original contributions

Non–Small-Cell Lung Cancer: Real-World Cost Consequence Analysis

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QUESTION ASKED: What is the impact on costs and survival for non–small-cell lung cancer (NSCLC) management after the implementation of regional diagnostic and therapeutic pathway including all new and relevant diagnostic and therapeutic strategies?

SUMMARY ANSWER: The implementation of the diagnostic-therapeutic pathway in 2017 led to a mortality reduction (odds ratio, 0.93; $P = .02$) and average overall cost increase ($P = .009$), compared with a previous 2015 cohort.

WHAT WE DID: We analyzed data from 254 incidental cases of NSCLC diagnosed in 2015 and 228 diagnosed in 2017 within the territory of the Local Health Authority 16 (now ULSS16), in the province of Padua (Italy), as recorded by the Veneto Cancer Registry. TNM staging was done by the Veneto Cancer Registry according to 8th edition of the classification issued by the International Association for the Study of Lung Cancer, taking into account patients' medical records produced within 6 months of the date of incidence. The analysis of costs was performed on anonymized aggregate data with no chance of individuals being identifiable. Data on drug prescriptions, use of medical devices, hospital admissions, visits to outpatient clinics and the emergency room, and hospice admissions were drawn from the administrative databases into 2 years after diagnosis. In particular, the costs were drawn from the reimbursement rates established by the Veneto Regional Authority for each procedure or medical action.

WHAT WE FOUND: We observed a significant increase in the average overall costs of patients in the 2017 cohort ($P = .009$), as far as a lower mortality odd (odds ratio, 0.93; $P = .02$) than the 2015 cohort. The overall cost increase was mainly because of the increase in the average cost of drugs (coefficient = 5,953, $P = .008$), while a decrease in the average cost of hospice care (coefficient = –1,822.6, $P = .022$) was observed. However, monthly overall costs did not increase. The proportion of patients treated with targeted or immune checkpoint inhibitors, into 2 years after diagnosis, increased by 523% for patients in stage III and by 250% for those in stage IV.

BIAS, CONFOUNDING FACTORS, DRAWBACKS: This study is based on real-world data derived from administrative hospital flows, and it does not take into account indirect costs, which are known to be high, being NSCLC a highly invalidating disease. Second, at the time this study is being reviewed, additional new oncologic therapies are being commercialized even for the locally advanced disease, which will modify the stage-specific survival and costs. Moreover, the study does not take into account costs of drugs delivered in clinical trials. Finally, further studies with larger sample size are still needed to confirm these results.

REAL-LIFE IMPLICATIONS: Our findings underscore the importance of real-world assessments of costs in oncology, especially in the case of a disease like NSCLC; if on the one hand new target- and immuno-therapies are concretely helping in prolonging the survival for patients diagnosed with an advanced NSCLC, on the other hand, the issue about their economic sustainability should also be a reminder of the importance of primary and secondary prevention. Physicians should therefore be encouraged to follow new clinical pathways in the care of their patients, while the steadily rising related costs underscore the need for policymakers and health professionals to pursue the most rational utilization of public resources. In this context, evidence emerging from studies based on real-world data can provide them with the foundations for their assessment.

Author affiliations and disclosures are available with the complete article at ascopubs.org/journal/op.

Accepted on February 23, 2021 and published at ascopubs.org/journal/op on April 7, 2021: DOI https://doi.org/10.1200/OP.20.00863

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VALUE IN CANCER CARE

original contributions

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abstract

PURPOSE The present work aimed at conducting a real-world data analysis on the management costs and survival analysis comparing data from non–small-cell lung cancer (NSCLC) cases diagnosed in the Veneto region before (2015) and after (2017) the implementation of a regional diagnostic and therapeutic pathway including all new diagnostic and therapeutic strategies.

METHOD This study considered 254 incidental cases of NSCLC in 2015 and 228 in 2017 within the territory of the Padua province (Italy), as recorded by the Veneto Cancer Registry. Tobit regression analysis was performed to verify if total and each item costs (2 years after NSCLC diagnosis) are associated with index year, adjusting by year of diagnosis, sex, age, and stage at diagnosis. Logistic regression models were run to study overall mortality at 2 years, adjusting by the same covariates.

