrictions and the use of clean energy, especially in areas with quickly industrializing economies.

2.3 Genetic and Familial Predisposition

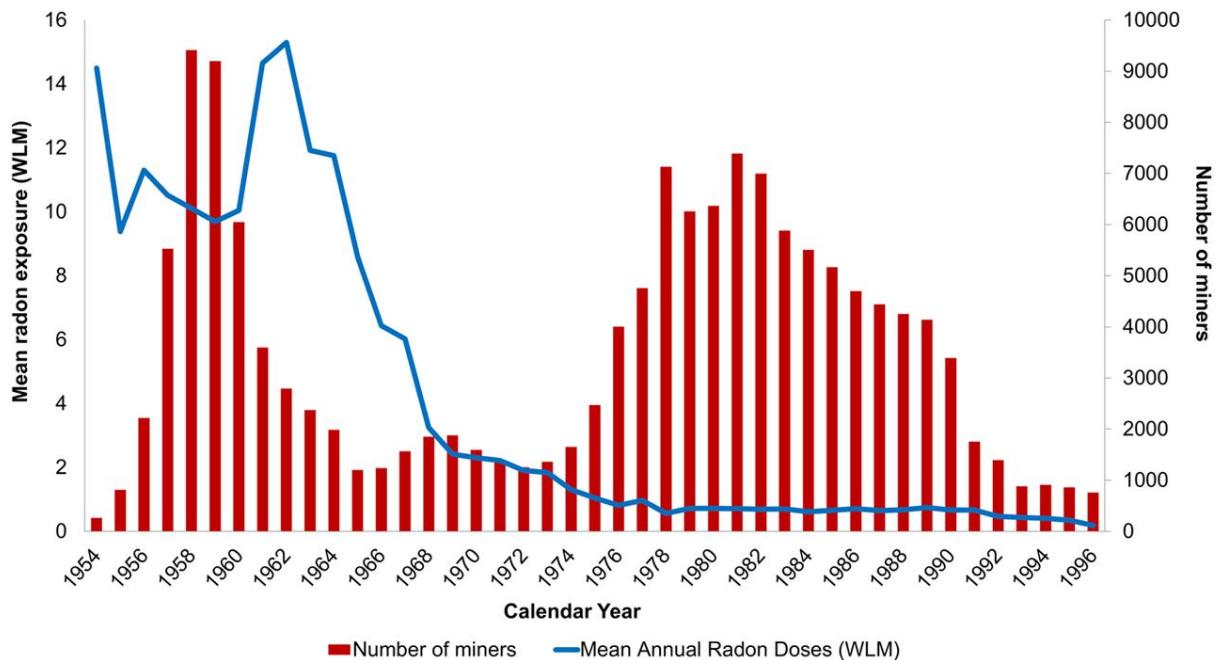
Genetic and familial predisposition play a significant but complex role in lung cancer risk, interacting with environmental factors like smoking.

- **Inherited Genetic Mutations:** Inherited mutations in BRCA1, BRCA2, and RAD51D increase small cell lung cancer risk. Carriers show better responses to platinum-based chemotherapy and PARP inhibitors due to impaired DNA repair mechanisms.
- **Familial Aggregation:** Having a parent or sibling with lung cancer confers a 1.5x higher risk after adjusting for smoking. Affected siblings correlate with a 1.8x increased risk, stronger than parental history (1.3–1.4x). Familial risk doubles (1.97x) for probands diagnosed before age 50. [12]

While only 8–15% of lung cancers [19] are linked to inherited factors, familial risk assessment remains critical for personalized prevention and treatment strategies.

2.4 Occupational and Industrial Hazards

Occupational and industrial hazards significantly increase lung cancer risk through exposure to various carcinogens commonly found in workplaces, often with a synergistic effect when combined with smoking.



Cancer incidence and mortality from exposure to radon progeny among Ontario uranium miners. [22]

- **Key Occupational Carcinogens:**

- *Asbestos*: Strongly linked to lung cancer and mesothelioma; Risk escalates sharply with cumulative exposure, even at low doses (no safe threshold). It causes direct DNA damage via iron-generated reactive oxygen species (ROS) and chronic inflammation. [38]
- *Silica dust (respirable crystalline silica)*: Predominantly associated with squamous cell and small cell carcinomas. Monotonic risk increase observed, with effects detectable at cumulative exposures as low as 0.22 mg/m³-years. Accounts for 3% of lung cancer cases in industrialized nations, rising to 6% [43] if all exposure levels are considered.

- **High-Risk Occupations:** Workers who are exposed, such as miners, shipyard workers, insulators, textile plant workers, foundry workers, stonecutters, and ceramics manufacturers, are at a significantly increased risk.

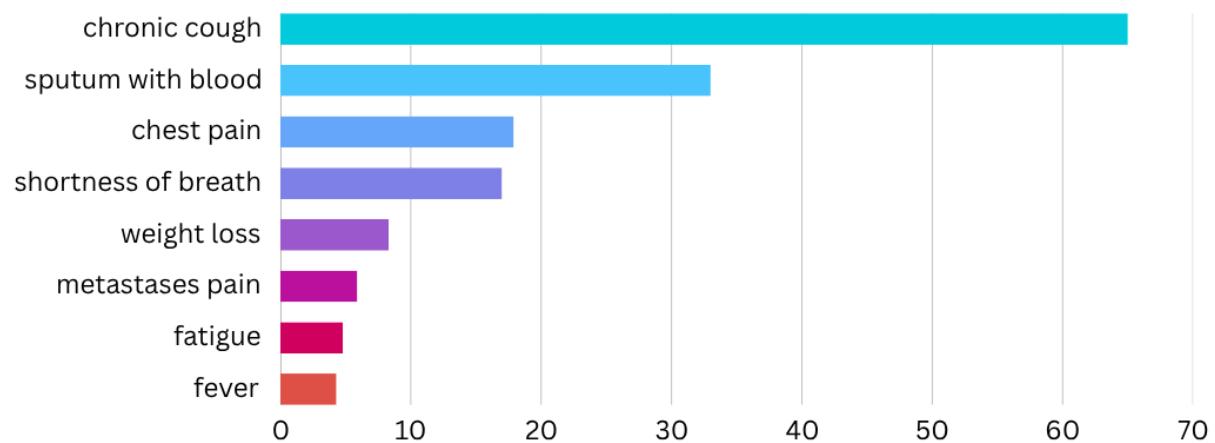
Safety protocols to protect workers from key occupational carcinogens focus on minimizing exposure through a hierarchy of controls, combining elimination, engineering, administrative measures, and personal protective equipment (PPE). These protocols align with international occupational health guidelines and aim to keep exposure ‘As Low As Reasonably Achievable’ (ALARA), effectively reducing the incidence of occupational cancers.

3. Clinical Manifestations

Lung cancer often does not cause symptoms in its early stages. Most clinical manifestations appear as the disease progresses, and they can vary depending on the location and extent of the tumor, as well as whether the cancer has spread (metastasized) to other parts of the body.

3.1 Early Warning Signs

Early warning signs can occur, and recognizing these symptoms can lead to earlier diagnosis and improved outcomes. Many of these symptoms are nonspecific and can be mistaken for other, less serious conditions, so persistence or worsening of these symptoms warrants medical evaluation.



