International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	LUNG CANCER IN NEVER SMOKERS: AN ANALYSIS OF RISK FACTORS, CLINICAL PROFILES, AND THERAPEUTIC INNOVATIONS WITHIN A SOCIAL AND TECHNOLOGICAL FRAMEWORK
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5644
RECEIVED	12 March 2026
ACCEPTED	04 June 2026
PUBLISHED	15 June 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

LUNG CANCER IN NEVER SMOKERS: AN ANALYSIS OF RISK FACTORS, CLINICAL PROFILES, AND THERAPEUTIC INNOVATIONS WITHIN A SOCIAL AND TECHNOLOGICAL FRAMEWORK

Aleksandra Ustaszewska *(Corresponding Author, Email: ustaszewska.a17@gmail.com)*
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0001-5651-5906

Zofia Parol
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0007-0885-2637

Mateusz Żyła
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0003-9005-620X

Aleksandra Oszczypała
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-5809-3934

Aleksandra Potempa
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0004-2698-4957

Michał Petkow
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-3398-9069

Liwia Prorok
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-3762-514X

Katarzyna Lipska
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0003-5670-7726

Monika Szyszkowska
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-5367-0026

Zuzanna Strojek
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0005-8857-5670

ABSTRACT

Lung cancer in never smokers (LCINS) is a clinically and biologically distinct disease- it is not simply a milder version of tobacco-related lung cancer. Every year, LCINS causes an estimated 200,000 deaths in the United States alone, making it more deadly than cancers of the cervix, ovary, or pancreas considered separately. Up to one in four people diagnosed with lung cancer has never smoked. This review examines why- tracing the environmental, genetic, and socioeconomic forces driving a disease that ranks among the top ten causes of cancer death worldwide. We conducted a systematic analysis of current literature focused on three main themes: the epidemiological shift in lung cancer, the molecular biology of LCINS- especially the EGFR and ALK pathways- and the psychosocial damage caused by the "smoker's disease" label. Key findings show clear regional differences: in East Asia, never smokers make up over 50% of all lung cancer patients, driven by specific genetic vulnerabilities and environmental exposures such as cooking fumes and PM2.5 air pollution. The review also highlights the growing role of artificial intelligence in radiology and liquid biopsy for early detection- tools that could fundamentally change how we identify LCINS before it becomes incurable. A core finding is that current screening programs, designed around tobacco use, miss the majority of never-smoker patients. A shift to risk-based, technology-enhanced screening is urgently needed. Finally, this analysis argues that social science, specifically addressing stigma and health equity, must be integrated into clinical oncology if we want to improve outcomes globally.

KEYWORDS

Lung Cancer in Never Smokers, EGFR Mutations, Air Pollution, Medical Stigma, Artificial Intelligence in Oncology, Health Policy

CITATION

Aleksandra Ustaszewska, Zofia Parol, Mateusz Żyła, Aleksandra Oszczypała, Aleksandra Potempa, Michał Petkow, Liwia Prorok, Katarzyna Lipska, Monika Szyszkowska, Zuzanna Strojek. (2026) Lung Cancer in Never Smokers: An Analysis of Risk Factors, Clinical Profiles, and Therapeutic Innovations Within a Social and Technological Framework. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5644

1.Introduction

For decades, lung cancer and tobacco smoking were treated as almost synonymous. This shaped how clinicians, researchers, and the public thought about the disease, associating it with personal behavior and individual choice.[5,21] That framing is now outdated. Lung cancer in never-smokers- defined as individuals who have smoked fewer than 100 cigarettes in their lifetime- is now recognized as a major global health concern in its own right. It ranks as the fifth to seventh leading cause of cancer-related mortality worldwide.[1,6] LCINS accounts for 15% to 25% of all lung cancer cases. Crucially, its incidence has remained stable or increased even as overall smoking rates have declined in many countries.[4,7]

LCINS is recognized as a biologically separate disease. It has a unique molecular profile, a distinct clinical course, and an uneven epidemiological pattern.[32] Compared to tobacco-related lung cancer, LCINS carries a lower overall tumor mutational burden- typically 0 to 3 mutations per megabase, versus up to 30 in heavy smokers- but it is far more likely to harbor specific, targetable mutations such as EGFR and ALK alterations.[7,31] Demographically, the disease hits women and younger adults harder than expected. In East Asia, never smokers account for more than half of all lung cancer diagnoses, a proportion that rises to over 80% among women in some Chinese datasets.[24,28]

