The Economic Burden of Lung Cancer in Greece: A Systematic Review of the Literature.

<u>Gourzoulidis G<sup>1</sup> Kastanioti C<sup>1</sup>, Mavridoglou G<sup>1</sup>, Kotsilieris T<sup>1</sup> Tzanetakos C<sup>2</sup></u>

<sup>1</sup>Department of Business and Organizations Administration, University of the Peloponnese, Kalamata, Greece <sup>2</sup>Health Through Evidence GP, Athens, Greece.

#### Background

Lung cancer is the most commonly diagnosed cancer site and the leading cause of cancer death globally[1].

In Greece, lung was estimated to be the 3rd most commonly diagnosed cancer site and lung cancer the leading cause of cancer death, with 8,960 new cases and 7,662 deaths annually (2020 estimates)[1].

There are two major types of lung cancer, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), while NSCLC accounts for 80-90% of lung cancers [2]

The economic burden of lung cancer accounts for a large proportion of all healthcare expenditure across many European countries[3]

•High direct costs associated with management of advanced NSCLC patients are mainly driven by hospitalization needed for drug administration and treatment of adverse events (AEs)[4-5], and these costs increase with disease progression compared to stable disease [6].



•In Greece, real-world evidence data on lung cancer is limited, with only a few studies available. Therefore, conducting a comprehensive and structured analysis of existing research is crucial to provide a clear understanding of the financial impact lung cancer has on the Greek healthcare system and society.

#### Objective

The objective of the current study was to conduct a systematic literature review and investigate the economic burden of lung cancer in Greece. Additionally, the study aimed to identify existing data gaps and provide insights to support the design of future real-world studies.

### Methods

- This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [7].
- A systematic search on studies published in English on cost of lung cancer in Greece was performed in electronic databases such as PubMed, Scopus and ScienceDirect.
- After conducting a literature search, identified studies were reviewed to remove duplicates. The remaining studies were then independently screened by two reviewers based on predetermined inclusion criteria using the PICOS framework (Population, Interventions, Comparators, Outcomes, and Study Design). The PICOS criteria used in the search strategy are detailed in Table 1. A standardized data extraction form, developed for the purpose of this review, was used by the same two reviewers to independently extract data. A third reviewer, where necessary, was involved to resolve potential discrepancies on extracted data between the two reviewers.



## Results

- The study by Leftakis and Geitona [10] analyzed hospitalization costs for lung cancer patients undergoing thoracic surgery in the ICU of Sotiria Hospital in Athens (September 1997 - February 1998). The total cost per patient was estimated at US\$6,958, with ICU expenses making up 29% (US\$2,011).
- The study by Gkogkozotou et al. [13] evaluated staging costs for NSCLC using PET/CT and brain MRI (December 2014 November 2016) in 30 patients. Average diagnostic test costs were €1,823.70 for those receiving chemotherapy alone, while surgical treatment after neoadjuvant chemotherapy cost up to €9,068.20.
  Table 2: Characteristics of included studies

Study	Study Design and	Population and	Disease stage	<b>Study Duration</b>	Treatment Status at	Costing	Perspective of	Funding
	data source	sample size			study inception	method	analysis	
Leftakis et al. (2001)	Prospective study; hospital ICU patient records,(Athens)	95, patients with lung cancer treated in the ICU	All stages undergoing surgery	1997–1998 (6 months)	Postoperative patients after thoracic surgery	Bottom-up	Public payer perspective (Greek NHS)	Not reported
Zarogoulidou et al. (2015)	Prospective hospital- based (Thessaloniki)	113, patients diagnosed with NSCLC or SCLC	Local and extended disease (NSCLC/SCLC	2011–2014 (32 months)	Newly diagnosed patients undergoing chemotherapy	Bottom-up	Public payer and societal perspective	None
Gkogkozotou et al. (2018)	Retrospective cohort study; hospital patient records,(Athens)	30, patients diagnosed with NSCLC	Early and advanced stages (I-IV)	2014–2016 (2 years)	Patients undergoing surgery or chemotherapy treatments	Bottom-up	Public payer perspective (Greek NHS)	None
Souliotis et al. (2019)	Retrospective study; hospital medical records, (Athens)	144, patients with terminal stage NSCLC or SCLC	Stage III B / IV	2011–2014 (3 years)	Lung cancer patients at end-of-life stage	Bottom-up	Public payer perspective (Greek NHS	None
Mountzios et al. (2021)	Retrospective, medical charts/records, clinical centers across Greece	59 patients diagnosed with EGFR mutation- positive NSCLC	Locally advanced or metastatic (Stage III/IV	2015–2020 (5 years)	Patients treated with afatinib (1st, 2nd line, or beyond)	Bottom-up	Public payer perspective (Greek NHS	Hellenic Cooperative Oncology Group internal research grant (HE_TRANS_NSCL
Kokkotou et al. (2021)	Retrospective, hospital-based registry,(Athens)	122, patients terminal stage NSCLC or SCLC	Stage IV	2015–2018 (4 years)	Lung cancer patients at end-of-life stage	Bottom-up	Public payer perspective (Greek NHS)	None
Linardou et al. (2023)	Retrospective, multicenter; data from 18 clinical centers across Greece	346, patients diagnosed with advanced NSCLC	Stage IV	2015–2019 (4 years)	Patients previously treated with other therapies, starting Nivolumab	Bottom-up	Public payer perspective (Greek NHS	Hellenic Cooperative Oncology Group

This extraction form was designed to capture information concerning authors, publication year, study design, year of data collection, sample size, study perspective as well as the cost outcome of each study. The economic burden of lung cancer is generally categorized into direct and indirect cost.