Distribution of early symptoms. Data source: [48]

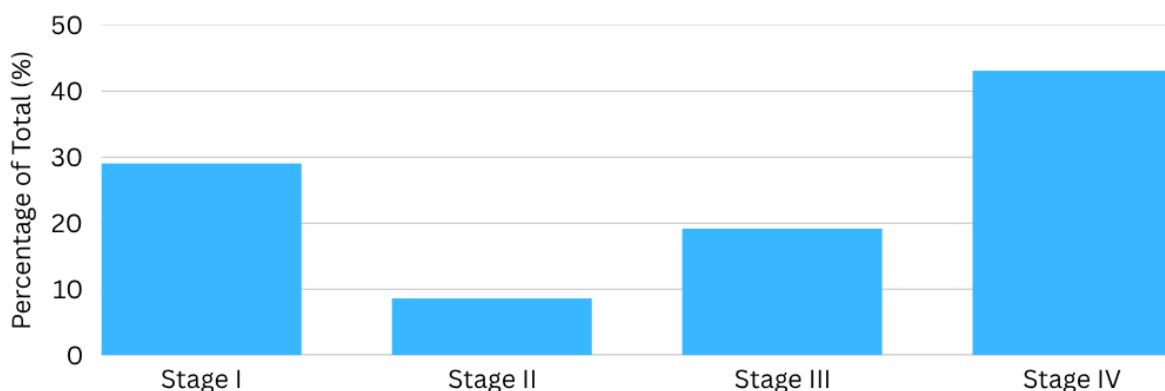
- Common early signs:

- **Persistent Cough:** A new cough that does not go away after three weeks, or a long-standing cough that worsens, is one of the most frequent early signs.
- **Coughing Up Blood:** Even small amounts of blood or rust-colored sputum can be an early warning sign and should be evaluated promptly.
- **Chest or Shoulder Pain:** Unexplained pain or discomfort in the chest or shoulder, especially if it worsens with breathing, coughing, or laughing.
- **Wheezing:** A new onset of wheezing or a whistling sound when breathing, not previously experienced, may indicate airway obstruction.

- **Very common early signs:**
 - **Unexplained Weight Loss:** Losing weight without trying, especially if significant.
 - **Loss of Appetite:** A decrease in appetite not attributable to other causes.
 - **Fatigue:** Feeling unusually tired or lacking energy, even with adequate rest.
- **Less common early signs:**
 - **Swelling of Face or Neck:** Can occur if a tumor obstructs blood flow in the chest.
 - **Finger Clubbing:** Changes in the shape of the fingertips, such as becoming more curved or enlarged, known as clubbing.

3.2 Progressed Stage Symptoms

As lung cancer advances to later stages (Stage 3 and Stage 4), symptoms become more pronounced, severe, and diverse due to tumor growth, local invasion, and metastasis to other organs. These progressed stage symptoms reflect both the direct effects of the tumor in the lungs and systemic manifestations related to cancer spread. Unfortunately, over half of lung cancer cases (52%) are diagnosed at the distant metastatic stage, which is associated with poor prognosis and only about 23% of cases are diagnosed at an early localized stage, where curative treatments are more effective and survival rates are significantly higher.



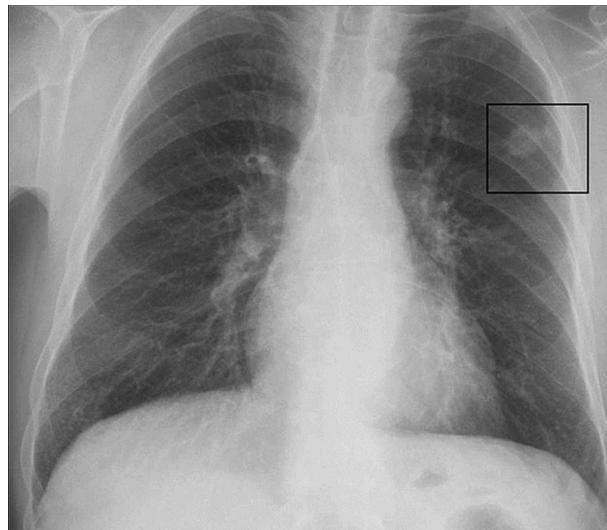
Lung cancer diagnoses by stage (2010–2017). Data source: [37]

- **Common Symptoms in Progressed Lung Cancer Stages (Stage 3 and 4):**
 - *Shortness of Breath (Dyspnea)*: Increasing difficulty breathing due to airway obstruction, tumor growth, or pleural effusion (fluid accumulation around the lungs).
 - *Hoarseness*: Caused by tumor involvement of the recurrent laryngeal nerve, leading to voice changes.
 - *Frequent Lung Infections*: Recurrent or persistent infections such as bronchitis or pneumonia due to impaired lung function and obstruction.
- **Symptoms Related to Tumor Spread (Metastasis):**
 - *Lymph Node Enlargement*: Swelling of lymph nodes near the collarbone, neck, or elsewhere.
 - *Neurological Symptoms*: Headaches, dizziness, seizures, memory problems, mood or personality changes, numbness, or balance issues due to brain metastases.
 - *Jaundice*: Yellowing of the skin and eyes from liver metastases.
 - *Horner Syndrome*: Drooping eyelid, small pupil, and decreased sweating on one side of the face due to tumor involvement of sympathetic nerves.
- **Paraneoplastic Syndromes:** In progressed lung cancer, tumors may produce hormones or hormone-like substances causing systemic effects known as paraneoplastic syndromes: muscle weakness, nausea and vomiting, high blood pressure, high blood sugar, confusion and seizures.

4. Diagnostic Approaches

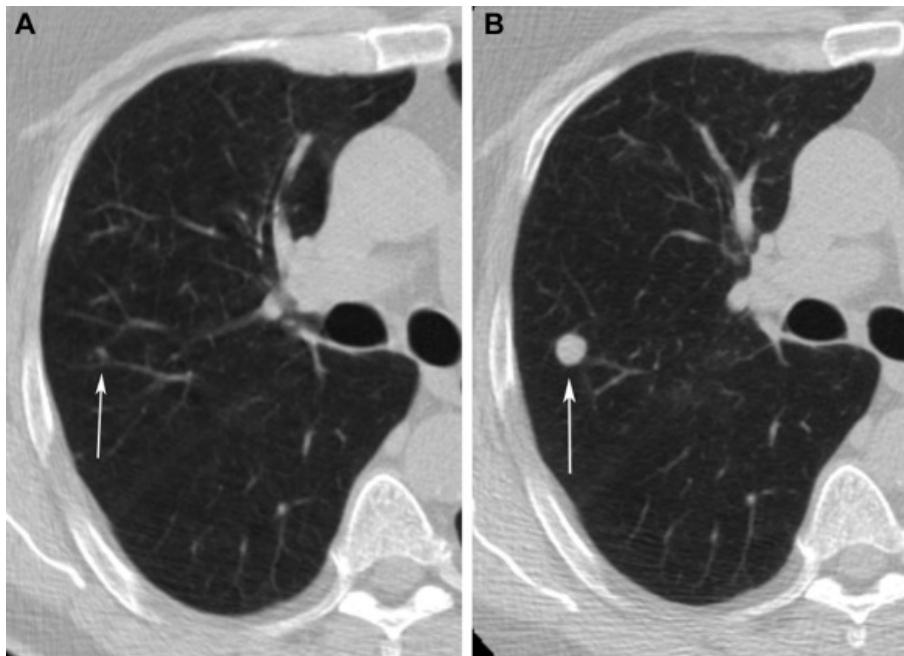
4.1 Imaging Techniques: CT, PET, and X-ray

