Outcomes and cost of lung cancer patients treated surgically or medically in Catalunya: cost–benefit implications for lung cancer screening programs

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Lung cancer screening programs with computed tomography of the chest reduce mortality by more than 20%. Yet, they have not been implemented widely because of logistic and cost implications. Here, we sought to: (1) use real-life data to compare the outcomes and cost of lung cancer patients with treated medically or surgically in our region and (2) from this data, estimate the cost–benefit ratio of a lung cancer screening program (CRIBAR) soon to be deployed in our region (Catalunya, Spain). We accessed the Catalan Health Surveillance System (CHSS) and analysed data of all patients with a first diagnosis of lung cancer between 1 January 2014 and 31 December 2016. Analysis was carried forward until 30 months (*t*=30) after lung cancer diagnosis. Main results showed that: (1) surgically treated lung cancer patients have better survival and return earlier to regular home activities, use less healthcare related resources and cost less tax-payer money and (2) depending on incidence of lung cancer identified and treated in the program (1–2%), the return on investment for CRIBAR is expected to break even at 3–6 years, respectively, after its launch. Surgical treatment of lung cancer is cheaper and offers better outcomes. CRIBAR is estimated to be cost-effective soon after launch. *European Journal of Cancer Prevention* XXX: 000–000 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Lung cancer is the first cause of cancer death in the world, both in men and females (Malvezzi *et al.*, 2017). Yet, it can be cured by surgical removal (Asamura *et al.*, 2017; Pérez-Martínez *et al.*, 2018; Waller, 2018). Unfortunately, this occurs only in a minority of patients because, in practice, about three quarters of patients are diagnosed when lung cancer is advanced (Postmus *et al.*, 2017) and surgery cannot be offered. Early lung cancer diagnosis is, therefore, in addition to primary prevention, of paramount importance.

In 2011, the National Lung Screening Trial (NLST) showed that the use of low-dose helical computed tomography (CT) was effective to detect early lung cancer and, as a result, mortality was reduced by 20% (Aberle *et al.*, 2011). Just a few days ago, the results of the NELSON study (a European equivalent to the NLST) confirmed these results (De Koning *et al.*, 2018).

Several international societies have recommended the implementation of CT screening programs for lung cancer (Kauczor *et al.*, 2015; Garrido *et al.*, 2017; Oudkerk *et al.*, 2017; Pedersen *et al.*, 2017). Yet, because this recommendation faces significant logistic hurdles and has important economic implications (Cressman *et al.*, 2014; Chin *et al.*, 2015; Oudkerk *et al.*, 2017; Wade *et al.*, 2018), lung cancer screening programs have not been widely adopted. Here, we reasoned that a detailed analysis and comparison of the cost and outcomes of lung cancer patients treated in early stages (surgically) or advanced stages (medically) in real-life may provide relevant background information in this setting. Accordingly, in this study, we sought to: (1) use real-life data to quantify the outcomes and cost of lung cancer patients treated medically (because they were not surgical candidates) or surgically (sometimes combined with other medical treatments) from 2014 to 2016 in our region (Catalunya, Spain), which enjoys

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a publically funded health care system that covers all residents in the region and (2) use this real-life derived data to estimate the cost–benefit ratio of a lung cancer screening program (CRIBAR) soon to be deployed in our region.

Materials and methods

Study design and ethics

This retrospective, observational, comparative analysis includes 13.186 residents in Catalunya (Spain) diagnosed of lung cancer (see ICD-9-CM codes in Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A271*) for the first time between 1 January 2014 and 31 December 2016 ($t=0$) in the public healthcare system. Patients treated with chemo and radiotherapy before 1 January 2014 and with a diagnosis of any metastasis before the date of lung cancer diagnosis were excluded from the analysis. All included patients were treated medically or surgically according to best practice international recommendations (Reck *et al.*, 2013; Hirsch *et al.*, 2017). Analysis was carried forward until 30 months ($t=30$) after the diagnosis of lung cancer ($t=0$).