RESULTS The 2017 cohort had a lower mortality odd (odds ratio, 0.93; $P = .02$) and a significant increase in the average overall costs ($P = .009$) than the 2015 cohort. The Tobit regression analysis by cost item showed a very significant increase in the average cost of drugs (coefficient = 5,953, $P = .008$) for the 2017 cohort, as well as a decrease in the average cost of hospice care (coefficient = –1,822.6, $P = .022$).

CONCLUSION Our study showed a survival improvement for patients with NSCLC as well as an economic burden growth. Physicians should therefore be encouraged to follow new clinical care pathways, while the steadily rising related costs underscore the need for policymakers and health professionals to pursue.

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INTRODUCTION

In 2018, lung was the third most common site of cancer in Europe (excluding nonmelanoma skin cancers), with 470,000 new cases diagnosed yearly (12% of all cancers). It was the most frequent cancer in males, responsible for 267,000 deaths, and the second most frequent in woman, with 138,000 deaths.[1] The rates and temporal patterns of lung cancer incidence or mortality largely reflect the tobacco epidemic in men and women in the different European countries.[2] In general, the decreasing or stabilizing lung cancer rates in men seen in many parts of Europe in recent years contrast with the uniformly increasing rates among women, often in the same countries.[3,4]

Approximately 85% of lung cancers are diagnosed as non–small-cell lung cancer (NSCLC),[5] among which the most common subtypes are adenocarcinoma and squamous cell carcinoma. The majority of patients present with locally advanced or metastatic disease at diagnosis,[6,7] which partially explains the poor survival rates. Over the past 20 years, the availability of targeted therapies has allowed to improve progression-free survival and overall survival (OS) in some subgroups of patients with advanced NSCLC.[8-15]

Given the high mortality and morbidity of this disease, and the high cost of therapies,[16] the management of patients with NSCLC poses a major challenge for public health and healthcare services worldwide. Because of the complexity of multidisciplinary management, and with the aim of ensuring the most rational allocation of resources, national and international agencies have developed clinical practice guidelines (CPG) to provide evidence-based recommendations for physicians and other healthcare professionals.[17-20] Clinical pathways have been derived from CPG to facilitate the organization and

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on February 23, 2021 and published at ascopubs.org/journal/op on April 7, 2021: DOI https://doi.org/10.1200/OP.20.00863

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timing of patient care within a clearly defined integrated network of hospital and primary care.[21,22] For this purpose, the Rete Oncologica Veneta has adapted Italy's national CPG to its regional context, creating a diagnostic, therapeutic, and care pathway (*percorso diagnostico terapeutico assistenziale*) for NSCLC that aims to assure for all the patients access to timely and appropriate diagnosis, staging and treatments, as well as ensuring correct resource allocation and sustainability.[23] A recent work analyzed the different phases of this clinical pathway in depth.[24]

Although a number of studies have shown that the costs of cancer care are generally rising, only a have examined the impact of introducing new therapies in terms of outcomes and costs at population level. A good way to do so is to conduct a cost-consequence analysis, which demands an estimation of the costs as well as the health-related consequences. The cost-consequence format is easy to approach for healthcare decision makers, can be readily understood and applied, and generates information on the affordability of any new recommendations at population level. It takes an incidence-based perspective and estimates the costs and consequences for an individual or disease cohort. Health outcomes are presented annually for the population, as are the related costs, aggregated by cost category.[25] This method is a straightforward way to present the impact on cost and outcome data side by side for a new health technology in respect to comparator in situations where the research design might otherwise become excessively complex. An example would be a comparison between the costs and consequences of different models of care across a care pathway in an observational study.[26]

The purpose of the present work was to offer a real-world data analysis on the costs of managing NSCLC and to conduct a cost-consequence analysis comparing the management of cases diagnosed in the Veneto region (north-east Italy) in 2015 and 2017, that is, before and after the implementation of a regional diagnostic and therapeutic pathway including all new and relevant diagnostic and therapeutic strategies.

