

# Lung Cancer in Vietnam



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## Introduction

Vietnam, a low-middle-income Southeast Asian country with a population of 96.5 million, is the 15th most populous country in the world.<sup>1</sup> In 1986, the Vietnamese Government introduced Doi Moi economic reform, transforming Vietnam from a socialist to a market economy. As a result, Vietnam achieved an annual gross domestic product growth rate of 6.2% to 7.02% from 2011 to 2019.<sup>1</sup> Rapid economic growth was associated with improved general health. Life expectancy at birth increased from 71 years in 1990 (66.0 y for men and 75.1 y for women) to 73.6 years (71.0 y for men and 76.3 y for women) in 2019.<sup>1</sup> Along with rapid economic development, levels of air and water pollution intensified and a western lifestyle was widely adopted, including high tobacco use, consumption of energy-dense diets, and reduced physical activity. Cancer incidence and mortality also increased.

## Epidemiology

Nine provinces as follows have regional cancer registries: Hanoi, Thai Nguyen, Hai Phong, Thanh Hoa, Hue, Da Nang, Can Tho, Kien Giang, and Ho Chi Minh City (Fig. 1). The Hanoi and Ho Chi Minh City cancer registries, in the two largest cities, cover 45 and 30 hospitals, respectively, and have the best overall data quality.<sup>2</sup> The International Agency for Research on Cancer and the Global Burden of Disease 2019 used data from these two registries to estimate the global burden of cancer in Vietnam.<sup>3</sup>

Cancer accounts for approximately 19% of all deaths in Vietnam. Lung cancer has been the second most common cancer and second leading cause of cancer deaths among Vietnamese since 2012, with an estimated 26,262 incident cases and 23,797 cancer deaths in 2020.<sup>3</sup> The Global Burden of Disease 2019 reported that age-standardized lung cancer mortality

rates steadily increased between 1990 and 2019, with an estimated 26.11 per 100,000 in 2019, placing Vietnam at the 37th position for worldwide lung cancer mortality.<sup>4</sup> Lung cancer is the most common cancer diagnosis among men and the fourth leading cancer diagnosis among women. On the basis of 2013 to 2017 data from Hanoi and Ho Chi Minh City, the age-standardized incidence rate per 100,000 was 32.03 for men and 10.48 for women (Fig. 2A). The age-specific incidence rate in 2013 to 2017 was low below 40 years and increased steeply after that, reaching a peak in the 65 to 79 age group among both men and women (Fig. 2B). Although the age-standardized incidence rates are trending

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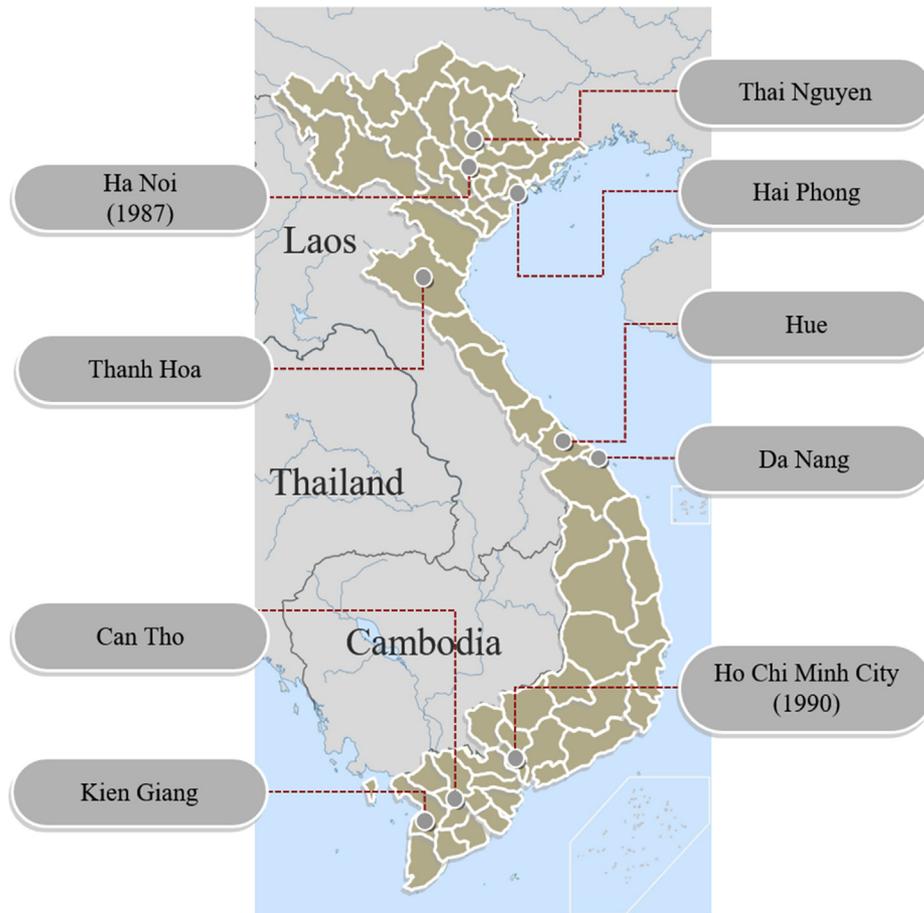