Because we used anonymized administrative databases for analysis, we did not obtain signed informed consent from each patient. Likewise, because this analysis includes all the population served by the Catalan Health Care system (not a random sample), formal sample size calculation is not required.

Sources of information

The Catalan Health Surveillance System (CHSS) includes detailed information on the use of healthcare resources of this population at individual level, including primary care attention, hospitalization, sociosanitary resources use, emergency care, mental healthcare and dispensed medication. Besides, it also includes information on hospital outpatient clinic, radiotherapy sessions, dialysis utilization, outpatient rehabilitation, nonemergency sanitary transport and home respiratory therapies (oxygen, noninvasive ventilation and others). The CHSS incorporates an automatic validation system that checks for internal consistency and, periodically, there are external audits to guarantee the quality and validity of the stored information, which is then used to pay healthcare providers. The CHSS does not include the care type and cost of lung cancer treatment provided by private healthcare companies (~15% of the total activity in the region for lung cancer), which is not accessible.

Analysis of real-life data

In each patient, we analysed the following variables: (1) demographics at $t=0$; (2) vital status from $t=0$ until $t=30$ months by Selwood analysis, as reported earlier (Vela *et al.*, 1999); (3) place of residence (home, hospital, nursing home, long-term care facility), which was analysed in 7-day periods from $t=0$ until $t=30$; (4) drug dispensation (Supplementary Table S2, Supplemental digital content 1, *http://links.lww.com/EJCP/A271*) from 12 months before $t=0$ until $t=30$; (5) annual healthcare resources utilization (HCRU), including primary care, emergency care, day-hospital visits, hospitalization events, long-term care needs and nonurgent sanitary transport use from $t=0$ until $t=30$. The annual rate of HCRU per person/year was calculated using the time at risk of each patient during each of these time periods, which finished either when the patient died or the study was censored (31 December 2016). This rate was estimated as total HCRU during the time period considered over the total number of patients/year; and, finally, (6) annual cost (€) per patient, as reported elsewhere (Vela *et al.*, 2017). Costs were calculated as the average value (€) per patient and category (surgical vs. medical treatment) during a given period of time, according to the Catalan Health System (Catsalut) tariffs.

Estimation of CRIBAR cost/benefit

Because CRIBAR will use the same inclusion and exclusion criteria, and three-year follow-up protocol, than those of the NLST (Aberle *et al.*, 2011), we anticipate a similar lung cancer detection rate (1–2%). On the other hand, as detailed in the on-line supplement, Supplemental digital content 1, *http://links.lww.com/EJCP/A271*, we estimated a total population to screen of 1.193 residents in three reference areas of our hospital. As a result, we anticipated total *cost* of CRIBAR for 3 years for these patients in our healthcare system context of 1 427 871 € (Supplementary Table S3, Supplemental digital content 1, *http://links.lww.com/EJCP/A271*).

To estimate the potential *benefits* of CRIBAR, we used life-years gained (LYG) (Torrance and Feeny, 1989) in two different efficacy scenarios (lung cancer incidence during screening of 1 or 2%), according to the results of the NSLT (Aberle *et al.*, 2011). To do so, we used the actual survival of surgical and medical patients at $t=30$ determined in our real-life analysis detailed above; survival after 5 and 10 years was estimated from the literature (Goldstraw *et al.*, 2016). We then applied a value of 30 000€ per LYG (and a discount rate of 3%) according to the most common value used to assign a societal value to LYG in Spain (Sacristán *et al.*, 2002), although this value varies between countries (Neumann *et al.*, 2014),

Statistical analysis

Results are presented as mean ± SD or proportion, as appropriate. Chi-square test (for categorical variables) and Student's *t* test (for continuous variables) were used to explore differences between groups. Given the observational nature of this study, no correction for multiple testing was applied. The threshold for statistical significance was set at a two-sided α-value of 0.05. All analyses were performed in R (version 3.4.3).