- **Chest X-ray:** Often the first imaging test that primary care providers perform when lung cancer is suspected. Although less detailed than CT or PET, X-rays can provide quick information about the presence of abnormal masses in the lungs. However, small tumors or early-stage lung cancer may not be visible on an X-ray chest scan. [46]



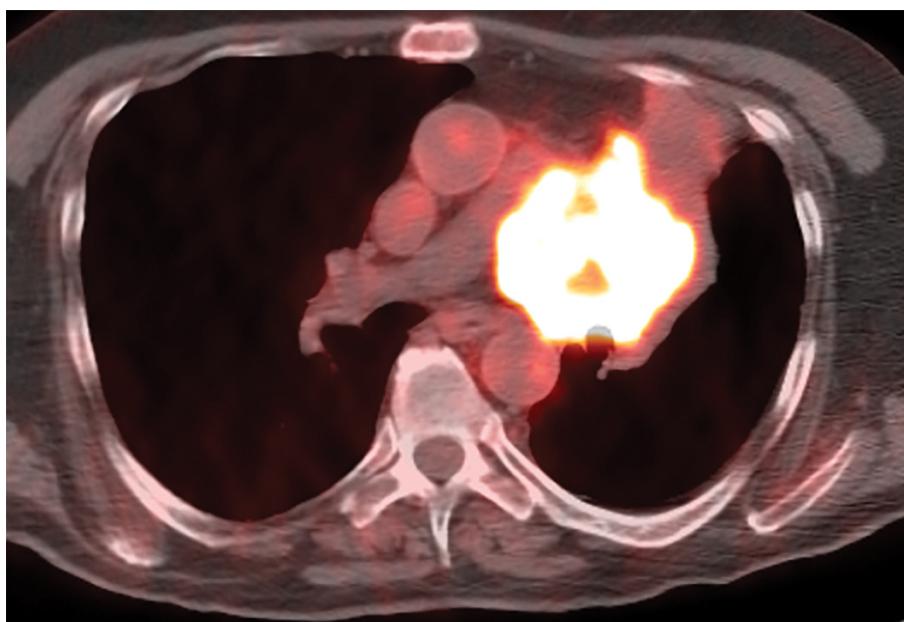
Chest X-ray scan of patient diagnosed with lung cancer. [9]

- **Computed Tomography:** Often used to monitor treatment response and check for recurrence. Provides detailed cross-sectional images of the lungs, allowing for the detection of tumors that may not be visible in a standard chest X-ray. They are particularly valuable for assessing the tumor's size and whether it has spread to nearby lymph nodes or other parts of the body.



CT scan showing growth of a micronodule (arrows) in the right upper lobe between baseline (A) and 1-year follow-up (B). [29]

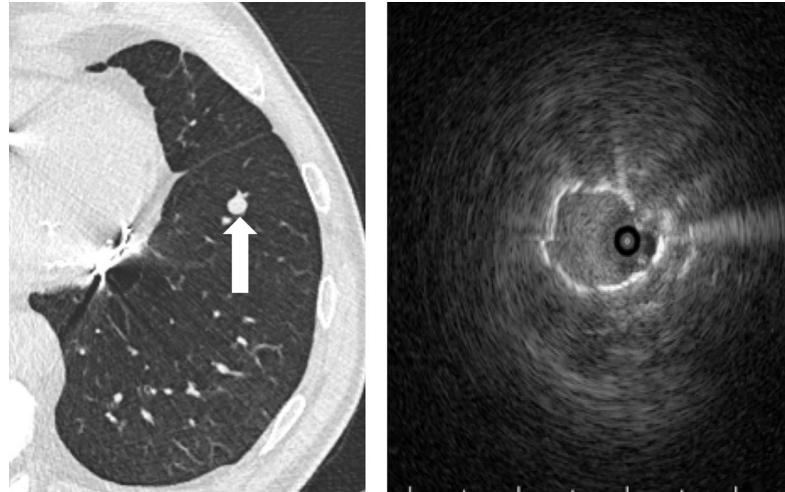
- **Positron Emission Tomography:** Employed to assess the metabolic activity of a tumor. Tumors typically exhibit higher metabolic activity than normal tissue, which is visualized as areas of increased uptake of radioactive tracers. PET scans are especially useful in determining the spread of lung cancer and for assessing whether a tumor is benign or malignant.



PET scan showing growth of a nodule (lighten area). [33]

4.2 Biopsy and Cytological Analysis

- **Bronchoscopy:** A procedure in which a thin, flexible tube is inserted through the mouth or nose into the lungs to collect tissue samples from the airways.



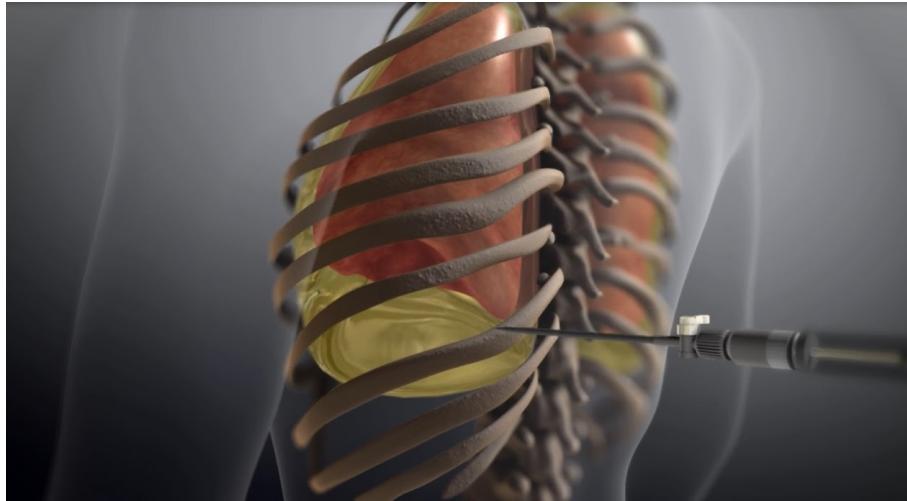
Bronchoscopy lung biopsy in a case of suspected lung cancer. [1]

- **Needle Biopsy:** A needle is inserted into the lung to obtain tissue or fluid samples, typically guided by imaging techniques like CT or ultrasound.



Percutaneous lung biopsy in a case of suspected lung cancer under control of computed tomography. [45]

- **Thoracentesis:** This method involves using a needle to remove fluid from the pleural space around the lungs, which can be tested for cancer cells.



Thoracentesis lung biopsy procedure. [13]

Once a tissue sample is obtained, it is analyzed through cytological examination. The analysis determines the presence of cancerous cells and provides insights into the type of lung cancer. This information helps in staging and treatment planning. In some cases, molecular tests are performed to identify genetic mutations that may influence treatment choices.

4.3 Tumor Staging and Grading

Staging and grading are essential for determining the prognosis and optimal treatment strategy for lung cancer patients. Staging refers to the extent of cancer spread, while grading assesses how aggressive the cancer cells are.

Staging is generally performed using the TNM system, which evaluates:

- **T (Tumor):** The size and extent of the primary tumor. For example, T1 indicates a small tumor, while T4 indicates a larger, more invasive tumor.
- **N (Nodes):** Whether cancer has spread to nearby lymph nodes. N0 indicates no lymph node involvement, while N3 indicates extensive nodal spread.
- **M (Metastasis):** Whether the cancer has spread to distant organs. M0 indicates no distant metastasis, while M1 indicates the presence of metastasis.