#### Table 1: Study selection criteria considered in the search strategy

	Inclusion criteria	Exclusion criteria
Population	Lung Cancer	-
Interventions	• -	_
Comparators	• -	-
Outcomes	<ul> <li>Original studies investigating direct or indirect cost for lung cancer</li> </ul>	-
Study design/type		<ul><li>Reviews or meta-analysis</li><li>Editorials</li></ul>
	<ul> <li>Prospective, retrospective, observational studies,</li> </ul>	• Comments

- The study by Mountzios et al. [9] examined 59 patients with advanced NSCLC and EGFR mutations treated from 2015 to 2020, reporting an average direct cost of €25,334 per patient, primarily driven by drug acquisition (€21,865), with additional monitoring (€3,325) and adverse event management (€143) costs.
- In a study by Linardou et al. [8] involving 346 NSCLC patients previously treated with immunotherapy, the average cost per patient was €58,974, largely due to drug acquisition (€58,008), with minor costs for monitoring (€570), administration (€203), and adverse event treatment (€192). This was based on an average of 27.53 nivolumab treatment cycles per patient.
- Both studies emphasize drug acquisition as the dominant cost driver, with afatinib and nivolumab accounting for a large portion of the total costs. In Mountzios et al.,[9] afatinib represented the majority of the €25,333.68 per patient, while in Linardou et al.,[8] nivolumab's €58,008 was the primary cost component.
- The study by Zarogoulidou et al. [12] examined direct and indirect costs of lung cancer management in

Countries	• Greece	<ul> <li>Countries other than Greece</li> </ul>
Date of publication	<ul> <li>Study published until June 2024</li> </ul>	_
Language restrictions	<ul> <li>English language publications</li> </ul>	-
		<ul> <li>Pharmacoeconomic modelling studies</li> </ul>
		Presentations at scientific conferences
	<ul> <li>(Published full-paper of original study)</li> </ul>	<ul> <li>Letters to the Editor</li> </ul>

Results

- 7 studies[8-14] met the selection criteria and were included in the review (Figure 1).
- 88% of the studies were conducted over an adequate time horizon of one year or more, whereas two studies[8-9] described as multicentric or nationwide while five were conducted at a single center[8-14] (Table 2).
- Most of the included studies were retrospective (5 studies)[8,9,11, 13,14] and all used a bottom-up costing approach. In addition, all the studies[8-14] were conducted from a Greek public payer perspective while only one study had been also considered the societal perspective[12] (Table 2).
- Key components of direct medical costs in healthcare for lung cancer include hospitalizations, drug acquisition, diagnostic testing, and physician services, with drug and hospital costs forming the bulk of expenses (Table 2).

Greece for 113 patients with NSCLC or SCLC at the University of Thessaloniki. The total direct cost was  $\in 1,853,984$ , with chemotherapy drugs as the largest expense (70%, or  $\in 1,216,421$ ), followed by growth factors ( $\in 147,373$ ) and hospitalization ( $\in 85,308$ ). The average direct cost per patient was estimated at  $\in 16,407$ . Indirect costs included 28,774 lost productivity days, mostly borne by patients (95%), highlighting the significant economic impact beyond healthcare costs.

Two studies [11,14] assessed the end-of-life care cost for lung cancer patients in the last six months of life and found that the most significant component of direct costs was pharmaceutical expenditures.

# Conclusions

The economic burden of lung cancer has increased substantially over the past decade in Greece. However, there is limited evidence on both direct and indirect costs, as well as on the costs associated with different types of lung cancer. Further real-world studies are needed in Greece to address this gap.

		Re	ferences
1.	Sung, H., CA Cancer J Clin, 2021. 71(3): p. 209-249.	8.	Linardou, H., et al., RAnticancer Res, 2023. 43(6): p. 2799-2812.
2.	Sun, S., et al. Nat Rev Cancer, 2007. 7(10): p. 778-90.	9.	Mountzios, G., et al., A Lung Cancer (Auckl), 2021. 12: p. 93-102.
3.	Luengo-Fernandez, R., et al., Lancet Oncol, 2013. 14(12): p. 1165-1174.	10.	Leftakis, A. and M. Geitona, C Intensive Crit Care Nurs, 2001. 17(6): p. 322-30
4.	Corral, J., et al.,BMC Health Serv Res, 2015. 15: p. 70.	11.	Souliotis, K., et al., Health Serv Res Manag Epidemiol, 2019. 6:
5.	Vergnenegre, A., et al., Curr Med Res Opin, 2014. 30(3): p. 463-70	12.	Zarogoulidou, V., et al., E J Thorac Dis, 2015. 7(Suppl 1): p. S12-9.
6.	Isla, D., et al., T. Clin Transl Oncol, 2011. 13(7): p. 460-71.	13.	Gkogkozotou,V.I., et al., PELung Cancer Manag, 2018. 7(2):
7.	Moher, D., et al., PLoS Med, 2009. 6(7):	14.	Kokkotou, E., et al., J Comp Eff Res, 2021. 10(4): p. 315-324.

ISPOR ANNUAL EUROPEAN CONGRESS, 17 – 20 NOVEMBER 2024, BARCELONA, SPAIN **Contact details**: g.gourzoulidis@hte.gr