Results

Characteristics of patients at the time of lung cancer diagnosis ($t=0$)

Table 1 compares the main demographic and clinical characteristics at the time of lung cancer diagnosis ($t=0$) in patients treated medically ($n=10\,866$; 82.4%) or surgically ($n=2230$; 17.6%). Males predominate in both groups and surgical patients tended to be slightly younger (about 4 years). Comorbidities were prevalent in both groups.

Outcomes

As expected, survival after lung cancer diagnosis was higher ($P<0.001$) in surgical patients (Fig. 1, Table 2). Besides, surgically treated patients regained autonomy and returned home after $t=0$ much sooner than those treated medically (Table 2).

Healthcare resources utilization

Table 3 presents the HCRU rates by medical and surgical patients before and after the diagnosis of lung cancer ($t=0$), as well as their rate ratio. HCRU after $t=0$ was most often higher in medical patients (higher rate ratio).

Cost assessment

Figure 2 shows that the average annual cost of medical and surgical patients during the year that preceded lung cancer diagnosis was similar but, at $t=30$, cost was 36% lower in surgical patients.

Table 1 Main clinical characteristics of participants by type of treatment received (medical vs. surgical)

	Medical treatment		Surgical treatment		
	N	%	*N*	%	*P* value
Cases	10866	82.4	2320	17.6	
Sex					0.007
Men	8410	77.4	1735	74.8	
Women	2456	22.6	585	25.2	
Age, years					<0.001
0–44 years	262	2.4	69	3.0	
45–64	3550	32.7	948	40.9	
65–74	3098	28.5	857	36.9	
75–84	2828	26.0	432	18.6	
85 or more	1128	10.4	14	0.6	
COPD	3820	35.2	902	38.9	<0.001
Diabetes	2800	25.8	545	23.5	0.024
Cardiac failure	1434	13.2	136	5.9	<0.001
Ischaemic Illness	1648	15.2	270	11.6	<0.001
Stroke	1408	13.0	199	8.6	<0.001
Chronic renal failure	1484	13.7	196	8.4	<0.001
Dementia	373	3.4	21	0.9	<0.001
Depression	1697	15.6	418	18.0	0.005
Nursing home	134	1.2	8	0.3	<0.001
Risk strata high (Dueñas-Espín *et al.*, 2016; Vela *et al.*, 2018)	3322	30.6	521	22.5	
Medium	4414	40.6	1,160	50.0	<0.001
Low	2255	20.8	493	21.2	
Basal	875	8.0	146	6.3	

COPD, chronic obstructive pulmonary disease .

Cost–benefit analysis

As detailed in Table 4 and presented graphically in Fig. 3, depending on the efficiency of the screening program (1 or 2% detection of incident lung cancer), we estimated that the cost–benefit ratio of CRIBAR will break even between 3 and 6 years after launch and will generate healthcare cost savings thereafter.

Discussion

This real-life study confirms previous studies that show that the best therapeutic option for a lung cancer patients is the surgical removal of the tumour (Speicher *et al.*, 2016; Couñago *et al.*, 2018) because lung cancer patients treated surgically here have better survival and return earlier to regular home activities than those treated medically (Fig. 1). It also shows that lung cancer patient treated surgically uses less healthcare related resources and cost less tax-payer money (Fig. 2). Using these real-life data, we estimated that the cost–benefit ratio of a lung cancer screening program in our region will break even between 3 and 6 years after launching and will generate healthcare cost savings thereafter (Fig. 3).