METHODS

Context

Italy's healthcare system is a regionally managed National Health Service (NHS) that provides universal coverage at the point of delivery completely free of charge for patients with cancer. The system is based on fundamental values of universality, free access, freedom of choice, pluralism in provision, and equity. Regional authorities plan and organize healthcare facilities and activities in accordance with a national health plan designed to assure an equitable provision of comprehensive care, called essential levels of assistance, throughout the country. Geographically disseminated local health authorities (LHAs) deliver public health and community health services and primary care directly. Secondary care and some specialized care are provided by community hospitals, whereas tertiary and highly specialized care is provided by scientific institutions such as cancer centers, teaching hospitals, or accredited private providers.[27] To guarantee all residents an equitable, uniform, and effective cancer care, in 2013, the Regional Government of Veneto established the Rete Oncologica Veneta, whose task, among others, was to set up and implement diagnostic and therapeutic pathways shared among all stakeholders including not only clinicians but also patients' advocacy groups and payers. These pathways are tools of clinical governance that, depending on the type of tumor or clinical problem, identify the best practicable pathway within the regional health organization. PDTAs are based on available scientific evidence and refer to main international and national guidelines and recommendations. Reference is also made to Italian national and regional legislation and to existing literature on network organization models for oncology service.[27]

When new pharmaceutical treatments are considered innovative, they are assessed by the European Medicines Agency, and their assessment has to be translated and acquired by the *Agenzia Italiana Farmaco* in its appraisal. To be considered innovative, a medicinal product has to demonstrate its added therapeutic value. A positive assessment could even suffice to justify a treatment's consideration as a sustainable expenditure for the NHS.[28] The attribution of innovative status ensures the immediate availability of medicines reimbursed by the NHS (see below). In Italy, the prices of medicines reimbursed by the NHS are set at central level by the Italian Medicines Agency (*Agenzia Italiana Farmaco*), which is a national regulatory authority.[29] Then, the Prices and Reimbursement Committee negotiates with pharmaceutical companies to set the prices of medicinal products reimbursed by the NHS based on transparent methods, timelines, and procedures.[30] Prices are decided at ex-factory level and usually fixed for 24 months.[27] The price may be lower at regional level, however, as regional authorities or LHAs are free to impose a share of co-payment on their price, mainly for cost-containment purposes or as a disincentive against inappropriate drug use. Various approaches are used to decide additional discounts (eg, success fee, cost sharing, risk sharing, payment by results, and budget cap).

The budget cap for regional authorities' pharmaceutical spending was introduced to oblige regional authorities to implement effective cost-containment initiatives. The national government set up a special fund amounting to a billion euros for innovative medicines included in a specific list (500 million for oncologic medicines, and 500 million for other medicines). Law No. 232 of 11 December 2016 (2017 Budget) establishes that acknowledgment of a drug's innovative nature and its inclusion in the list of innovative medicines may have a maximum duration of 36 months. After this time, cancer drugs that are still

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innovative in daily clinical use are no longer funded for their innovative nature and are covered by the ordinary fund for the reimbursement of costs for drugs.

Patients' Data

This study considered 254 incidental cases of NSCLC diagnosed in 2015 and 228 diagnosed in 2017 within the territory of the LHA 16 (now ULSS16), in the province of Padua (Italy), as recorded by the Veneto Cancer Registry. TNM staging was done by the Veneto Cancer Registry according to 8th edition of the classification issued by the International Association for the Study of Lung Cancer,[31] taking into account patients' medical records produced within 6 months of the date of incidence. Cases lacking sufficient information for proper staging were identified as not diagnosed.

Costs

The analysis was performed on anonymized aggregate data with no chance of individuals being identifiable. Data on drug prescriptions, use of medical devices, hospital admissions, visits to outpatient clinics and the emergency room, and hospice admissions were drawn from the administrative databases.

In particular, the costs were drawn from the reimbursement rates established by the Veneto Regional Authority for each procedure or medical action.