Figure 1. Nine regional cancer registries in Vietnam.

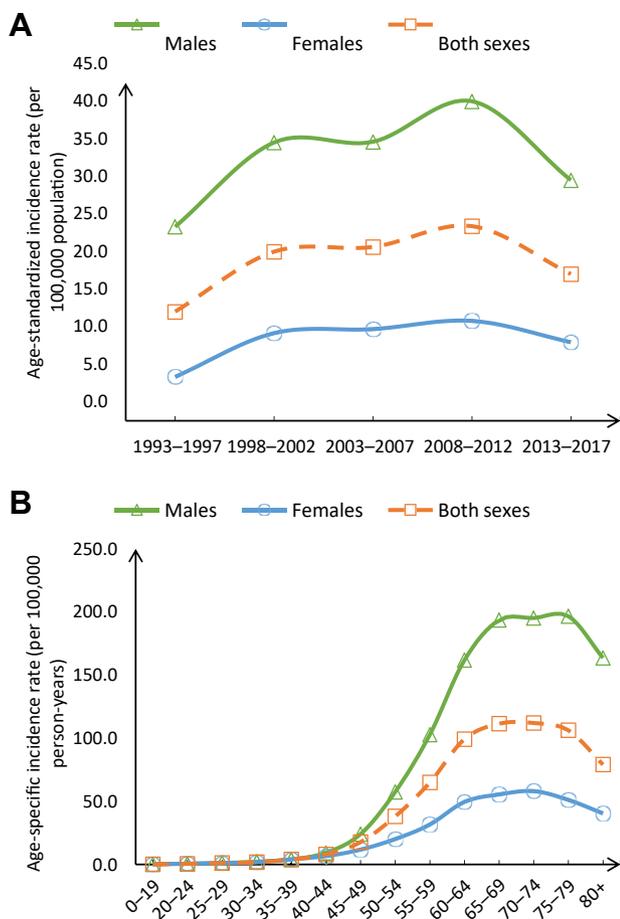
downward, the absolute number of incident lung cancer cases is expected to increase continuously in both cities, with projected 6198 male cases and 2311 female cases in 2025, owing to population growth, aging, and the impact of smoking and secondhand smoke exposure.<sup>2</sup> The aggregate 5-year lung cancer survival rate in Vietnam is 14.8%.

## Smoking

Vietnamese men had one of the highest smoking rates in the world with a prevalence of current smoking of 72.8% in 1997 although smoking rate was only 4.3% in women.<sup>5</sup> In 2000, the Vietnamese Government identified tobacco control as a public health priority and introduced the National Tobacco Control Policy, including public education, prohibitions on tobacco advertising, promotion, and sponsorship, health warnings, tax and price increases, smoking cessation advocacy, and restriction on public smoking. The goal was to reduce smoking rate among men to 20%. Vietnam signed the Framework Convention on Tobacco Control (FCTC) on August 8, 2003, ratified it into law, and became a member of FCTC on November 17,

2004.<sup>6</sup> In 2009, ratification of the Action Plan for the Implementation of the WHO FCTC prohibited smoking in indoor public places and public transport. Sanctions were imposed for smoking in public places by the first comprehensive tobacco control law established in 2012.<sup>7</sup>

These policies have had modest impact: aggregate smoking prevalence decreased from 23.8% in 2010 to 22.5% in 2015; 47.4% to 45.3% among men; and 1.4% to 1.1% among women.<sup>7</sup> Indoor secondhand smoke exposure declined from 84.9% to 80.7% in restaurants, 73.1% to 59.9% in homes, 55.9% to 42.6% at workplaces, 34.4% to 19.4% in public transportation, and 22.3% to 16.1% in schools. Nevertheless, the estimated number of smokers in Vietnam, 15.5 million in 2015, has not changed from that in 1997. The prevalence of smoking among patients with lung cancer ranges between 80% and 90% among males and 0% and 3.4% among females in recent studies, highlighting the importance of tobacco control and the need to identify risk factors beyond tobacco, particularly in women.