The rise of LCINS also raises important social and technological questions. The label "smoker's disease" has created a persistent stigma around all lung cancer- one that follows patients regardless of their smoking history.[8,9] This stigma has measurable consequences: it contributes to delayed diagnosis, psychological distress, and lower research research investment relative to other cancers of similar mortality burden.[36,39] At the same time, rapidly emerging technologies- including deep learning algorithms for imaging analysis and multi-omics liquid biopsies- now offer realistic pathways to detect LCINS in people who fall entirely outside traditional, tobacco-based screening criteria.[11,33]

This review brings together clinical data, social context, and emerging technology to build a fuller picture of LCINS- one that goes beyond biology and asks why some people are more exposed, less screened, and less treated than others. The goal is to go beyond biomedical facts and address the socioeconomic drivers and technological tools that could transform how LCINS is detected, treated, and discussed in public health policy.[26,37]

2.Methodology

This review article adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The research process involved a systematic search across major medical and scientific databases, including PubMed, MEDLINE (via Ovid), EMBASE, and Scopus, covering literature published primarily between 2017 and 2026 to capture the most recent genomic and technological improvements.

Inclusion criteria were defined as:

1. Primary research, systematic reviews, and meta-analyses exploring LCINS.
2. Studies reporting on clinical, molecular, or socioeconomic outcomes.
3. Research involving adult populations (≥18 years).
4. Studies are adjusting for major confounding factors to reduce the influence of hidden tobacco exposure.

Exclusion criteria involved:

1. Studies focusing on former or light smokers without a separate analysis of never-smokers.
2. Non-English language publications.
3. Animal or in vitro studies without clear clinical translation.

A total of 6,725 reports were initially identified through database searching. Following a double-blind screening of titles and abstracts, 54 high-quality studies were selected for final inclusion.

3.Global and Regional Incidence Trends

In the United States, the annual incidence of lung cancer in non-smoking individuals is approximately 14 to 21 per 100,000 person-years in females and 5 to 13 per 100,000 in males.[19,20] To put that in context: the CDC estimates that about 10% to 20% of all U.S. lung cancer deaths occur in people who never smoked-translating to roughly 20,000 to 40,000 deaths per year.[19] This sex disparity is even more pronounced in Asian populations. In Taiwan, lung cancer is the leading cause of cancer mortality, and 53% of those who succumb to the disease are never smokers.[28] In mainland China, estimates suggest that 86.1% of lung cancers in females and 44.9% in males occur in individuals with no history of tobacco use.[42] Globally, LCINS tends to affect slightly younger patients: while smoking-related lung cancer typically presents at a median age of around 70, never-smoker cohorts show a median age closer to 67, with a notable proportion of cases appearing before age 55.[28]

Table 1. Regional incidence of LCINS and associated factors.

North America	10% – 20%	Radon, Secondhand Smoke, Asbestos
Western Europe	10% – 25%	Air Pollution, Radon, Occupational
East Asia	30% – 50%+	Genetic Susceptibility, Cooking Fumes, PM2.5
South Asia (India)	~41%	Indoor Air Pollution, Solid Fuels
Ethiopia	< 25% (smokers), rest NS	Biomass Fuel, Prior TB, Low SES

LCINS is on the rise globally, likely driven by aging populations and growing exposure to environmental carcinogens.[6,7] It also tends to appear earlier than tobacco-related lung cancer (median age 67 versus 70) with a meaningful share of cases occurring before age 55.[28]

Environmental Risk Factors and Hazard Ratios

The pathogenesis of LCINS is driven by a complex array of non-tobacco determinants. Meta-analyses of over 16 million never smokers have identified several key environmental and clinical factors associated with increased incidence.[2,14]

4. Environmental, Genetic, and Socioeconomic Risk Factors

4.1 Radon and Ionizing Radiation

Radon-222 is a colorless, odorless radioactive gas that forms naturally from uranium decay in soil and rock. It seeps into buildings through foundations and can accumulate to dangerous concentrations indoors. When inhaled, radon's decay products release alpha radiation that causes DNA double-strand breaks in lung tissue. In Europe and North America, radon is estimated to cause approximately 2% to 9% of all lung cancer deaths.[40] The U.S. Environmental Protection Agency estimates that radon is responsible for about 21,000 lung cancer deaths annually in the United States, making it the second leading cause of lung cancer overall after smoking.[19] Meta-analysis data confirm that residential radon exposure is associated with an adjusted odds ratio (aOR) of 1.82- nearly doubling the risk in non-smoking populations.[14]

4.2 Ambient and Indoor Air Pollution

Exposure to fine particulate matter (PM2.5) is a well-established driver of LCINS. PM2.5 particles can penetrate deep into the lung tissue, triggering chronic inflammation and oxidative stress. For every 10 μg/m³ increase in PM2.5, the risk of lung cancer incidence rises by approximately 16% (aHR 1.16).[43] In developing countries and high-income Asian regions, indoor air pollution from the combustion of solid fuels (wood, coal, animal dung) and high-temperature cooking oil fumes (COF) are critical factors. Heating oils to high temperatures produces mutagenic polycyclic aromatic hydrocarbons and volatile organic compounds (VOCs). Cooking oil fumes are associated with an aHR of 1.29, with specific methods like deep-frying further elevating the risk.[22,23]