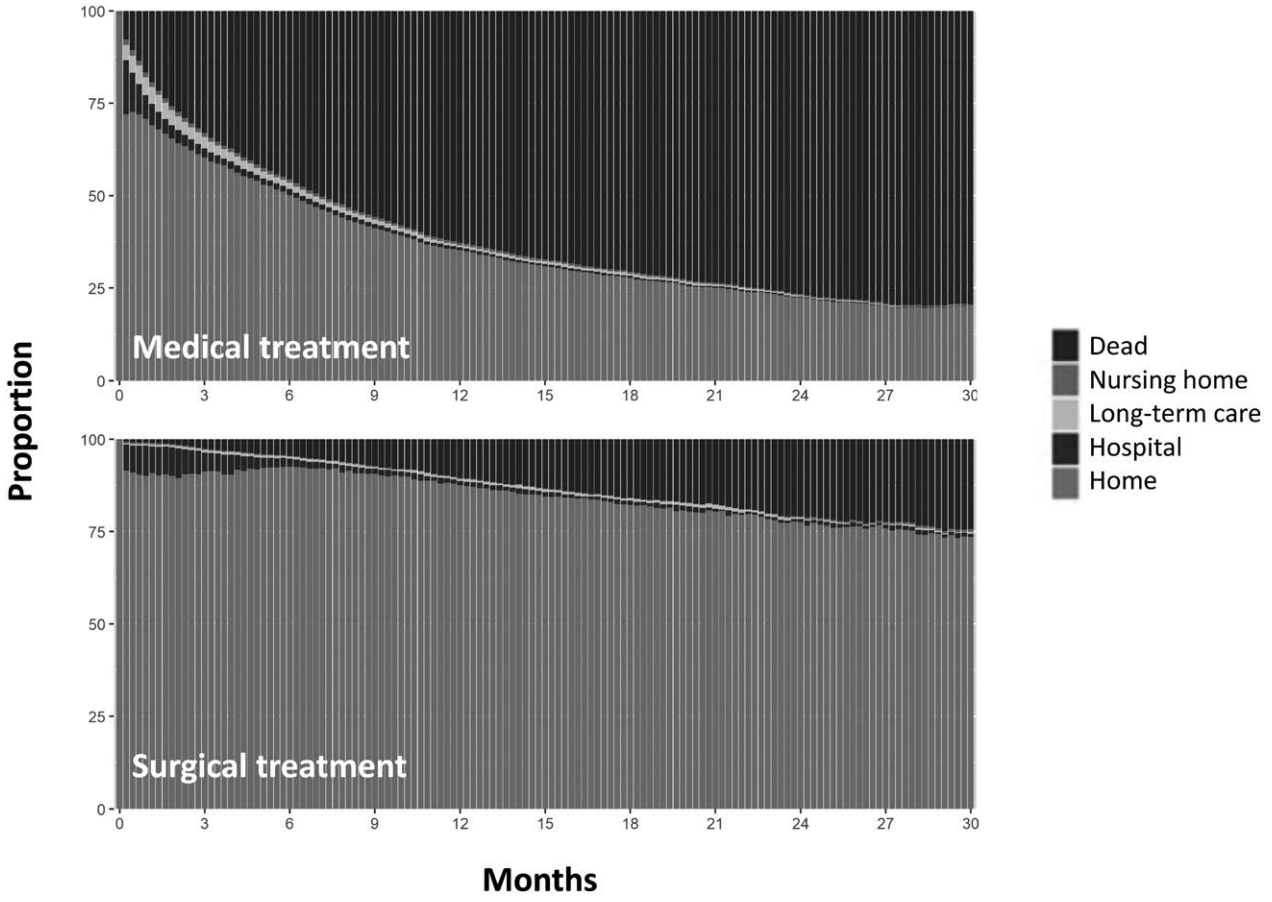
Previous studies

The publication of the NLST results in 2011 (Aberle *et al.*, 2011) generated a great deal of interest to explore the cost-effectiveness of lung cancer screening programs. Initially, most studies used mathematical models in data bases of private healthcare insurance companies. All of them concluded that lung cancer screening programs were highly cost-effective, in line with other accepted cancer screening interventions (McMahon *et al.*, 2011; Pyenson *et al.*, 2012; Villanti *et al.*, 2013). More recently, Black *et al.* (2014) investigated the cost-effectiveness of the original NLST program and reported that screening for lung cancer with low-dose CT would cost about 81 000 USD (about 70 000€) per quality-adjusted life-years gained. Importantly, though these authors also reported that modest changes in some of their assumptions may greatly alter this figure, they eventually concluded that 'the determination of whether screening outside the trial will be cost-effective will depend on how screening is implemented' (Black *et al.*, 2014). This is, precisely, the goal of our study.