**Figure 2.** (A) Age-standardized incidence rates of lung cancer annually, 1993 to 2017, in Hanoi and Ho Chi Minh City, stratified by sex. (B) Age-specific incidence rate (per 100,000 person-years) for lung cancer 2013 to 2017 in Hanoi and Ho Chi Minh City, stratified by sex.

## Health Care Infrastructure

Health care in Vietnam is administratively categorized into the following four levels: (I) central or tertiary hospitals, (II) provincial hospitals, (III) district hospitals, and (IV) commune health centers. Most level I hospitals are owned by the Ministry of Health. Level II, III, and IV hospitals are owned by local provincial governments and directly supervised by the corresponding provincial or the District Department of Health.<sup>8</sup> Private hospitals and clinics account for 6% of all health care facilities. Vietnam Government launched a National Health Insurance (NHI) scheme in 1993, which covered 77% of the population in 2015, with a target of 90% by 2020.<sup>8</sup> The NHI law, enacted in 2008, was revised in 2021 to make health care more accessible for all citizens.

There are five comprehensive cancer centers, as follows: Vietnam National Cancer Hospital, Hanoi Oncology Hospital (North); Hue Oncology Hospital (Central); Ho

Chi Minh City Oncology Hospital, and Cho Ray Hospital (South Vietnam). Furthermore, 70 oncology departments were located within level I and II hospitals. Most patients with cancer are diagnosed and treated in level I and II hospitals. The seven largest hospitals providing thoracic oncology services in Vietnam have 55 specialty thoracic surgeons, 434 medical oncologists, 99 radiation oncologists, 60 pulmonologists, 127 radiologists, 69 pathologists, and 60 palliative care specialists (Table 1). The public health care workforce of Vietnam cannot meet current care delivery needs, and cancer centers are overcrowded; the health care system only meets 30% to 40% of cancer care demands. Therefore, more patients are seeking cancer treatment at private hospitals.

## Lung Cancer Screening

There are no national lung cancer screening guidelines or programs. Implementation of low-dose computer tomography (LDCT) screening for lung cancer is currently infeasible owing to lack of equipment, infrastructure, expertise, logistic difficulties, and financing. The NHI does not cover LDCT lung cancer screening. Ad hoc LDCT lung cancer screening is available in some private and level I hospitals.

## Diagnosis

NHI reimbursement for advanced diagnostic techniques including bronchoscopy and imaging modalities, such as CT and magnetic resonance imaging, in level I and II hospitals has been associated with increased detection of thoracic malignancies. Approximately 15% to 30% of lung cancer cases are incidentally detected by CT scans during routine checkup or evaluation for other illnesses. The use of positron emission tomography–CT scans for lung cancer diagnosis and staging is increasing. Nevertheless, there are currently only nine positron emission tomography–CT scanners in Vietnam.

Invasive diagnostic and staging approaches, such as endobronchial ultrasound, endoscopic ultrasound, transthoracic needle aspiration, video-assisted mediastinoscopy, and video-assisted thoracoscopic surgery, are available in level I hospitals. Most patients with lung cancer are diagnosed three to 6 months after onset of typical cancer-related symptoms, most at advanced stage. Unpublished data from the five largest oncology hospitals suggest that 1%, 4%, 19%, 55%, and 21% of patients with lung cancer are diagnosed at stages I, II, III, IV, and unknown, respectively. Histologic diagnosis of SCLC or NSCLC is required before treatment. Moreover, more than 80% of the cases are NSCLC, approximately 70% of which are adenocarcinoma.

**Table 1. Human Resources for Specialty Lung Cancer Care in Tertiary Cancer Centers in Vietnam, 2020**

Human Resources	Vietnam National Cancer Hospital	Hanoi Oncology Hospital	Viet Duc University Hospital	National Lung Hospital	108 Military Central Hospital	Ho Chi Minh Cho Ray City Oncology Hospital	Overall
Radiologists	35	20	20	10	14	18	127
Pathologists	20	8	5	5	9	8	69
Pulmonologists	12	5	2	5	10	26	60
Medical oncologists	214	126	20	10	25	19	434
Surgeons	103	25	500	12	450	220	1402
Specialty–lung cancer surgeons	7	2	8	12	8	13	55
Radiation oncologists	42	15	0	10	10	12	99
Palliative care specialists	8	6	12	2	5	12	60
Estimated number of newly diagnosed lung cancer cases receiving thoracic surgery in 2020	430	25	120	–	20	300	1067
Estimated number of newly diagnosed lung cancer cases receiving radiation therapy in 2020	753	273	60	–	220	80	1411
Estimated number of newly diagnosed patients with lung cancer receiving chemotherapy in 2020	1720	715	20	–	250	500	4925