- The outpatient database collects information about medical acts and procedures that can be delivered at outpatient facilities under NHS funding valued at the rate reported in the *Nomenclature Tariffario delle Prestazioni Ambulatoriali*, an outpatient formulary.[32]
- The hospital admissions database defines the Diagnosis-Related Groups of each admission valued at the rate reported in the *Nomenclature Tariffario delle Prestazioni Ospedaliere*, an inpatient formulary,[33] covering all hospital activity from acute or day hospital admissions.
- The pharmaceutical distribution database and hospital drug consumption database are regional databases used to assess the costs for medical therapies taking the dose administered into account.
- The emergency room admissions database includes the costs of each admission derived from the rates for all medical acts and procedures performed during A&E admissions.
- The medical devices database reports the costs sustained by regional authorities to deliver medical devices.
- Hospice admission costs are derived by multiplying a regional daily rate by the number of days spent in the hospice.

Each patient was linked via an anonymous unique identification code to all administrative data regarding his or her hospital admissions, ambulatory care services, drug prescriptions, emergency department visits, medical device usage, and hospice admissions. We considered overall costs within 2 years of follow-up after NSCLC was diagnosed. The average per-patient, stage-specific, real-world costs were calculated and stratified by stage of disease at diagnosis.

Statistical Analysis

Descriptive analyses were used to analyze the cost and survival characteristics of the sample. Mann-Whitney-Wilcoxon Test was used to check for significant difference in costs. Logrank test was used to compare the survival function of 2015 and 2017 patients at each stage. Tobit regression analysis was performed to verify if total and each item costs (2 years after the diagnosis of NSCLC) are associated with index year, adjusting by year of diagnosis, sex, age, and stage at diagnosis. Logistic regression models were run to study overall mortality at 2 years (dependent variable), adjusting by year of diagnosis, sex, age, and stage at diagnosis. The R 3.6.2 and SAS 9.4 statistical packages were used for record linkage and all statistical analyses.

Ethical Issue

The study was conducted in accordance with the principles established in the Declaration of Helsinki. The study did not need specific authorization from an ethics committee as it is a retrospective observational study based on cases routinely collected by the Cancer Registry of the Veneto Region, which is authorized by the Italian Guarantor for the Protection of Personal Data to use health-related data for research purposes. All data were anonymized, following the Italian regulations, and were handled for monitoring and quality assurance purposes.

RESULTS

A total of 482 cases with an NSCLC (8.51% stage I, 5.19% stage II, 17.43% stage III, 52.07% stage IV, and 16.80% stage not defined) were included in this population study: 254 cases (52.7%) diagnosed in 2015 and 228 (47.3%) in 2017. Among these cases 66.39% (320) were male, and the mean age was 73.7 years (standard deviation ± 10.6, median 75, range 32-98 years). The main clinical and pathologic characteristics per year are summarized in Table 1.

Table 2 shows the mean per-patient total cost and OS 2 years after diagnosis for the two cohorts considered. For the 2015 cohort, the mean per-patient cost was 31,212€, and the 2-year OS rate was 26.0%, whereas for the 2017 cohort, the cost increased by 12,122€ (to a mean cost of 43,334€), and so did OS (30.7% at 2 years).

Table 3 shows the mean per-patient differences by cost item in the first and second years after diagnosis. There was a significant increase in the average cost for the 2017 cohort of drugs (+3,155€, up 118%) and medical devices (+225€, up 90%) in the first year, and a marked reduction in the average cost of hospice care (–294€, down 44%).

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TABLE 1. Sample Characteristics by Years

Characteristic	2015 Cases (N = 254)	2017 Cases (N = 228)	*P*
Sex, % (n)			
Male	54.4 (174)	45.6 (146)	.33
Age, mean (SD)	73.3 (± 10.7)	74.0 (± 10.4)	.49
Stage, % (n)			.013
I	58.5 (24)	41.5 (17)	
II	52.0 (13)	48.0 (12)	
III	51.2 (43)	48.8 (41)	
IV	47.0 (118)	53.0 (133)	
ND	69.1 (56)	30.9 (25)	
Morphology, % (n)			
Epithelial tumor	5.5 (14)	5.7 (13)	
Squamous cell carcinoma, NOS	13.0 (33)	11.4 (26)	
Adenocarcinoma, NOS	43.3 (110)	29.4 (67)	
Carcinoid tumor, NOS	1.6 (4)	0.4 (1)	
Acinar cell carcinoma	1.6 (4)	4.8 (11)	
Other morphology	3.5 (9)	5.3 (12)	
ND	31.5 (80)	43 (98)	

Abbreviations: ND, not diagnosed; NOS, not otherwise specified; SD, standard deviation.