Interpretation of current observations

Several observations of our analysis deserve specific discussion. First, not surprisingly (but reassuringly) our real-life analysis confirmed that surgery is the best (and cheapest) therapeutic option (both in terms of survival, speed of recovery and cost) for lung cancer (Figs. 1 and 2, Table 2). Second, according to CHSS, the prevalence of lung cancer in the general population of Catalunya is 0.14%. This figure is well below that reported in the NLST (1–2%), indicating that an identical lung cancer screening program in our region has great potential to

Fig. 1



Survival and place of residence of lung cancer patients treated medically (top panel) or surgically (bottom panel). For further explanations, see text.

Table 2 Survival and place of residence at different times after lung cancer diagnosis (t=0) in patients treated medically or surgically

	Medical treatment				Surgical treatment			
	t=3	t=12	t=24	t=30	t=3	t=12	t=24	t=30
Dead (%)	33.1	62.7	76.6	79.3	2.7	10.5	20.9	24.4
Living at home (%)	60.4	35.3	22.6	20.3	91.3	87.6	77.5	73.6
Long-term care facility/hospitalized (%)	6.5	2.0	0.8	0.4	6.0	1.9	1.6	2.0

't' indicates number of months after lung cancer diagnosis (t=0).

identify, diagnose, operate and cure many asymptomatic lung cancer patients. Third, our analysis shows that the return on investment will break even between 3 and 6 years after launching CRIBAR and that it will generate significant health-care cost savings thereafter (Table 4, Fig. 3). All in all, these observations clearly support the implementation of lung cancer screening programs in our healthcare system, as proposed by a recent European Union position statement (Oudkerk *et al.*, 2017).

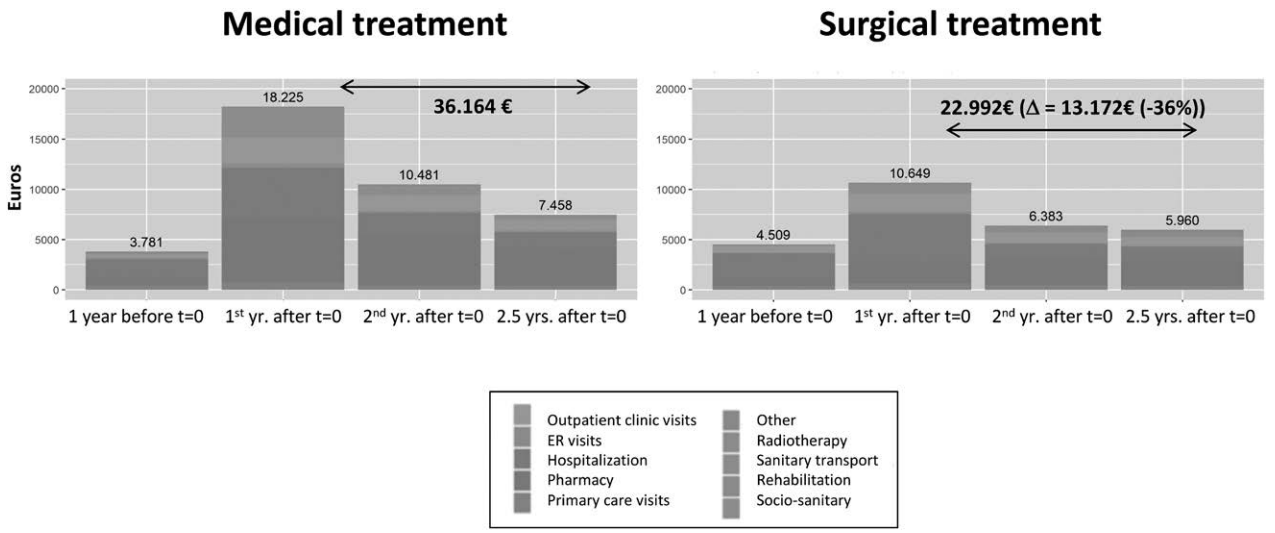
On the other hand, however, the cost–benefit ratio of any screening program depends critically on the technology used to screen for the presence of the disease of interest as well as the characteristics of the population to be screened (Molina *et al.*, 2016; Carozzi *et al.*, 2017). The NSLT included asymptomatic men and women, 55–74 years of age, with a history of >30 pack-years of cigarette smoking and who were either current smokers or had been smokers within the previous 15 years (Aberle *et al.*, 2011). Very recently, extended follow-up results during more than 11 years confirmed the original observations (National Lung Screening Trial Research, 2019). It is possible, however, that the inclusion of other lung cancer-related markers, such as circulating tumour markers (Molina *et al.*, 2016; Guida *et al.*, 2018), abnormal spirometry (de-Torres et al., 2015, 2016) or others can contribute