4.3 Secondhand Smoke (Passive Smoking)

Despite not smoking themselves, many people who never smoke are chronically exposed to environmental tobacco smoke. Meta-analyses of spousal smoking show a 27% to 30% increase in the risk of lung cancer for the non-smoking spouse. [14] Passive smoke contains over 7,000 chemicals, dozens of which are known carcinogens. While it does not always leave the distinct "Signature 4" tobacco mutation pattern in the tumor, it contributes to the overall cellular transformation and mutation.[7]

4.4. Occupational and Socioeconomic Factors

Occupational exposure to substances like asbestos, arsenic, chromium, and cadmium remains a concern. Asbestos exposure alone can increase lung cancer risk six-fold, and while often associated with historical industrial work in men, it remains a latent risk factor globally.[4] Socioeconomic status (SES) also plays an important role; low education and limited wealth are independently associated with higher lung cancer risk in never smokers, likely due to a clustering of risks such as poor housing (radon, lack of ventilation), dietary imbalances, and higher exposure to solid fuels.[25,26]

Table 2. Environmental and clinical risk factors for LCINS with hazard ratios.

Passive Smoking	1.30	1.22 – 1.40
PM2.5 (per 10 μg/m³)	1.16	1.03 – 1.30
PM10 (per 10 μg/m³)	1.10	1.09 – 1.11
Previous Cancer	2.04	1.95 – 2.13
Rheumatoid Arthritis	1.41	1.15 – 1.73
Family History (East Asia)	1.56	1.23 – 1.98
Cooking Oil Fumes	1.29	1.22 – 1.37
Residential Radon	1.82 (OR)	1.31 – 2.54

5. The Clinical and Molecular Profile

LCINS is not just epidemiologically different — it is biologically different. It has its own histological patterns, its own metastatic behavior, and a genomic landscape that bears little resemblance to the tumors that grow in heavy smokers.[1,7] Understanding these distinctions is essential, because they directly determine how the disease is treated and how patients respond.

5.1 Clinical Presentation and Metastatic Behavior

The histological picture in LCINS is striking. Never smokers are diagnosed with adenocarcinoma in 60% to 80% of cases- a much higher rate than the roughly 40% seen in smokers.[21,28] Squamous cell carcinoma and small cell lung cancer, both strongly linked to tobacco, are rare in this group: squamous cell carcinoma occurs in about 10% to 15% of LCINS cases, and small cell lung cancer in fewer than 10%.[5] This histological dominance of adenocarcinoma matters clinically, because adenocarcinoma is the subtype most likely to harbor the targetable mutations that make precision therapy possible.

One of the most dangerous features of LCINS is how late it is diagnosed. Because never smokers are excluded from standard lung cancer screening programs, the disease often goes undetected until it causes symptoms- or is found accidentally on a scan done for an unrelated reason. By then, many patients are already at an advanced stage. Symptoms mirror those seen in smokers (cough, breathlessness, chest pain), but never smokers more often present with signs of distant spread: bone pain, headaches, or neurological symptoms.[37] Retrospective cohort data show that never smokers are significantly more likely to have Stage IV disease at diagnosis- 89.2% vs. 78.3% in smokers in some series- with bone metastases found in 40.5% and brain metastases in 26.7% of non-smoking patients.[28]

Table 3. Symptom prevalence in smokers vs. never smokers at diagnosis.

Cough	48.1%	41.2%	0.07
Chest Pain	24.1%	14.5%	0.002
Back Pain	7.0%	12.8%	0.01
Haemoptysis	15.2%	8.8%	0.01
Neurological Sx	4.9%	8.8%	0.04

Retrospective cohort studies show that never smokers are significantly more likely to present with Stage IV disease and metastasis at the time of diagnosis (89.2% for non-smokers vs. 78.3% for smokers in some studies). Metastatic involvement of the bone (40.5%) and brain (26.7%) is significantly more prevalent in the non-smoking cohort.[28]

5.2 The Genomic and Molecular Landscape

The biggest biological difference between LCINS and tobacco-related lung cancer lies in the DNA. Smoking causes a recognizable pattern of mutations called “Signature 4”- characterized by C>A transversions driven by direct carcinogen exposure from tobacco combustion. LCINS tumors show none of this. Instead, they display “clock-like” mutational signatures (SBS1 and SBS5) that reflect natural, age-related DNA damage from endogenous processes- changes that accumulate in any dividing cell over time, regardless of lifestyle.[29,30,31] This fundamental difference is why the two diseases behave differently and why they respond to treatment so differently.