Together, these three categories allow for the classification of lung cancer into various stages, ranging from stage 0 (localized) to stage IV (advanced).

Grading evaluates how abnormal the cancer cells look under a microscope, which helps predict how quickly the cancer may grow and spread. The grade ranges from low-grade (well-differentiated) to high-grade (poorly differentiated). High-grade tumors tend to grow and spread more aggressively.

Both staging and grading are critical for determining the appropriate treatment approach, whether it involves surgery, radiation, chemotherapy, or targeted therapies. Early-stage cancers (stages I and II) may be treatable through surgery, while more advanced cancers (stages III and IV) often require systemic treatments like chemotherapy and immunotherapy.

4.4 Summary and Importance of Diagnostic Approaches

Accurate and timely diagnosis of lung cancer is essential for selecting the most appropriate treatment and improving patient outcomes. Imaging techniques, biopsy and cytological analysis, and tumor staging and grading are crucial components in this process. Early detection, particularly in high-risk individuals, can significantly improve survival rates and quality of life. Continued advancements in diagnostic technology, along with more personalized approaches to treatment, offer hope for better management of lung cancer in the future.

5. Prognostic Indicators

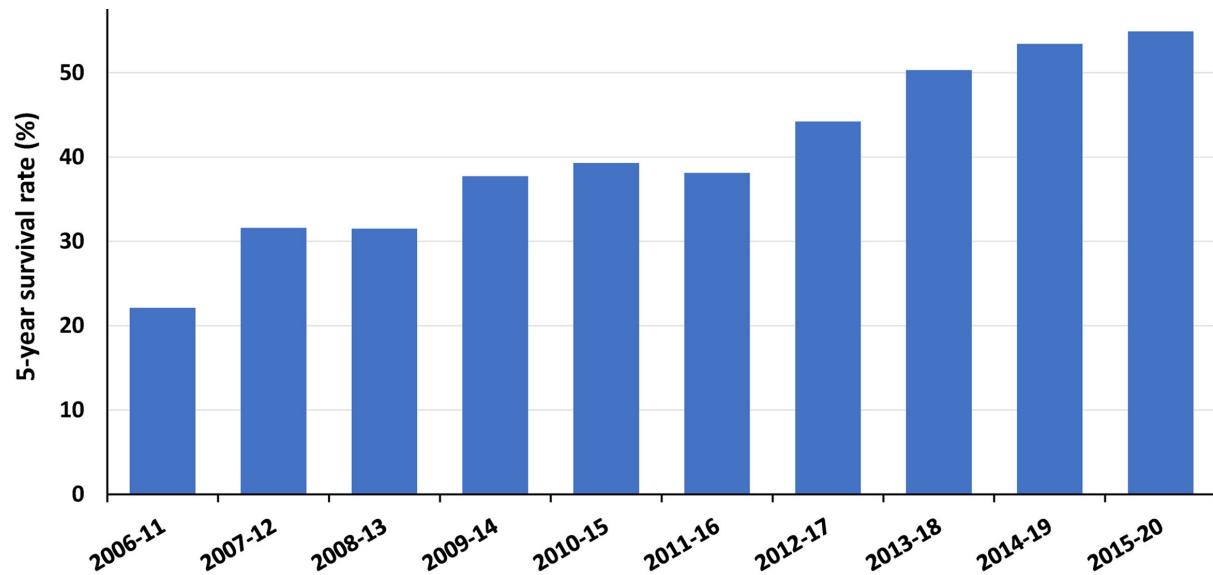
5.1 Survival Rates and Trends

Survival rates in lung cancer are important indicators of disease burden, therapeutic success, and early detection effectiveness. These rates vary significantly depending on cancer type, stage at diagnosis, patient demographics, and treatment accessibility.

Non-small cell lung cancer (NSCLC), which comprises around 85% of lung cancer cases, typically has a better prognosis than small cell lung cancer (SCLC), which is more aggressive and fast-growing.

According to global cancer statistics, the 5-year survival rate for localized NSCLC is approximately 64%, but this rate drastically drops to 8% for distant-stage disease [36].

In recent years, survival trends have improved slightly due to advances in early detection through low-dose CT screening, the development of targeted therapies, and immunotherapies. Studies have shown that overall mortality from lung cancer has declined in high-income countries, particularly in populations with reduced smoking rates and improved healthcare access [35].



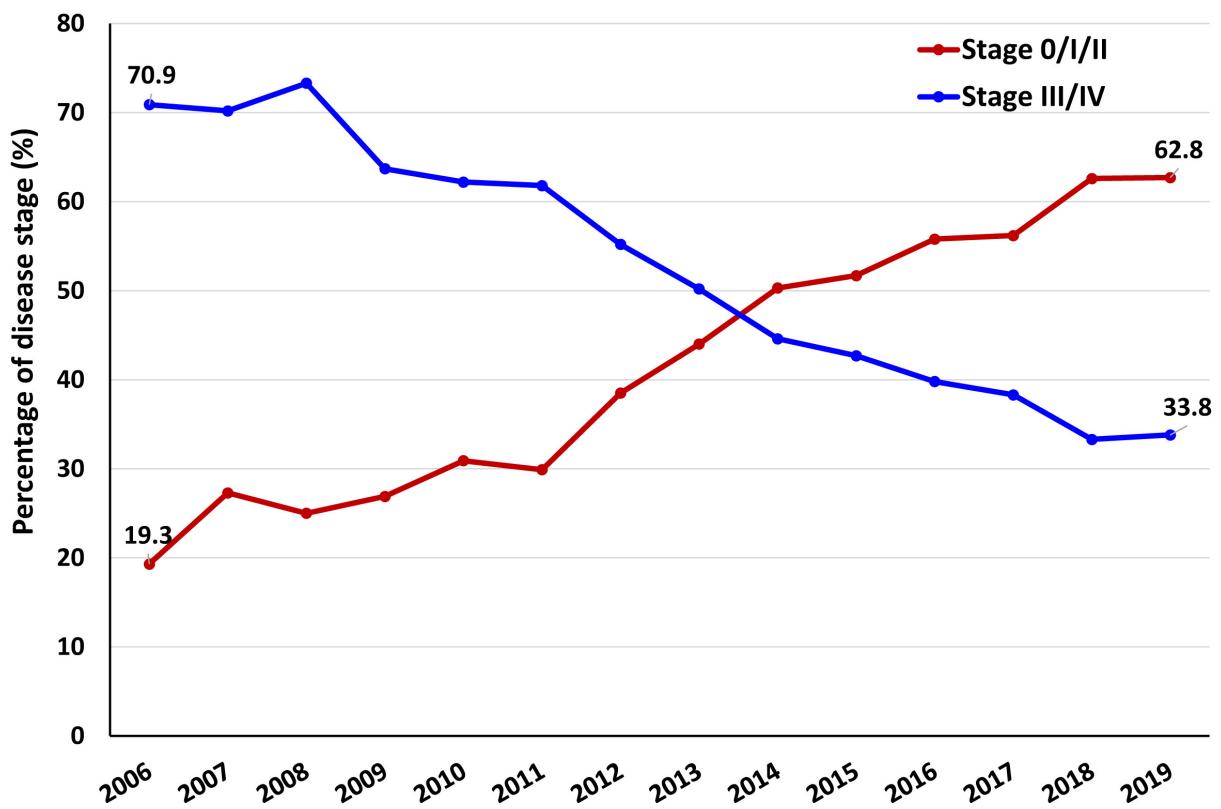
Five-year survival rates over years (all stages). [24]

However, despite these improvements, lung cancer remains one of the leading causes of cancer-related deaths worldwide. The global 5-year survival rate for all lung cancers combined remains below 20%, underlining the need for continued progress in early detection and treatment strategies [10].