The rise in the cost of drugs continued in the second year (+6,436€, up 141%). Moreover, in the second year, a relevant increase was noticed in the average cost of hospitalization (+1,037.55, +38.19%). Table 4 shows the results of our logistic regression analysis on mortality 2 years after the diagnosis of NSCLC. The 2017 cohort had a lower mortality odd (odds ratio 0.93, $P = .016$) than the 2015 cohort.

Table 5 shows the results of the Tobit regression analysis on total costs, adjusted for age, stage of disease at diagnosis, sex, and cohort, at 2 years after the diagnosis of lung cancer. There was a significant increase in the average costs of patients in the 2017 cohort ($P = .009$). As for the results of Tobit regression analysis by cost item, there was a very significant a decrease in the average cost of hospice care (coefficient = –1,822.6, $P = .022$), as well as an increase in the average cost of drugs (coefficient = 5,953, $P = .008$) for the 2017 cohort . However, monthly overall costs did not increase (data not shown). The proportion of patients treated with targeted or immune checkpoint inhibitors increased by 523% for patients in stage III and by 250% for those in stage IV with 2 years of follow-up after NSCLC was diagnosed (data not shown).

DISCUSSION

This real-world data analysis on patients with NSCLC showed that the survival rate improved significantly in the 2017 cohort vis-à-vis the 2015 cohort, overall, but especially for the advanced stages, who are the ones benefitting of the new oncologic drugs introduced in between the slot of time considered here. Consistent with this, our study showed that the mean costs of care have increased as well,

TABLE 2. Descriptive Analysis: Survival and Mean Per-Patient Total Cost at 2 Years After Diagnosis (for 2015 and 2017 Cohorts), Marginal Effect, and Costs

	2015				2017						
Disease Stage at Diagnosis	No. (%)	% Survival at 2 Years (No. Deaths)	Mean Total Cost at 2 Years	Average Cost Ratio Compared With Stage I	No. (%)	% Survival at 2 Years (No. Deaths)	Mean Total Cost at 2 Years	Average Cost Ratio Compared With Stage I	Difference in Cost	Absolute Risk (%)	Log-Rank Test, *P*
I	24 (9.45)	100 (0)	23.642,61€	1.00	17 (7.46)	100 (0)	28.799,27€	1.00	5.156,66€	0.00	—
II	13 (5.12)	84.62 (2)	27.783,24€	1.26	12 (5.26)	83.33 (2)	34.244,51€	1.19	6.461,27€	1.29	.999
III	43 (16.93)	37.21 (27)	41.187,41€	1.71	41 (17.98)	46.34 (22)	48.229,86€	1.67	7.042,45€	– 9.13	.653
IV	118 (46.46)	5.93 (111)	39.389,07€	1.68	133 (58.33)	14.29 (114)	49.621,96€	1.72	10.232,89€	– 8.36	.276
ND	56 (22.05)	14.29 (48)	25.696,11€	1.01	25 (10.96)	20 (20)	31.748,13€	1.10	6.052,02€	– 5.71	.835
Total	254 (100)	25.98 (188)	30.116,76€	1.32	228 (100)	30.7 (158)	40.098,95€	1.39	9.982,19€	– 4.72	.594

Abbreviation: ND, not diagnosed.