5.3 Targetable Driver Mutations

The practical consequence of this genomic profile is that never smokers are far more likely to have mutations that can be directly targeted with drugs. EGFR mutations, the most therapeutically important, are found in 43% to 65% of never smokers with adenocarcinoma, compared to only 11% to 13% of smokers. ALK gene rearrangements occur in 12% of never smokers versus just 2% of smokers.[7,32] Both EGFR and ALK alterations have approved targeted therapies with response rates that outperform standard chemotherapy by a large margin. Importantly, these mutations are typically mutually exclusive- a tumor driven by EGFR will not also carry ALK- meaning a single dominant driver usually defines the biology of each individual patient's cancer.[1]

Table 4. Key molecular alterations: frequency in never smokers vs. smokers.

EGFR	43% – 65%	11% – 13%
ALK	12%	2%
KRAS	Rare	Common (~25-30%)
TP53	~59% (SCLC)	~85% (SCLC)
TMB	Low (0-3 mut/Mb)	High (0-30 mut/Mb)

5.4 The Sherlock-Lung Subtypes

The landmark Sherlock-Lung study, conducted by the U.S. National Cancer Institute, used whole-genome sequencing of tumors from 232 never-smokers to classify LCINS into three molecular subtypes — named after musical dynamics to reflect differences in mutational tempo and aggressiveness.[29,30,31]

1. "Piano" Subtype: The dominant subtype, characterized by low mutational burden, slow growth, high intra-tumor heterogeneity, and frequent KRAS mutations. It appears to arise from progenitor cells and grows slowly over many years.
2. "Mezzo-forte" Subtype: Features specific chromosomal amplifications and is frequently associated with EGFR mutations. These tumors exhibit faster growth than the "piano" type.
3. "Forte" Subtype: Characterized by whole-genome doubling, like the genomic instability often seen in smokers' tumors, leading to aggressive disease.

5.5 Therapeutic Advances and Outcomes

The high frequency of actionable mutations in LCINS has fundamentally changed how these patients are treated. Before the era of targeted therapy, a diagnosis of advanced lung cancer carried a median survival of less than a year. For never smokers with sensitizing EGFR or ALK mutations, modern Tyrosine Kinase Inhibitors (TKIs) have changed that equation dramatically.[7,27]

- EGFR TKIs: Third-generation inhibitors like osimertinib have demonstrated a 45% reduction in the risk of progression or death. Median survival for non-smokers with advanced disease and actionable mutations can exceed 3 to 5 years, compared to just 1 to 2 years for those without such mutations.[7,27]
- ALK/ROS1 Inhibitors: Agents like alectinib and crizotinib offer highly effective, targeted options with superior response rates compared to chemotherapy.[1]
- Immunotherapy Challenges: While immune checkpoint inhibitors (ICIs) have revolutionized care for smokers, they are generally less effective in never smokers. This is due to the low tumor mutational burden (TMB) and low neoantigen load, which fail to trigger a robust T-cell response.[3]

6. Diagnostic Approaches and Screening Strategies

6.1 Artificial Intelligence (AI) in Early Detection

Artificial Intelligence is increasingly utilized to enhance the sensitivity of routine imaging. Deep learning models, such as the "CXR-Lung-Risk" model developed by MGH researchers, can analyze a single standard chest X-ray- a test performed millions of times annually for unrelated reasons to identify asymptomatic never smokers at high risk for lung cancer. In external validation, 28% of patients were identified as high risk, with 2.9% later developing lung cancer, significantly exceeding the thresholds where CT screening is typically recommended.[12] Furthermore, AI-derived imaging biomarkers like qXR-LNMS (Lung Nodule Malignancy Score) have shown a negative predictive value of 93.4% in differentiating benign from malignant nodules on chest X-rays, supporting the triage of high-risk non-smokers into advanced LDCT screening.[18]

6.2 Liquid Biopsy and Biomarker Integration

Liquid biopsy offers a non-invasive method to monitor DNA changes and detect cancer at early stages. By analyzing circulating tumor DNA (ctDNA), microRNA, and volatile organic compounds (VOCs) in blood or breath, clinicians can identify molecular signatures of lung cancer before they are visible on imaging.[34] AI algorithms, including Support Vector Machines (SVM) and Convolutional Neural Networks (CNN), are being trained on multi-omics datasets to improve the specificity of these tests, potentially lowering the high false-positive rates (up to 30%) associated with traditional CT scans.[13,34]