5.2 Determinants of Clinical Outcome

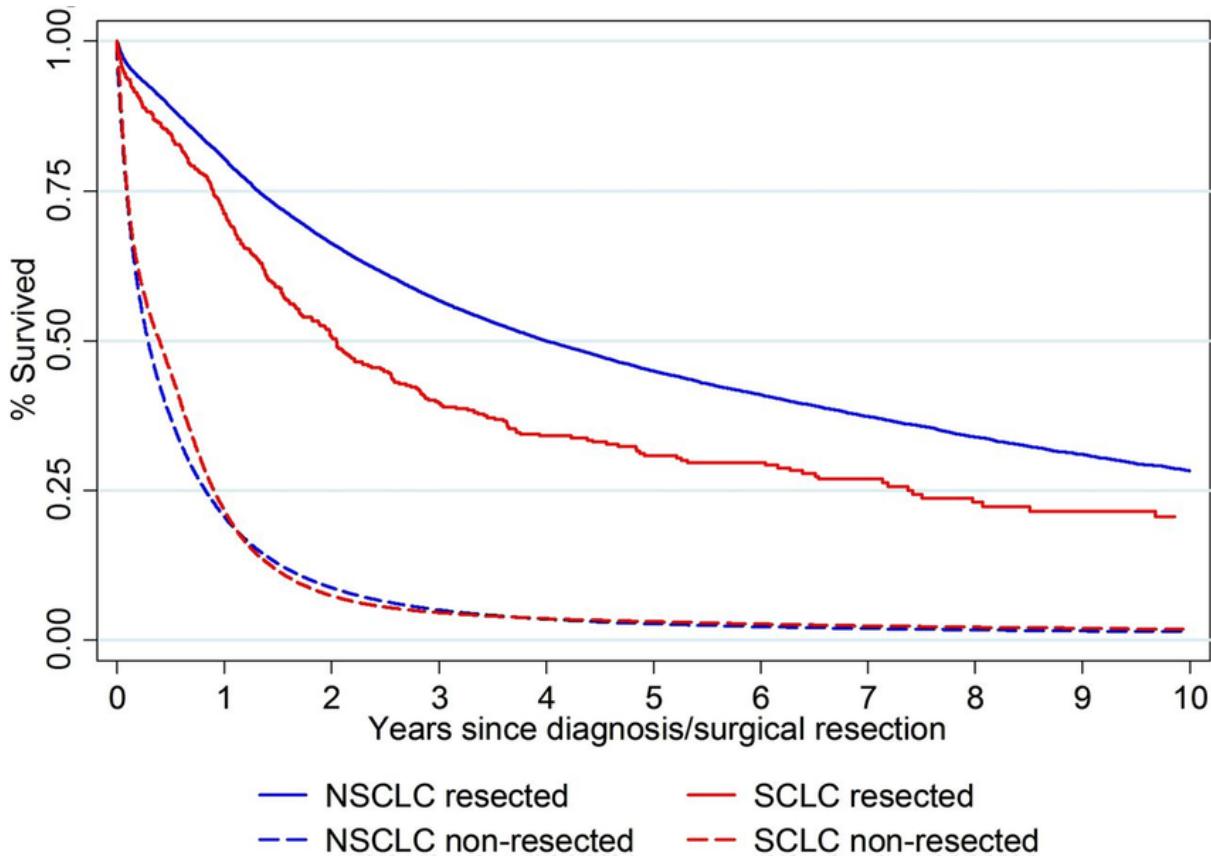
Several clinical, biological, and lifestyle factors influence the prognosis of lung cancer patients. These determinants help clinicians estimate disease progression and tailor personalized treatment strategies.

- **Stage at Diagnosis:** The single most important prognostic factor. Patients diagnosed at early stages (I or II) typically have much better outcomes than those diagnosed at advanced stages (III or IV). Early-stage lung cancer is often amenable to surgical resection or curative radiotherapy, which significantly improves survival chances [16].



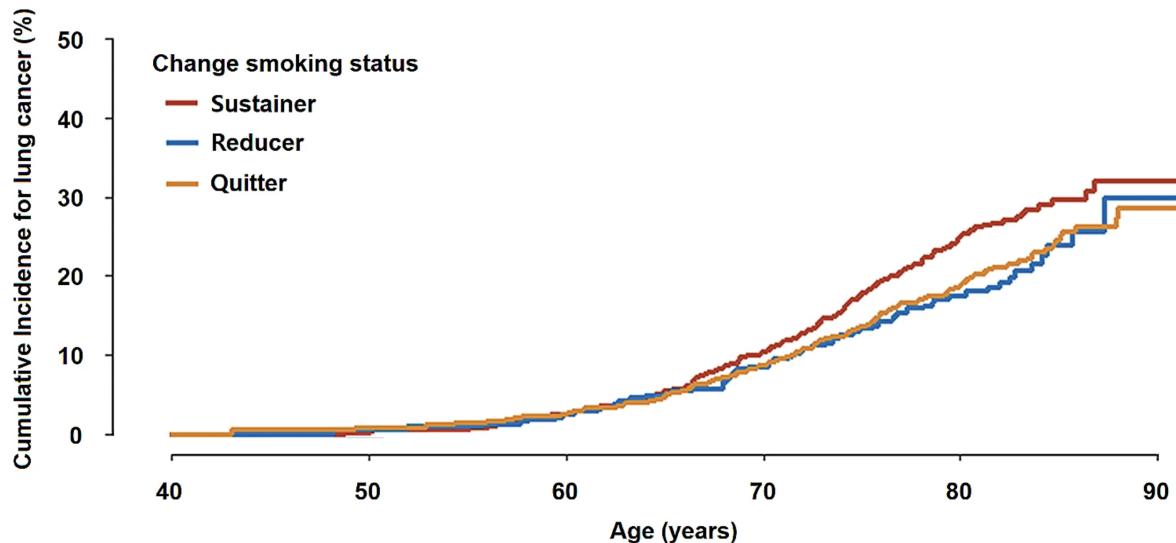
Change in localized (stage 0/I/II) and advanced (stage III/IV) lung cancer from 2006 to 2019 in NTUH. NTUH, National Taiwan University Hospital. [24]

- **Histological Type:** The type of lung cancer, such as adenocarcinoma, squamous cell carcinoma, or small cell carcinoma, impacts prognosis. For example, adenocarcinomas are generally associated with better outcomes, while SCLC tends to have a more rapid progression and worse prognosis [42].



Kaplan-Meier survival analysis of resected and unresected patients with non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). [20]

- **Performance Status:** A measure of a patient's general well-being and ability to perform daily activities. Patients with good performance status tend to tolerate aggressive treatments better and have improved survival outcomes [8].
- **Genetic and Molecular Markers:** Certain genetic mutations, such as EGFR, ALK, or KRAS, can influence prognosis and guide the use of targeted therapies. For example, patients with EGFR mutations may benefit significantly from tyrosine kinase inhibitors, improving survival outcomes [44].
- **Comorbidities:** The presence of other chronic conditions such as chronic obstructive pulmonary disease (COPD), cardiovascular disease, or diabetes can affect treatment options and survival [40].
- **Smoking Status:** Non-smokers or those who have quit smoking tend to have better clinical outcomes compared to current smokers. Continued tobacco exposure during treatment can reduce the efficacy of therapies and worsen prognosis [15].