**Table 2. Systemic Therapy for Advanced NSCLC**

Systemic Therapy	Advanced NSCLC With Tumor Driver Mutations				Pan-Negative Advanced NSCLC
Targeted therapy/ immunotherapy	EGFR+	ALK +	ROS-1+	BRAF <sup>V600E</sup> +	PD-L1+ (≥1%)
First line	Gefitinib <sup>a</sup> erlotinib <sup>a</sup> afatinib <sup>a</sup> osimertinib <sup>b</sup>	Alectinib <sup>b</sup> ceritinib <sup>‡</sup> crizotinib <sup>b</sup>	Ceritinib <sup>b</sup> crizotinib <sup>b</sup>	Dabrafenib + trametinib <sup>b</sup>	Pembrolizumab <sup>b</sup>
Second line	Osimertinib (with T790M mutation) <sup>b</sup>	Alectinib <sup>b</sup> brigatinib <sup>b</sup> ceritinib <sup>b</sup>		Dabrafenib + trametinib <sup>b</sup>	Atezolizumab <sup>b</sup> nivolumab <sup>b</sup> pembrolizumab <sup>b</sup>
Chemotherapy	Platinum-doublet chemotherapy: cisplatin <sup>c</sup> or carboplatin <sup>c</sup> , combined with either pemetrexed <sup>a</sup> , a taxane (paclitaxel <sup>c</sup> or docetaxel <sup>c</sup> ), etoposide <sup>c</sup> , gemcitabine <sup>c</sup> , or vinorelbine <sup>c</sup> , ± bevacizumab <sup>b</sup> . Pemetrexed <sup>a</sup> and bevacizumab <sup>b</sup> are not used for squamous cell carcinoma				

Note: All patients with NSCLC are recommended for *EGFR* mutation testing by polymerase chain reaction; specimens without *EGFR* mutation are to be simultaneously tested for *ALK* and *ROS1* rearrangements by fluorescence in situ hybridization; negative specimens are then tested by immunohistochemistry for PD-L1 protein expression.<sup>9</sup> Although guidelines recommend biomarker testing and testing for *EGFR*, *ALK*, and *ROS1* is partially covered by the National Health Insurance scheme, few laboratories in Vietnam perform them. Patients must pay out-of-pocket for other recommended biomarker tests, such as *BRAF*<sup>V600E</sup>, *HER-2*, *MET*, *KRAS*, and *PIK3CA*. There is no official guideline for treatment of SCLC from the Vietnam Ministry of Health.

<sup>a</sup>The National Health Insurance approved 50% reimbursement.

<sup>b</sup>Not covered by the National Health Insurance.

<sup>c</sup>The National Health Insurance approved 100% reimbursement.

## Surgery

Patients with stages I to IIIA NSCLC are advised to undergo resection at level I and II hospitals. Lobectomy is performed in 85% to 95% of cases; bilobectomy and pneumonectomy account for 3.5% and 0.5%, respectively. A 2016 analysis of 282 lobectomies with complete lymphadenectomy for stages I to IIIA NSCLC at the Vietnam National Cancer Hospital reported 1-, 2-, 3-, and 4-year overall survival rates of 89%, 73%, 67%, and 61%, respectively. Nevertheless, there are no guidelines standardizing lymph node staging, lymphadenectomy, or pathologic evaluation.

Initially introduced in 1996, video-assisted thoracoscopic surgery lobectomy has been widely performed since 2012. Approximately 50% of resections are now done by this technique. Robotic-assisted thoracic surgery was recently introduced in three hospitals but is seldom performed because of high cost and only partial reimbursement by the NHI. Although only 10% to 15% of patients with lung cancer undergo resection in Vietnam, the annual case volume is growing. Approximately 1070 lung cancer resections were performed at seven large hospitals in 2020, despite the coronavirus disease 2019 pandemic (Table 1).