6.3 The TALENT Trial and the Move Toward Population Screening

The most compelling evidence for screening never smokers comes from the Taiwan Lung Cancer Screening in Never-Smoker Trial (TALENT)- the first large prospective study of its kind. It enrolled 12,011 high-risk never smokers and used low-dose CT (LDCT) to screen them. The lung cancer detection rate was 2.6%- more than double the 1.1% detection rate seen in the landmark NLST trial, which screened heavy smokers. Even more strikingly, 96.5% of the cancers found were at Stage 0 or Stage I, meaning they were curable with surgery. Based on this evidence, Taiwan became the first country in the world to implement a national lung cancer screening program specifically for never smokers with a family history of the disease.[15,16,35]

7.Discussion: Socio-Technological Implications and Health Equity

The clinical findings reviewed above do not exist in a vacuum. Who gets LCINS, who gets diagnosed early, and who gets access to the best treatments are all shaped by social factors: stigma, income, geography, and healthcare infrastructure, as much as by biology.[26] This section addresses those intersections directly.

The Psychology of Stigma and the "Smoker's Disease" Label

Lung cancer carries a stigma that other major cancers do not. Studies consistently show that patients-smokers and never smokers alike, report feeling blamed for their own illness, and that this perceived blame has measurable effects on their health and behavior.[8,38] For never smokers, the stigma is especially disorienting: they are judged for a habit they never had. A 2012 study in the European Journal of Oncology Nursing found that never-smoker patients reported significantly higher levels of stigma-related distress than ever-smokers, because the social narrative around lung cancer offered them no framework for understanding why they became ill.[8] This health-related stigma results in three concrete harms:

- ✓ Blame and Victimhood: Never smokers often feel a sense of injustice, repeatedly having to defend their non-smoking status to healthcare providers or friends and family.[10,38]
- ✓ Psychological Distress: Lung cancer stigma is strongly associated with higher levels of depression and lower quality of life. In many cases, it accounts for more variance in QOL than age or sex.[9,36]
- ✓ Delayed Diagnosis: Fear of adverse judgment can lead patients to minimize symptoms or delay seeking medical attention. Furthermore, clinicians may not suspect lung cancer in a non-smoker, attributing symptoms like cough to asthma or allergies.[39]

Public health efforts must shift from a "blame-the-smoker" narrative to a "humanize-the-disease" approach. Campaigns that emphasize that "anyone with lungs can get lung cancer" are essential to take care of mental health and encourage earlier diagnosis.[10,37]

Socioeconomic Determinants and Health Equity

Socioeconomic status shapes LCINS risk in concrete ways. In low-income settings, around 3 billion people worldwide still cook and heat their homes using solid fuels like wood, coal, and animal dung- releasing carcinogenic particles directly into their living spaces.[25] In India, indoor air pollution from solid fuels

accounts for approximately 41% of all lung cancer cases in never smokers. In Ethiopia, biomass fuel exposure, prior tuberculosis infection, and low household income cluster together as risk factors in never-smoker patients.[25] In high-income countries, by contrast, the dominant non-tobacco risk factors are radon accumulation in poorly ventilated housing and outdoor PM2.5 exposure, both of which disproportionately affect lower-SES neighborhoods with older building stock and proximity to traffic.[40]

New technologies offer hope, but they also carry a risk of making existing inequalities worse. AI-powered chest X-ray analysis and liquid biopsy are currently available only in well-resourced hospitals in high-income countries. Populations in low- and middle-income countries (LMICs) where LCINS burden is rising fastest, face a double disadvantage: higher environmental exposure and lower access to early detection tools. Without deliberate policy action, the global rollout of precision screening could leave behind the very populations that need it most. Scalable, low-cost solutions — including point-of-care biomarker testing and AI tools trained on diverse, non-Western datasets — must be prioritized in research and health policy agendas.[26,34]

8. Conclusions

Never smoking is not protection. Lung cancer in never smokers ranks as the seventh leading cause of cancer mortality worldwide, and its incidence is not falling.[1,4,7] Roughly one in four lung cancer cases arises not from tobacco, but from radon in homes, polluted air, cooking fumes, inherited genetic risk, and the cumulative disadvantages of poverty- factors that current screening programs largely ignore. Molecularly, LCINS is defined by a low tumor mutational burden but a remarkably high rate of actionable driver mutations, particularly EGFR (43–65% in never smokers) and ALK (12%), that can be directly targeted with drugs to extend survival from months to years.[7,31,32]

Yet the clinical potential of these targeted therapies is being undermined by the two problems this review has repeatedly highlighted: late diagnosis and the burden of stigma. The “smoker’s disease” label delays both patient help-seeking and clinical suspicion, meaning that by the time LCINS is detected, 89% of never-smoker patients already have Stage IV disease in some cohorts.[9,36,39] Artificial intelligence and liquid biopsy offer realistic tools for detecting the disease earlier — the CXR-Lung-Risk model identified 28% of patients as high-risk from a routine chest X-ray, and the TALENT trial found 96.5% of screen-detected LCINS at Stage 0 or I- but these technologies need to reach the right populations to have an impact.[11,12,34]