Table 3 Health-care resources utilization rate per 100 patients and year (and ratio rate between medical and surgical patients), during the year before *t*=0 and the first two years after it

	First year before *t*=0				First year after *t*=0				Second year after *t*=0			
	Medical	Surgical	Ratio rate (M/S)	*P* value	Medical	Surgical	Ratio rate (M/S)	*P* value	Medical	Surgical	Ratio rate (M/S)	*P* value
Primary care visits	1490.7	1266.3	1.177	<0.001	2471.9	2048	1.207	<0.001	1650.1	1477.8	1.117	<0.001
Out-patient visits	414.8	750.0	0.553	<0.001	1731.7	1753.8	0.987	0.048	1136.2	1090.5	1.042	0.001
ER visits	189.0	119.9	1.576	<0.001	370.2	214	1.73	<0.001	216.4	139.3	1.553	<0.001
Day-hospital sessions	57.1	91.7	0.623	<0.001	902.7	436	2.07	<0.001	509.7	200.2	2.546	<0.001
Hospitalization	89.1	101.4	0.879	<0.001	200.9	190.5	1.054	0.006	100.2	71.6	1.399	<0.001
Long-term care facility	20.0	1.8	10.994	<0.001	144.5	17.2	8.396	<0.001	66.3	18.7	3.539	<0.001
Nonemergency transport	105.7	47.7	2.217	<0.001	673.7	234.7	2.87	<0.001	283.6	153.7	1.845	<0.001
Radiotherapy sessions	–	–	–	–	76.3	23.9	3.192	<0.001	18.4	11.6	1.597	<0.001
Drug dispensations	1576.5	1602.2	0.984	0.005	2438.9	1704.1	1.431	<0.001	1672.9	1343.8	1.245	<0.001
Cancer drugs	–	–	–	–	2666.1	932.2	2.86	<0.001	2550.4	678.4	3.759	<0.001
Anxiolytics	840.8	833.6	1.009	0.28	396.2	321.3	1.233	<0.001	353.8	304.7	1.161	<0.001
Sedatives	357.4	337.5	1.059	<0.001	149.8	120.2	1.246	<0.001	132.3	123.8	1.069	0.064
Antidepressive	587.3	605.7	0.97	0.001	224	210.2	1.066	<0.001	246	229.1	1.074	0.006
Opioids	387.2	273.3	1.417	<0.001	1049.4	418.8	2.506	<0.001	846.8	327.5	2.586	<0.001
Analgesics	1484.7	1082.5	1.371	<0.001	2024.4	1418.4	1.427	<0.001	1629.5	845.2	1.928	<0.001

M, medical; S, surgical.

Fig. 2



Mean annual cost (€) per patient before and after the diagnosis of lung cancer in patients treated medically (left panel) or surgically (right panel). For further explanations, see text.

to better define the population to screen, and as a result, can improve the cost–benefit ratio of future lung cancer screening programs. This is a hypothesis that requires future prospective research.