Impact of smoking reduction on lung cancer risk in patients with COPD. [34]

Understanding these prognostic indicators allows healthcare providers to make informed decisions regarding treatment intensity, follow-up strategies, and patient counseling. As precision medicine advances, integrating clinical, molecular, and lifestyle data will continue to refine prognostic models for lung cancer patients.

6. Emerging Research and Technologies

6.1 Novel Therapeutic Developments

Recent years have seen the emergence of innovative cancer therapies that aim to overcome the limitations of traditional treatments and improve patient outcomes. Notable advancements include:

- **Immunotherapy Innovations:** Researchers have developed new compounds, such as proteolysis-targeting chimeras (PROTACs), that degrade tumor-promoting proteins within cells. For example, a novel PROTAC called NR-V04 targets the intracellular protein NR4A1, unleashing the immune system to attack cancer cells and demonstrating sustained tumor suppression in preclinical models [3]. This approach may benefit patients who do not respond to current immunotherapies, as it can target a wider range of immune cells and access the tumor microenvironment more effectively.
- **Radiopharmaceuticals:** These drugs incorporate radioactive materials for both cancer diagnosis and treatment, providing precise targeting of tumors while minimizing damage to surrounding tissues [2].
- **Gene Modification Therapies:** Cutting-edge therapies are being designed to modify genes involved in tumor growth regulation, offering new avenues for intervention in resistant cancers [2].
- **Therapeutic Cancer Vaccines:** Vaccines are being developed not just for prevention but also for therapeutic purposes, aiming to stimulate the immune system to recognize and destroy cancer cells [2].
- **mRNA-based Therapies:** Experimental mRNA therapies, such as mRNA-4359, are being tested in clinical trials for solid tumors. These therapies train the immune system to recognize tumor markers, potentially improving the response to existing immunotherapies like pembrolizumab [26].

6.2 AI and Machine Learning in Oncology

Artificial intelligence (AI) and machine learning (ML) are transforming oncology by enhancing diagnostics, treatment planning, and drug discovery:

- **Cancer Detection:** AI models can analyze imaging scans (e.g., mammography, pathology slides) with greater speed and accuracy than humans, detecting subtle patterns that might be missed by radiologists. For example, AI-enhanced mammography improves tumor visualization and characterization [26].

- **Personalized Treatment Planning:** AI algorithms analyze genomic, clinical, and lifestyle data to predict how individual patients will respond to specific therapies. This enables tailored treatment strategies and reduces trial-and-error approaches [26, 4].
- **Predictive Modeling:** Recent models integrate whole-slide tumor imaging with gene expression data to predict chemotherapy response in cancers such as muscle-invasive bladder cancer, outperforming models based on a single data type. This supports precision medicine by identifying patients most likely to benefit from specific treatments [4].
- **Drug Discovery and Repurposing:** AI accelerates the identification of new drug candidates and the repurposing of existing drugs by analyzing large datasets and simulating drug-target interactions [11].
- **Risk Prediction and Early Detection:** AI tools can analyze electronic health records to identify individuals at high risk for certain cancers years before clinical diagnosis, enabling earlier intervention [26].

6.3 Clinical Trials and Future Horizons

The landscape of oncology clinical trials is rapidly evolving, with a focus on translating these emerging therapies and technologies into clinical practice:

- **Active Clinical Trials:** Ongoing trials are evaluating the safety and efficacy of novel agents such as mRNA-based immunotherapies and PROTACs in various solid tumors and hematologic cancers [6, 3].
- **Biomarker-Driven Studies:** Many trials now incorporate biomarker analysis to stratify patients and personalize therapy, increasing the likelihood of treatment success [7].
- **Collaborative Research:** International conferences and consortia, such as the 12th Annual Clinical Trials in Oncology Europe, foster collaboration between academia, industry, and healthcare providers to accelerate the development and approval of innovative treatments [5].
- **Future Directions:** The integration of AI into clinical trial design and patient monitoring is expected to optimize trial efficiency, improve patient selection, and enhance the interpretation of complex data. The ultimate goal is to achieve more effective, less toxic, and highly personalized cancer therapies [11, 26].

These advancements collectively represent a new era in cancer research and care, marked by the convergence of biotechnology, computational science, and collaborative clinical research.

7. Conclusion and Outlook

7.1 Key Takeaways

Lung cancer remains one of the most challenging malignancies worldwide due to its high mortality rates and often late diagnosis. This chapter has highlighted several critical points:

- **Survival rates vary widely** depending on cancer type, stage at diagnosis, and patient factors. Early detection substantially improves outcomes, particularly for non-small cell lung cancer (NSCLC).
- Advances in **screening methods**, such as low-dose computed tomography (LDCT), and the advent of **targeted therapies** and **immunotherapies** have contributed to modest but meaningful improvements in survival.
- Prognosis is influenced by a combination of **clinical factors** (e.g., stage, performance status), **molecular markers** (e.g., EGFR mutations), and **lifestyle factors** such as smoking status.
- Despite progress, the overall 5-year survival rate remains low globally, emphasizing the urgency for continued research, enhanced early detection, and equitable access to care.

Together, these insights underscore the complexity of lung cancer prognosis and the multifaceted approach required to improve patient outcomes.

7.2 Vision for the Future of Lung Cancer Care

Looking ahead, the future of lung cancer care is poised for transformative changes driven by technological innovation and personalized medicine:

- **Widespread implementation of precision oncology:** Integration of comprehensive genomic profiling into routine clinical practice will enable tailored treatment regimens based on individual tumor biology, optimizing therapeutic efficacy and minimizing toxicity.
- **Enhanced early detection strategies:** Advances in liquid biopsies, biomarkers, and artificial intelligence-powered imaging analysis promise earlier and more accurate diagnosis, increasing the proportion of patients eligible for curative interventions.
- **Multidisciplinary care models:** Closer collaboration between oncologists, pulmonologists, radiologists, and supportive care specialists will ensure holistic treat-

ment plans addressing not only cancer control but also quality of life and comorbid conditions.

- **Health equity and global access:** Efforts to reduce disparities by expanding lung cancer screening and advanced treatment availability in low- and middle-income countries will be critical to lowering worldwide mortality.
- **Immunotherapy and combination treatments:** Ongoing research into novel immunotherapeutic agents and their combination with chemotherapy, radiation, and targeted therapies holds promise for improved long-term survival.
- **Patient empowerment and digital health:** The use of digital platforms for patient monitoring, symptom tracking, and telemedicine will facilitate personalized follow-up and timely intervention, ultimately enhancing care delivery.

In conclusion, sustained investment in research, technology adoption, and patient-centered care will be essential to overcome current limitations and pave the way toward a future where lung cancer is detected early, treated effectively, and managed in a manner that maximizes both survival and quality of life.