Improving outcomes for never smokers will require three things to happen simultaneously. First, screening eligibility needs to reflect actual risk- not just smoking history. Tools like the FORMOSA model already show how family history, radon exposure, PM2.5 levels, and genetic susceptibility can be combined into a practical risk score for never smokers.[13,15,37] Second, public health campaigns need to say clearly what the data already shows: lung cancer is not a smoker's disease. It never was for a quarter of the people who get it[10,37] Third, research and health policy must ensure that the tools being developed- AI screening, liquid biopsy, targeted therapies- are made accessible in low- and middle-income countries, where the burden is rising fastest and resources are most constrained.[3,26,44] Lung cancer in never smokers is a growing global emergency. It deserves to be treated as one.

Author Contributions:

Conceptualization: Aleksandra Ustaszewska

Methodology: Aleksandra Ustaszewska, Zofia Parol

Literature review: Aleksandra Potempa, Michał Petkow, Katarzyna Lipska

Data analysis and interpretation: Liwia Prorok, Aleksandra Oszczypała, Mateusz Żyła

Writing - original draft: Aleksandra Ustaszewska, Aleksandra Oszczypała, Aleksandra Potempa, Katarzyna Lipska, Liwia Prorok, Mateusz Żyła, Michał Petkow, Monika Szyszkowska, Zofia Parol, Zuzanna Strojek

Writing - review & editing: Aleksandra Ustaszewska, Zuzanna Strojek, Monika Szyszkowska