Strengths and limitations

The fact that we analysed real life data from the entire population of patients with lung cancer (n=13.186) served by the Catalan Health Service followed up for 30 months is a clear strength of our analysis. On the other hand, however, there are some limitations that deserve specific comment. First, data on private healthcare information (about 15% of total activity in Catalunya) are not included in the public databases used for our analysis and could not therefore be accessed. Second, there is a relative paucity of clinical information in the administrative databases accessed. In particular, we lack information on the clinical stage of lung cancer at diagnosis. Likewise, we miss information on specific causes of death in both groups. Finally, some surgical patients (stage IIIA) might have received neoadjuvant chemotherapy. Unfortunately, we do not know the precise figure, but in any case, in our analysis, its cost has been attributed to the surgical group, so real differences between groups would have been larger in favour of the surgical group.

Conclusion

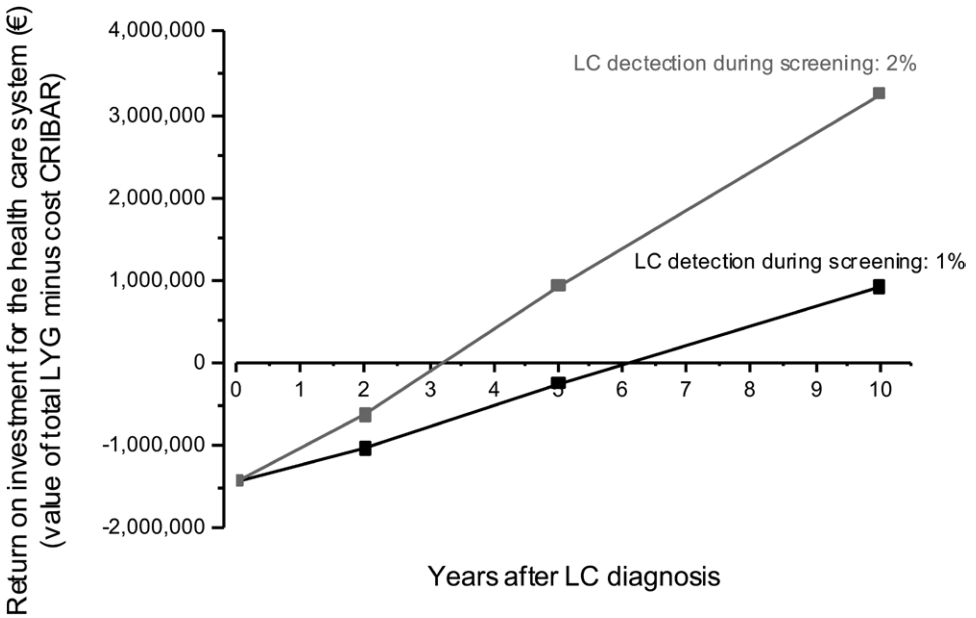
Using real-life data, our study confirms that surgical treatment of lung cancer is cheaper and offers better

Table 4 Cost–benefit analysis of CRIBAR

Number of patients identified by screening	*N*=12 (1% incidence of lung cancer)	*N*=24 (2% incidence of lung cancer)
2 years		
Survival surgical patients	79%	79%
Survival medical patients	23%	23%
LYG	13.4	26.7
Economic value of LYG	401 040.00 €	802 080.00 €
Return on investment (Value LYG – cost CRIBAR)	−1 026 831.03 €	−625 791.03 €
5 years		
Survival surgical patients	76%	76%
Survival medical patients	10%	10%
LYG	39.4	78.7
Economic value of LYG	1 180 800.00 €	2 361 600.00 €
Return on investment (Value LYG – cost CRIBAR)	−247 071.03 €	933 728.97 €
10 years		
Survival surgical patients	72%	72%
Survival medical patients	7%	7%
LYG	78.0	156.0
Economic value of LYG	2 340 000.00 €	4 680 000.00 €
Return on investment (value LYG – cost CRIBAR)	912 128.97 €	3 252 128.97 €

LYG, Life-years gained.

Fig. 3



Estimated return on investment over 10 years after the launch of CRIBAR assuming a 1% (black lines) or 2% (red lines) lung cancer detection (Aberle *et al.*, 2011). For further explanations, see text.

outcomes and shows that lung cancer screening programs in our region are highly likely to be cost-effective within a few years after launching.

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Conflicts of interest

There are no conflicts of interest.

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