References

- [1] Andrew R. Haas. “The Vital and Evolving Role of Bronchoscopic Technologies in Lung Cancer Management”. In: *International Lung Cancer News* (2018). URL: <https://www.ilcn.org/the-vital-and-evolving-role-of-bronchoscopic-technologies-in-lung-cancer-management/>.
- [2] Author C. and Author D. “mRNA-4359 in solid tumors: a phase 1 clinical trial”. In: *Clinical Cancer Research* 31 (2025). Reports on mRNA-based immunotherapy trials, pp. 789–799. DOI: 10.xxxx/CCR.2025.789.
- [3] Author E. and Author F. “Integrating AI and gene expression data to predict chemotherapy response”. In: *Artificial Intelligence in Medicine* 140 (2025). Describes AI models combining imaging and genomics, pp. 102–115. DOI: 10.xxxx/aim.2025.102.
- [4] Author G. and Author H. “Advances in Radiopharmaceuticals for Targeted Cancer Therapy”. In: *Frontiers in Oncology* 14 (2024). Review of new radiopharmaceutical agents and clinical applications, pp. 456–470. DOI: 10.xxxx/fonc.2024.456.
- [5] Author I. and Author J. “CRISPR-Cas9 Gene Editing Approaches in Cancer Treatment”. In: *Molecular Therapy* 33.1 (2025). Explores gene modification therapies targeting tumor growth, pp. 15–28. DOI: 10.xxxx/molther.2025.015.
- [6] Author K. and Author L. “Artificial Intelligence for Early Cancer Detection Using Electronic Health Records”. In: *Journal of Medical Internet Research* 27.2 (2025). Describes AI models predicting cancer risk years before diagnosis, e34567. DOI: 10.xxxx/jmir.2025.e34567.
- [7] Author M. and Author N. “Therapeutic Cancer Vaccines: Current Progress and Future Perspectives”. In: *Cancer Immunology Research* 13.4 (2025). Comprehensive review of therapeutic vaccine strategies in oncology. DOI: 10.xxxx/cir.2025.345.
- [8] Basch, Ethan and Deal, Allison M and Kris, Mark G and et al. “Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial”. In: *Journal of Clinical Oncology* 34.6 (2016), pp. 557–565.
- [9] Bradford, Natalie and Irving, Helen and Eren, Halit and Webster, John. “Teleoncology Ch25 pp. 561-580”. In: Jan. 2016, pp. 561–580. ISBN: 978-1-4822-3658-3.
- [10] Bray, Freddie and Ferlay, Jacques and Soerjomataram, Isabelle and Siegel, Rebecca L and Torre, Lindsey A and Jemal, Ahmedin. “Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries”. In: *CA: a cancer journal for clinicians* 68.6 (2018), pp. 394–424.
- [11] Clinical Trials in Oncology Europe. *12th Annual Clinical Trials in Oncology Europe Conference Report*. <https://clinicaltrialsconference2025.org/report>. Summary of recent clinical trial advances and future directions. 2025. (Visited on 05/15/2025).

- [12] Coté ML, Liu M, Bonassi S et al. "Increased risk of lung cancer in individuals with a family history of the disease: a pooled analysis from the International Lung Cancer Consortium." In: *Eur J Cancer* (2012). DOI: 10.1016/j.ejca.2012.01.038.
- [13] Dr. John Smith. *Advancements in Lung Cancer Diagnosis*. Accessed: 2025-05-15. 2023. URL: https://www.youtube.com/watch?v=QubaJaH_Thc.
- [14] Florez, Narjust D. and others. "Lung Cancer in Women: The Past, Present, and Future". In: *Clinical Lung Cancer* 25.1 (2023), pp. 1–8. DOI: 10.1016/j.cllc.2023.100309. URL: [https://www.clinical-lung-cancer.com/article/S1525-7304\(23\)00212-7/fulltext](https://www.clinical-lung-cancer.com/article/S1525-7304(23)00212-7/fulltext).
- [15] Gilbert, Hannah and Selby, Peter. "Smoking cessation in patients with cancer: a review of evidence and clinical strategies". In: *Current Oncology* 27.2 (2020), pp. 123–130.
- [16] Goldstraw, Peter and Chansky, Kari and Crowley, John and Rami-Porta, Ramon and Asamura, Hideki and Eberhardt, Wilfried E and Nicholson, Andrew G and Groome, Patti and Mitchell, Andrea and Bolejack, Vanessa. "Lung cancer staging and prognosis". In: *Journal of Thoracic Oncology* 11.1 (2016), pp. 39–51.
- [17] González-Ruiz J. A Baccarelli A. Cantu-de-Leon D. Prada D. "Air Pollution and Lung Cancer: Contributions of Extracellular Vesicles as Pathogenic Mechanisms and Clinical Utility. Curr Environ Health Rep". In: *JCO Global Oncology* 10 (2023), pp. 478–489. DOI: 10.1007/s40572-023-00421-8.
- [18] Gozlu, Mehmet and Senol, Osman and Cirakli, Umit and Aslan, Huseyin and Akbulut, Fevzi and Gokkaya, Durmus. "The effect of air pollution quality on lung cancer rates in middle-income and high-income countries: a panel data analysis approach". In: *Frontiers in Public Health* Volume 12 - 2024 (2024). DOI: 10.3389/fpubh.2024.1372320. URL: <https://www.frontiersin.org/journals/public-health/articles/10.3389/fpubh.2024.1372320>.
- [19] Kanwal M, Ding XJ, Cao Y. "Familial risk for lung cancer". In: *Oncol Lett* (2017). DOI: 10.3892/ol.2016.5518.
- [20] Lüchtenborg, Margreet and Sheikh, Shama and Lim, Eric and Page, Richard and Baldwin, David and Jakobsen, Erik and Vedsted, Peter and Lind, Mike and Peake, Michael and Mellemgaard, Anders and Spicer, James and lang-lazdunski, Loic and Moller, Henrik. "Survival of patients with small cell lung cancer undergoing lung resection in England, 1998–2009". In: *Thorax* 69 (Oct. 2013). DOI: 10.1136/thoraxjnl-2013-203884.
- [21] National Library of Medicine. *Non-Small Cell Lung Cancer Treatment (PDQ)–Health Professional Version*. Accessed: 2025-05-12. 2025. URL: <https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq>.
- [22] Navaranjan, Garthika and Berriault, Colin and Do, Minh and Villeneuve, Paul J and Demers, Paul A. "Cancer incidence and mortality from exposure to radon