Supervision: Aleksandra Ustaszewska

Final approval: All authors

Conflicts of Interest: No conflicts of interest to declare.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Chen, P.-M., Huang, Y.-H., & Li, C.-Y. (2026). Lung cancer in never-smokers: Risk factors, driver mutations, and therapeutic advances. *Diagnostics, 16*(2), 245. https://doi.org/10.3390/diagnostics16020245
2. Naidu, S. B., Wisking, A., Karoshi, A., Burdett, S., Godolphin, P. J., Popat, S., Janes, S. M., & Navani, N. (2025). Risk factors associated with incidence of lung cancer in never-smokers: A systematic review and meta-analysis. *JTO Clinical and Research Reports, 6*, 100910. https://doi.org/10.1016/j.jtocrr.2025.100910
3. de Alencar, V. T. L., Figueiredo, A. B., Corassa, M., Gollob, K. J., & Cordeiro de Lima, V. C. (2022). Lung cancer in never smokers: Tumor immunology and challenges for immunotherapy. *Frontiers in Immunology, 13*, 984349. https://doi.org/10.3389/fimmu.2022.984349
4. Murphy, C., Pandya, T., Swanton, C., & Solomon, B. J. (2025). Lung cancer in nonsmoking individuals: A review. *JAMA, 334*(20), 1836–1845. https://doi.org/10.1001/jama.2025.17695
5. Schabath, M. B., & Cote, M. L. (2019). Cancer progress and priorities: Lung cancer. *Cancer Epidemiology, Biomarkers & Prevention, 28*(10), 1563–1579. https://doi.org/10.1158/1055-9965.EPI-19-0221
6. LoPiccolo, J., Gusev, A., Christiani, D. C., & Janne, P. A. (2024). Lung cancer in patients who have never smoked: An emerging disease. *Nature Reviews Clinical Oncology, 21*(2), 121–146. https://doi.org/10.1038/s41571-023-00844-0
7. Chen, P.-M., Huang, Y.-H., & Li, C.-Y. (2026). Lung cancer in never-smokers: Risk factors, driver mutations, and therapeutic advances. *Diagnostics, 16*(2), 245. https://doi.org/10.3390/diagnostics16020245
8. Cataldo, J. K., Jahan, T. M., & Pongquan, V. L. (2012). Lung cancer stigma, depression, and quality of life among ever and never smokers. *European Journal of Oncology Nursing, 16*(3), 264–269. https://doi.org/10.1016/j.ejon.2011.06.008
9. Chambers, S. K., Dunn, J., Occhipinti, S., Hughes, S., Baade, P., Sinclair, S., Aitken, J., Youl, P., & O'Connell, D. L. (2016). Psychological distress and quality of life in lung cancer: The role of health-related stigma, illness appraisals and social constraints. *Psycho-Oncology, 25*(11), 1569–1576. https://doi.org/10.1002/pon.3829
10. American Lung Association. (2023). *Making lung cancer stigma a thing of the past*. https://www.lung.org/blog/making-lung-cancer-stigma-past
11. Habbab, F. M., Bédard, E. L. R., Joy, A. A., Alam, Z., Abraham, A. G., & Roa, W. H. Y. (2025). Early detection of lung cancer: A review of innovative milestones and techniques. *Journal of Clinical Medicine, 14*(21), 7812. https://doi.org/10.3390/jcm14217812
12. Radiological Society of North America. (2023). *AI identifies non-smokers at high risk for lung cancer*. https://www.rsna.org/media/press/i/2482
13. Duranti, L., Tavecchio, L., Rolli, L., & Solli, P. (2025). New perspectives on lung cancer screening and artificial intelligence. *Life, 15*(3), 498. https://doi.org/10.3390/life15030498
14. Naidu, S. B., Wisking, A., Karoshi, A., Burdett, S., Godolphin, P. J., Popat, S., Janes, S. M., & Navani, N. (2025). Risk factors associated with incidence of lung cancer in never-smokers: A systematic review and meta-analysis. *JTO Clinical and Research Reports, 6*, 100910. https://doi.org/10.1016/j.jtocrr.2025.100910
15. Chang, G., Chiu, C., Yu, C., et al. (2023). Low-dose CT screening among never-smokers with or without a family history of lung cancer in Taiwan: A prospective cohort study. *The Lancet Respiratory Medicine, 12*, 141–152. https://doi.org/10.1016/S2213-2600(23)00338-7
16. International Association for the Study of Lung Cancer. (2021). *TALENT study supports NLCST and NELSON trial results*. https://www.iaslc.org/iaslc-news/press-release/talent-study-supports-nlcst-and-nelson-trial-results
17. Robbins, H. A., Katki, H. A., Cheung, L. C., & Berg, C. D. (2024). Risk prediction models for lung cancer in people who have never smoked: A protocol of a systematic review. *BMJ Open, 14*(2), e077609. https://doi.org/10.1136/bmjopen-2023-077609
18. Qure.ai. (2023). *The invisible majority: Using AI to detect lung cancer early in non-smokers*. https://www.qure.ai/us/evidence/Lung-Cancer-Diagnosis-in-Non-Smokers
19. Centers for Disease Control and Prevention. (2024). *Lung cancer among people who never smoked*. https://www.cdc.gov/lung-cancer/nonsmokers/index.html
20. Yale Medicine. (2024). *Lung cancer in nonsmokers*. https://www.yalemedicine.org/conditions/lung-cancer-in-nonsmokers
21. Pelosof, L., Ahn, C., Gao, A., Kim, B., Yan, J., Xie, Y., Minna, J. D., Dowell, J., & Moran, C. (2017). Proportion of never-smoker non-small cell lung cancer patients at three diverse institutions. *Journal of the National Cancer Institute, 109*(7), djw295. https://doi.org/10.1093/jnci/djw295
22. Hong, Y., Jang, K., & Xie, H. (n.d.). Meta-analysis of the association between indoor environmental pollution and lung cancer risk in never-smokers. *American Journal of Translational Research*. https://doi.org/10.62347/MKBQ5855
23. McAllister, B. J., Malhotra Mukhtyar, R., Cai, S., Brown, K., Lock, S., & Khan, S. (2025). Relationship between household air pollution and lung cancer in never smokers in high-income countries: A systematic review. *BMJ Open, 15*(6), e093870. https://doi.org/10.1136/bmjopen-2024-093870