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TABLE 3. Mean Per-Patient Itemized Costs, and Differences for Itemized Costs and Total Costs in the First and Second Year After Diagnosis

	First Year After Diagnosis					Second Year After Diagnosis				
Item	2015 (%Total)	2017 (Total)	Cost Difference (2017-2015)	Cost Variation (%)	*P*, Mann-Whitney-Wilcoxon Test	2015 (%Total)	2017 (%Total)	Cost Difference (2017-2015)	Cost Variation (%)	*P*, Mann-Whitney-Wilcoxon Test
Hospitalization cost	9,763.9€ (55.4)	9,810.4€ (47)	+ 46.5€	+ 0.5	.87	2,716.7€ (21.7)	3,754.3€ (19.5)	+ 1,037.5€	+ 38.2	.22
Outpatient visits cost	3,463€ (19.7)	3,649€ (17.5)	+ 186€	+ 5.4	.97	3,389.9€ (27.1)	3,086.6€ (16.1)	– 303.4€	– 8.9	.40
Emergency room cost	292.2€ (1.7)	315.8€ (1.5)	+ 23.6€	+ 8.1	.51	162.9€ (1.3)	262€ (1.4)	+ 99.2€	+ 60.9	.46
Hospice cost	665.5€ (3.8)	371.2€ (1.8)	– 294.4€	– 44.2	.26	256.7€ (2.1)	86.3€ (0.4)	– 170.3€	– 66.4	.38
Hospital delivered drugs cost	2,670.9€ (15.2)	5,826.7€ (27.9)	+ 3,155.7€	+ 118.1	.60	4,553.1€ (36.4)	10,989.5€ (57.2)	+ 6,436.4€	+ 141.4	.12
Medical devices cost	250.3€ (1.4)	475.6€ (2.3)	+ 225.2€	+ 90	.03	769.3€ (6.2)	484.3€ (2.5)	– 285€	– 37.1	.50
Other drugs	514.6€ (2.9)	442.5€ (2.1)	– 72.1€	– 14	.07	647.7€ (5.2)	544.9€ (2.8)	– 102.8€	– 15.9	.53
Total	17,620.4€ (100)	20,891.1€ (100)	+ 3,270.6€	+ 18.6	.42	12,496.3€ (100)	19,207.8€ (100)	+ 6,711.5€	+ 53.7	.25

with drugs being the item most responsible for increase in our sample.

In fact, the differences between the clinical pathways adopted in 2015-2017 mainly concern the use of new drugs for metastatic patients, whereas the diagnostic and surgical procedures remained much the same. This observation is consistent with the better survival reported by previous studies on the efficacy of costly drugs included in updated NSCLC clinical pathways.[11,13,14] Our study design was based on real-world data, however, capturing the situation in a noninterventional, observational manner and in a natural, uncontrolled setting (outside any traditional clinical trials[34]), and providing evidence to complement the outcomes of randomized controlled trials. Data from real-world studies can help inform policymakers, clinicians, and patients about how an intervention performs outside the narrow confines of the research setting. They provide essential information on the long-term effectiveness of a new clinical pathway in large populations, and its economic performance in a naturalistic setting, enabling its comparison with other options. Real-world data also form a key part of healthcare technology assessments used by national and regional bodies to orient clinical decision making.[29]

Various studies examined the costs of managing patients with NSCLC in other European countries before the introduction of new targeted and immunotherapies,[35,36] but few have assessed these costs since the new drugs have been adopted. A study published by McGuire et al[37] compared NSCLC treatment costs for patients diagnosed in Germany, France, and England during the years 2008-2010, reporting considerable differences in average total costs for their 2-year follow-up (25,063€ for Germany, 17,777€ for France, and 32,500€ for England). Our study showed a comparable mean per-patient cost for our 2015 cohort (31,212€), before the new therapeutic strategies were adopted. A similar total mean cost (33,143€) was also

TABLE 4. Logistic Regression Analysis: Overall Mortality 2 Years After Diagnosis: Independent Variable Calendar Year 2017 (Reference 2015), Adjusted for Sex, Age, and Stage at Diagnosis

Variable	Exp (Coefficient)—OR	95% CI	*P*
Year (reference: 2015)			
2017	0.93	0.87 to 0.99	.02
Sex (reference: F)			
M	1.06	0.99 to 1.14	.06
Age at diagnosis	1.01	1.00 to 1.01	< .01
Stage at diagnosis (reference: stage I)			
II	1.19	1.01 to 1.41	.04
III	1.80	1.58 to 2.04	< .01
IV	2.38	2.13 to 2.66	< .01
ND	2.15	1.89 to 2.45	< .01

Abbreviations: ND, not diagnosed; OR, odds ratio.