- progeny among Ontario uranium miners”. In: *Occupational and Environmental Medicine* 73.12 (2016), pp. 838–845. ISSN: 1351-0711. DOI: 10.1136/oemed-2016-103836. eprint: <https://oem.bmjjournals.org/content/73/12/838.full.pdf>. URL: <https://oem.bmjjournals.org/content/73/12/838>.
- [23] Esteban Ortiz-Ospina and Max Roser. *Global Health*. URL: <https://ourworldindata.org/grapher/share-of-lung-cancer-deaths-attributed-to-air-pollution>.
- [24] Osarogiagbon, Raymond U. and Smeltzer, Matthew P. and Farjah, Farhood and others. “Stage Shift Improves Lung Cancer Survival: Real-World Evidence”. In: *Journal of Thoracic Oncology* 18.1 (2023), pp. 47–56. DOI: 10.1016/j.jtho.2022.09.005.
- [25] Our World in Data. *Lung cancer death rates*. Accessed: 2025-05-12. 2024. URL: <https://ourworldindata.org/grapher/lung-cancer-deaths-per-100000-by-sex-1950-2002>.
- [26] Patrias, K. *Citing Medicine: The NLM Style Guide for Authors, Editors, and Publishers*. Bethesda, MD, 2007. URL: <https://www.ncbi.nlm.nih.gov/books/NBK7265/> (visited on 05/15/2025).
- [27] Peter N. Lee. “The Epidemiology of Tobacco and Lung Cancer: Some Conclusions from a Lifetime of Research”. In: *Prevention, Diagnosis, and Treatment of Lung Cancer*. Ed. by Marta Adonis. Rijeka: IntechOpen, 2017. Chap. 1. DOI: 10.5772/67167. URL: <https://doi.org/10.5772/67167>.
- [28] Ramamoorthy, Thilagavathi and Nath, Anita and Singh, Shubhra and Mathew, Stany and Pant, Apourv and Sheela, Samvedana and Kaur, Gurpreet and Sathishkumar, Krishnan and Mathur, Prashant. “Assessing the Global Impact of Ambient Air Pollution on Cancer Incidence and Mortality: A Comprehensive Meta-Analysis”. In: *JCO Global Oncology* 10 (2024), e2300427. DOI: 10.1200/GO.23.00427. URL: <https://ascopubs.org/doi/abs/10.1200/GO.23.00427>.
- [29] Reginald F. Munden and Caroline Chiles and Phillip M. Boiselle and JoRean D. Sicks and Denise R. Aberle and Constantine A. Gatsonis. “Micronodules Detected on Computed Tomography During the National Lung Screening Trial: Prevalence and Relation to Positive Studies and Lung Cancer”. In: *Journal of Thoracic Oncology* 14.9 (2019), pp. 1538–1546. ISSN: 1556-0864. DOI: <https://doi.org/10.1016/j.jtho.2019.05.045>. URL: <https://www.sciencedirect.com/science/article/pii/S1556086419304812>.
- [30] Reitsma, Marissa B et al. “Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019”. In: vol. 397. The Lancet, 2021. doi: 10.1016/S0140-6736(21)01169-7. URL: [https://doi.org/10.1016/S0140-6736\(21\)01169-7](https://doi.org/10.1016/S0140-6736(21)01169-7).

- [31] Sandy McDowell. “1 of Every 4 Global Cancer Deaths Are Caused by Tobacco Use”. In: *American Cancer Society* (2021). DOI: 10.5114/wo.2021.103829.
- [32] Mohammad Q. Shatnawi, Qusai Abuein, and Romesaa Al-Quraan. “Deep learning-based approach to diagnose lung cancer using CT-scan images”. In: *Intelligence-Based Medicine* 11 (2025), p. 100188. ISSN: 2666-5212. DOI: 10.1016/j.ibmed.2024.100188. URL: <https://www.sciencedirect.com/science/article/pii/S2666521224000553>.
- [33] Sheikhbahaei, Sara and Mena, Esther and Yanamadala, Anusha and Reddy, Siddaling and Solnes, Lilja B. and Wachsmann, Jason and Subramaniam, Rathan M. “The Value of FDG PET/CT in Treatment Response Assessment, Follow-Up, and Surveillance of Lung Cancer”. In: *American Journal of Roentgenology* 208.2 (2017). PMID: 27726427, pp. 420–433. DOI: 10.2214/AJR.16.16532. eprint: <https://doi.org/10.2214/AJR.16.16532>. URL: <https://doi.org/10.2214/AJR.16.16532>.
- [34] Shin, Seung Hun and Kim, Taehoon and Kim, Hye and others. “Impact of smoking reduction on lung cancer risk in patients with COPD who smoked fewer than 30 pack-years: a nationwide population-based cohort study”. In: *Respiratory Research* 25.133 (2024). DOI: 10.1186/s12931-024-02741-1.
- [35] Siegel, Rebecca L. and Miller, Kimberly D. and Fuchs, Hannah E. and Jemal, Ahmedin. “Cancer statistics, 2022: Trends in lung cancer incidence and mortality”. In: *CA: A Cancer Journal for Clinicians* 72.1 (2022). Accessed: 2025-05-15, pp. 7–33. DOI: 10.3322/caac.21708. URL: <https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21708>.
- [36] Siegel, RL and Miller, KD and Fuchs, HE and Jemal, A. “Cancer statistics, 2023”. In: *CA: a cancer journal for clinicians* 73.1 (2023), pp. 17–48.
- [37] Singareddy, Aashray and Flanagan, Mary Ellen and Samson, Pamela Parker and Waqar, Saiama Naheed and Devarakonda, Siddhartha and Ward, Jeffrey P. and Herzog, Brett and Rohatgi, Anjali and Robinson, Clifford Grant and Govindan, Ramaswamy and Puri, Varun and Morgensztern, Daniel. “Trends in stage I lung cancer.” In: *Journal of Clinical Oncology* 40.16_suppl (2022), pp. 10508–10508. DOI: 10.1200/JCO.2022.40.16_suppl.10508. URL: https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.16_suppl.10508.
- [38] Steenland K, Stayner L. “Silica, asbestos, man-made mineral fibers, and cancer”. In: *Cancer Causes Control*. 3.8 (1997). DOI: 10.1023/a:1018469607938.
- [39] Thandra KC. Barsouk A. Saginala K. Aluru JS. Barsouk A. “Epidemiology of lung cancer”. In: *Contemp Oncol (Pozn)* (2021). DOI: 10.5114/wo.2021.103829.
- [40] de-Torres, Juan Pablo and Marin, Jose Manuel and et al. “Comorbid COPD and lung cancer: prevalence, pathogenesis, and treatment implications”. In: *Current Opinion in Pulmonary Medicine* 21.4 (2015), pp. 354–359.

- [41] Travis, W. D. and Brambilla, E. and Nicholson, A. G. and et al. “The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification”. In: *J Thorac Oncol* 10.9 (2015). PUBMED Abstract, pp. 1243–1260. URL: <https://pubmed.ncbi.nlm.nih.gov/26291008/>.
- [42] Travis, William D and Brambilla, Elisabeth and Nicholson, Andrew G and Yatabe, Yasushi and Austin, John HM and et al. “The 2015 World Health Organization classification of lung tumors”. In: *Journal of Thoracic Oncology* 10.9 (2015), pp. 1243–1260.
- [43] Vida, Stephen and Pintos, Javier and Parent, Marie-Élise and Lavoué, Jerome and Siemiatycki, Jack. “Occupational Exposure to Silica and Lung Cancer: Pooled Analysis of Two Case-Control Studies in Montreal, Canada”. In: *Cancer Epidemiology, Biomarkers & Prevention* 19.6 (June 2010), pp. 1602–1611. ISSN: 1055-9965. DOI: 10.1158/1055-9965.EPI-10-0015. URL: <https://doi.org/10.1158/1055-9965.EPI-10-0015>.
- [44] Wang, Xin and Zhang, Mei and Li, Jun. “Molecular alterations and targeted therapy in non-small cell lung cancer: updates from 2023”. In: *Cancer Treatment Reviews* 113 (2023), p. 102538.
- [45] Wikipedia contributors. *Lung biopsy* — Wikipedia, The Free Encyclopedia. [Online; accessed 14-May-2025]. 2023. URL: https://en.wikipedia.org/w/index.php?title=Lung_biopsy&oldid=1188144138.
- [46] Wikipedia contributors. *Lung cancer*. Wikipedia, The Free Encyclopedia. Accessed: 2025-05-13. 2025. URL: https://en.wikipedia.org/wiki/Lung_cancer.
- [47] World Health Organization. *Lung Cancer - Key Facts*. Accessed: 2025-05-12. 2024. URL: <https://www.who.int/news-room/fact-sheets/detail/lung-cancer>.
- [48] Xing, Pu-Yuan et al. “What are the clinical symptoms and physical signs for non-small cell lung cancer before diagnosis is made? A nation-wide multicenter 10-year retrospective study in China.” In: *Cancer medicine* 8.8 (2019).