24. Wakelee, H. A., et al. (2007). Lung cancer incidence in never smokers. *Journal of Clinical Oncology, 25*, 472–478. https://doi.org/10.1200/JCO.2006.07.2983
25. Estifanos, N., Egata, G., Addissie, A., Kebede, R. A., Worku, A., Bekele, A., Habtamu, B., Tesfaye, S., Endries, A. Y., Shigute, Z., Mebratie, A. D., Alemu, G., Bedi, A. S., & Deyessa, N. (2026). Lung cancer risk factors beyond smoking in Ethiopia: A multicenter matched case–control study. *Cancers, 18*(6), 914. https://doi.org/10.3390/cancers18060914
26. EMJ Reviews. (2026). *Social factors shape lung cancer in never smokers*. https://www.emjreviews.com/respiratory/news/social-factors-shape-lung-cancer-in-never-smokers/
27. CyberKnife Miami. (2023). *Lung cancer is increasing among non-smokers: What's their chance of survival compared to smokers & what's their best treatment option?* https://www.cyberknifemiami.com/lung-cancer-is-increasing-among-non-smokers-whats-their-chance-of-survival-compared-to-smokers-whats-their-best-treatment-option/
28. Vasudevan, S., Krishna, V., & Mehta, A. (2022). Lung cancer in non-smokers: Clinicopathological and survival differences from smokers. *Cureus, 14*(12), e32417. https://doi.org/10.7759/cureus.32417
29. Landi, M. T., Synnott, N. C., Rosenbaum, J., Zhang, T., Zhu, B., Shi, J., Zhao, W., Kebede, M., Sang, J., Choi, J., Mendoza, L., Pacheco, M., Hicks, B., Caporaso, N. E., Abubakar, M., Gordenin, D. A., Wedge, D. C., Alexandrov, L. B., Rothman, N., Lan, Q., Garcia-Closas, M., & Chanock, S. J. (2021). Tracing lung cancer risk factors through mutational signatures in never-smokers. *American Journal of Epidemiology, 190*(6), 962–976. https://doi.org/10.1093/aje/kwaa234
30. National Cancer Institute. (2021). *NIH study illuminates origins of lung cancer in never smokers*. https://dceg.cancer.gov/news-events/news/2021/sherlock-lung
31. Zhang, T., Joubert, P., Ansari-Pour, N., et al. (2021). Genomic and evolutionary classification of lung cancer in never smokers. *Nature Genetics, 53*, 1348–1359. https://doi.org/10.1038/s41588-021-00920-0
32. Couraud, S., Zalcman, G., & Milleron, B. (2012). Lung cancer in never smokers: A review. *European Journal of Cancer, 48*, 1299–1311. https://doi.org/10.1016/j.ejca.2012.03.007
33. Pulmonary & Sleep of Tampa Bay. (2024). *Advancements in early detection technologies for lung cancer*. https://pulmonaryandsleephealth.com/advancements-in-early-detection-technologies-for-lung-cancer/
34. Gupta, S., P, A., Reddy, G. H. V., Natarajan, K., Srivastava, V., & Goda, J. (2025). Artificial intelligence in radiology: Transforming cancer detection and diagnosis. *Cureus, 17*(11), e96518. https://doi.org/10.7759/cureus.96518
35. ASCO Post. (2021). *Taiwanese TALENT study supports effectiveness of low-dose CT for lung cancer in certain populations*. https://ascopost.com/news/february-2021/taiwanese-talent-study-supports-effectiveness-of-low-dose-ct-for-lung-cancer-in-certain-populations/
36. Brown Johnson, C. G., Brodsky, J. L., & Cataldo, J. K. (2014). Lung cancer stigma, anxiety, depression, and quality of life. *Journal of Psychosocial Oncology, 32*(1), 59–73. https://doi.org/10.1080/07347332.2013.855963
37. Dodd, C., Henshall, C., Jain, M., & Davey, Z. (2025). An integrative review to examine the care pathways and support available for individuals diagnosed with lung cancer who have never smoked. *Current Oncology, 33*(1), 4. https://doi.org/10.3390/curroncol33010004
38. Lung Cancer Research Foundation. (2023). *Are smokers the only ones who can get lung cancer?* https://www.lungcancerresearchfoundation.org/for-patients/print-and-digital-resources/living-with-lung-cancer/navigating-the-stigma/
39. Carter-Harris, L. (2015). Lung cancer stigma as a barrier to medical help-seeking behavior: Practice implications. *Journal of the American Association of Nurse Practitioners, 27*(5), 240–245. https://doi.org/10.1002/2327-6924.12227
40. UK Biobank. (2023). *Understanding lung cancer in never-smokers in the UK: An observational study of demographic and environmental risk factors*. https://www.ukbiobank.ac.uk/projects/understanding-lung-cancer-in-never-smokers-in-the-uk-an-observational-study-of-demographic-and-environmental-risk-factors/
41. Chamouni, G., Lococo, F., Sassorossi, C., Atuhaire, N., Ádány, R., & Varga, O. (2025). Ethical and legal concerns in artificial intelligence applications for the diagnosis and treatment of lung cancer: A scoping review. *Frontiers in Public Health, 13*, 1663298. https://doi.org/10.3389/fpubh.2025.1663298
42. European Society for Medical Oncology. (2024). *Population-based lung cancer screening can reduce mortality in people who have never smoked, study shows in China*. https://www.esmo.org/press-releases/population-based-lung-cancer-screening-can-reduce-mortality-in-people-who-have-never-smoked-study-shows-in-china
43. Díaz-Gay, M., Zhang, T., Hoang, P. H., et al. (2025). The mutagenic forces shaping the genomes of lung cancer in never smokers. *Nature, 644*, 133–144. https://doi.org/10.1038/s41586-025-09219-0
44. ClinicalTrials.gov. (2025). *Lung cancer screening in population who had never smoked (NCT07383454)*. https://clinicaltrials.gov/study/NCT07383454