## Radiation

There are 44 radiotherapy centers: 24 in North, seven in Central, and 13 in South Vietnam, most of which are located within level I and II hospitals. Access to radiotherapy facilities is limited. Three-dimensional conformal radiation therapy and intensity-modulated radiation therapy are used for 85% and 15% of patients, respectively. For those with early stage NSCLC who refuse surgery or are deemed inoperable, the 2018 national guidelines recommend radiation therapy at 65 to 70 Gy (2 Gy per fraction and five fractions per week) or stereotactic body radiation therapy.<sup>9</sup> Stereotactic body radiation therapy is available at five hospitals. Concurrent chemoradiotherapy is recommended for patients with inoperable stage III. Sequential therapy is an alternative approach for patients deemed unable to tolerate concurrent chemoradiotherapy.<sup>9</sup> For patients with SCLC with early stage, prophylactic cranial irradiation is recommended. Currently, Cyberknife and Gammaknife equipment are available in five hospitals in Vietnam.

The use of radiation therapy for lung cancer is predicted to increase in Vietnam. Although the number of linear accelerators increased from 13 in 2010 to 58 in 2020, this is insufficient to meet existing demand. Radiotherapy facilities are currently not available in many provinces. Vietnam Government plans to increase the number of linear accelerators and radiotherapy units and set up proton therapy units in the next few years.

## Systemic Therapy

Because 70% to 80% of patients are diagnosed at stage III or IV, systemic therapy is the mainstay of lung cancer treatment in Vietnam. Systemic therapy is based on pathology and biomarker profile. Systemic chemotherapy, delivered in 70 oncology departments, is used neoadjuvantly, adjuvantly, concurrently or sequentially with radiation, and palliatively. A strategy for personalized care of NSCLC was released in August 2018 (Table 2).<sup>9</sup> Although tests for *EGFR*, *ALK*, and *ROS1* are covered by the NHI, few laboratories in Vietnam perform them. Testing for *BRAF*<sup>V600E</sup>, *HER-2*, *MET*, *KRAS*, and *PIK3CA* is also recommended, but patients must pay out-of-pocket. A recent study of 350 Vietnamese patients with NSCLC from four hospitals revealed the following: 35% had *EGFR*, 23% *KRAS*, 7% *ALK*, 3% *ROS1*, 2% *BRAF*, and 0.6% *NRAS* gene mutations.<sup>10</sup> The prevalence of *EGFR* mutation in this study was remarkably lower than that in surrounding Southeast Asian countries, suggesting the study population and findings may not be generalizable. Drugs approved for advanced NSCLC and their reimbursement status are summarized in Table 2. An unpublished survey suggested that access to tyrosine kinase inhibitors and immune checkpoint inhibitors is limited: 22% of eligible patients with lung cancer received targeted therapy, 0.2% received immunotherapy, and greater than 74% received chemotherapy during their cancer treatment in 2016 to 2018.

For patients with nonsquamous NSCLC, four cycles of platinum-doublet chemotherapy, with or without bevacizumab, are recommended.<sup>9</sup> Pemetrexed and bevacizumab are not recommended for treatment of squamous cell carcinoma. Platinum-doublet chemotherapy is the standard first-line treatment for patients with NSCLC lacking driver mutations. Systemic chemotherapy is standard when targeted therapy and immunotherapy are not available for advanced NSCLC with driver mutations. For SCLC, four to six cycles of platinum and etoposide or topotecan are recommended. Chemotherapy for NSCLC and SCLC is typically reimbursed by the NHI in both public and private hospitals. The 2018 national guidelines which oncologists follow are based from the NHI reimbursement.<sup>9</sup>

## Conclusions

In recent decades, dramatic changes in the health care system of Vietnam have improved many aspects of lung cancer diagnosis and treatment. Nevertheless, lung cancer remains an oncologic public health challenge. High smoking rates, absence of lung cancer screening programs, limited access to optimal treatment, and reimbursement constraints are existing obstacles. Effective smoking cessation, early detection programs, and improvements in the quality of care are top priorities to reduce the adverse public health impact of lung cancer in Vietnam. The

growing burden of lung cancer in coming years will put a high demand on the care delivery infrastructure which will require a more coordinated response.

## CRediT Authorship Contribution Statement

**Huong T. T. Tran:** Conceptualization, Project administration, Writer—review and editing, Supervision.

**Sang Nguyen:** Writer—review and editing, Data curation, Project administration.

**Kiem K. Nguyen, Dung X. Pham, Uoc H. Nguyen, Anh T. Le, Giang H. Nguyen, Dung V. Tran, Son D. H. Phung, Hung M. Do:** Writer—review and editing, Data curation.

**Xiao-Ou Shu:** Conceptualization, Resources, Formal analysis, Methodology, Writing—review and editing.

**Raymond Osarogiagbon:** Conceptualization, Investigation, Resources, Project administration, Writing—review and editing, Supervision.

**Thuan V. Tran:** Writer—review and editing, Supervision.

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