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TABLE 5. Tobit Multivariate Regression Models (Adjusted for Sex, Age, and Stage at Diagnosis) for Different Itemized Costs and Total Costs, Two Years After Diagnosis: Independent Variable Calendar Year 2017 (Reference 2015)

Regression Model Dependent Variable	Coefficient, 2017 (Ref 2015)	95% CI	*P*
Hospitalization costs	6,878	2,191.9 to – 816.4	.37
Outpatient visits costs	384.0	1,635.3 to – 867.4	.548
Emergency room costs	79.6	187.8 to – 28.6	.149
Hospice costs	– 1,822.6	– 266.5 to – 3,378.6	.022
Hospital delivered drugs costs	5,953	10,328.1 to 1,577.8	.008
Medical devices costs	1,045	2,520.9 to – 430.6	.165
Other drugs costs	– 110.2	68.1 to – 288.5	.226
Mean cost by month alive	168.1	540.6 to – 204.4	.376
Total costs	6,013	10,513.9 to 1,511.4	.009

reported in a Dutch study by van der Linden et al,[38] who considered a sample of patients with NSCLC diagnosis between 2009 and 2011.

Our study then detected a 38% increase in the mean per-patient total cost for patients diagnosed in 2017 (up 12,121€), with the average cost of medication rising by 118% in the first year and 141% in the second. A previous study, which investigated how total cost of care for advanced NSCLC changed after the approval of immunotherapies, found lower mean per-patient total costs, and fewer hospitalizations and emergency department visits after the introduction of immunotherapy.[39] Overall, the previous American study[39] found that targeted therapies may lower monthly medical costs by prolonging survival and diminishing the use of other medical resources, despite the considerable drug costs. Our study contradicted these results; in fact, only the hospice medical costs seemed to be reduced during the first year.

In conclusion, our findings underscore the importance of real-world assessments of costs in oncology, especially in the case of a disease like NSCLC, which has such a high impact on treatment costs and patient outcomes. Our study showed an improvement in survival for patients with advanced-stage disease—a remarkable and necessary step forward in the treatment of a cancer that has been a global health scourge for decades. By contrast, this work also shows that the economic burden of NSCLC is steadily growing and that per-patient costs essentially increase in parallel with the stage at diagnosis. Physicians should therefore be encouraged to follow new clinical pathways in the care of their patients, while the steadily rising related costs underscore the need for policymakers and health professionals to pursue the most rational utilization of public resources. In this context, evidence emerging from studies based on real-world data can provide them with the foundations for their assessment. Moreover, if on the one hand new target- and immuno-therapies are concretely helping in prolonging the survival for patients diagnosed with an advanced NSCLC, on the other hand, the issue about their economic sustainability should also be a reminder of the importance of primary and secondary prevention. As it appears clearly from our analysis, the earlier the diagnosis, the longer the survival and the lower the costs.

This study also has some limitations, which have to be mentioned. First of all, being based on real-world data derived from administrative hospital flows, it does not take into account indirect costs, which are known to be high, with NSCLC being a highly invalidating disease.[40] Second, at the time this study is being reviewed, additional new oncologic therapies are being commercialized even for the locally advanced disease, which will modify the stage-specific survival and costs.[41] Finally, further studies with larger sample size are still needed to confirm these results.

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SUPPORT

Funding for this study was provided by ROV (Region Veneto Oncology Network) Regional health Research RSF-2017-557 and Ministry of Health grant NET-2016-02363853.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/OP.20.00863.

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Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Non–Small-Cell Lung Cancer: Real-World Cost Consequence Analysis

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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Research Funding: Roche, Novartis, Merck KGaA, Bristol-Myers Squibb
Expert Testimony: Roche, AstraZeneca
Travel, Accommodations, Expenses: Novartis, Celgene, AstraZeneca, Pfizer

No other potential conflicts of interest were reported.

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