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Economic burden of resected (stage IB-IIIA) non-small cell lung cancer in France, Germany and the United Kingdom: A retrospective observational study (LuCaBIS)

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ABSTRACT

Objectives: New adjuvant treatments are being developed for patients with resected non-small cell lung cancer (NSCLC). Due to scarcity of real-world data available for treatment costs and resource utilization, health technology and cost-effectiveness assessments can be limited. We estimated the burden and cost-of-illness associated with completely resected stage IB-IIIA NSCLC in France, Germany and the United Kingdom (UK).

Materials and methods: Eligible patients were aged ≥18 years with completely resected stage IB-IIIA NSCLC between August 2009 and July 2012. Patients (living or deceased) were enrolled at clinical sites by a systematic sampling method. Data were obtained from medical records and patient surveys. Direct, indirect and patient out-of-pocket expenses were estimated by multiplying resource use by country-specific unit costs. National annual costs were estimated based on disease prevalence data available from published sources.

Results: 39 centers provided data from 831 patients of whom patient surveys were evaluable in 306 patients. Median follow-up was 26 months. The mean total direct costs per patient during follow-up were: €19,057 (France), €14,185 (Germany), and €8377 (UK). The largest cost drivers were associated with therapies received (€12,375 France; €3694 UK), and hospitalization/emergency costs (€7706 Germany). Monthly direct costs per patient were the highest during the distant metastasis/terminal illness phase in France (€15,562) and Germany

Abbreviations: NSCLC, non-small cell lung cancer; UK, United Kingdom; EUCAN, European Cancer Observatory; CI, confidence interval; QoL, quality of life; SAS, Statistical Analysis Software; MRI, magnetic resonance imaging; PET, Positron emission tomography; CT, computed tomography; ED, emergency department; SD, standard deviation; LuCaBIS, Lung Cancer Burden of Illness Study

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(€6047) and during the adjuvant treatment period in the UK (€2790). Estimated mean total indirect costs per patient were: €696 (France), €2476 (Germany), and €1414 (UK). Estimates for the annual national direct cost were €478.4 million (France), €574.6 million (Germany) and €325.8 million (UK).

Conclusion: To our knowledge, this is the first comprehensive study describing the burden of illness for patients with completely resected stage IB-IIIA NSCLC. The economic burden was substantial in all three countries. Treatment of NSCLC is associated with large annual national costs, mainly incurred during disease progression.

1. Introduction

Lung cancer is the most commonly diagnosed cancer and frequent cause of cancer death worldwide [1]. The majority of lung cancers are diagnosed as non-small cell lung cancer (NSCLC) [2]. Complete surgical resection is the recommended therapy in all guidelines, and is used to treat NSCLC Stages (I–II) and specific cases of Stage IIIA disease [3–5]. Cisplatin-based adjuvant chemotherapy recommended for patients with Stage II-IIIA disease provides a small (5.8%) benefit in the 5-year rate of disease-free survival, although the associated toxicity is substantial [6,7]. With standard treatment, patients with resected NSCLC have a 5-year overall survival of 58–73% for Stage I, 36–46% for Stage II and 24% for Stage III [3,4].

There is a need for improved NSCLC treatments with higher efficacy and reduced toxicity compared to platinum-based regimens. New treatments for advanced NSCLC, such as targeted therapies, anti-angiogenic agents and immune checkpoint inhibitors, are currently being investigated in early stage NSCLC [8,9]. However, cost and affordability have been identified as major factors contributing to inequitable access to NSCLC anti-cancer drugs in European countries [10]. In many countries, decisions concerning drug access are made by health technology assessment agencies and reimbursement authorities. Data describing treatment patterns, outcomes in routine clinical practice, and an understanding of resource use and costs, which are not collected during clinical trials, are necessary to the quality of the decisions made by these agencies. To our knowledge, there are no comprehensive burden-of-illness data for patients with completely resected stage IB-IIIA NSCLC.

We report a retrospective, observational burden-of-illness study in France, Germany and the United Kingdom (UK) among 831 patients with completely resected stage IB-IIIA NSCLC (LuCaBIS: a burden-of-illness study in patients with stage IB-IIIA Non-Small Cell Lung Cancer in France, Germany, and the United Kingdom). Using medical charts and patient surveys, we identified low use of adjuvant therapy in patients with Stage IB disease (15.1%). Higher treatment rates were seen in more advanced disease stages (Stage IIA, 52.0%; Stage IIB, 58.2%; Stage IIIA, 71.4%), for which available evidence more consistently shows a survival benefit.

A similar pattern of adjuvant treatment use was observed in each country in terms of stage, although for each stage and overall, adjuvant chemotherapy was administered most frequently in France (61.8% of patients), intermediately in Germany (51.9%), and was used the least in the UK (33.4%). 40% of patients had disease recurrence or died during the study follow-up period (median follow-up of 26 months). Here we report the resource utilization and monetary costs associated with patients with completely resected stage IB-IIIA NSCLC from the same study.

The clinical aspects of this study are reported in a back-to-back manuscript in this issue.

2. Materials and methods

The study (ClinicalTrials.gov identifier: NCT01772225) was conducted in 39 specialist cancer centers, teaching hospitals and tertiary referral centers in France (14 centers), Germany (11 centers) and the UK (14 centers), providing a range of geographic locations and institution types within each country. Medical records in each center were screened for patients presenting with (or progressing to) stage IB-IIIA NSCLC between 1 August 2009 and 31 July 2012. Each center aimed to enroll between 5 and 30 patients. A limit of 30 patients per center was imposed in order to avoid potential bias arising from differences among centers in treatment practices combined with an imbalance in the number of patients included from each center. In sites with more than 30 potentially eligible patients, a systematic quasi-random sampling method (i.e. based on a generated random number) was used for patient selection to minimize the potential for selection bias and domination of one site over the others.

2.1. Inclusion and exclusion criteria

Patients (living or deceased) identified by medical record screening were eligible if they were ≥18 years of age, had undergone complete resection (no residual disease) of stage IB-IIIA NSCLC, and if the investigator/study site had been the main care provider for the patient during the period of NSCLC treatment or management.

Patients were excluded if they had undergone wedge resection, if their resection was less than 1 month before study screening, if they had received investigational adjuvant systemic treatment within a clinical trial, if they had received treatment for concomitant cancer, or if they were lost to follow-up. Patients who participated in randomized trials of treatment after recurrence of NSCLC were included.

2.2. Study objectives and procedures

The objectives of the cost analysis were to estimate the level of resource utilization, direct and indirect costs associated with managing patients with resected stage IB-IIIA NSCLC during adjuvant treatment, prior to disease recurrence/progression, and after disease recurrence/progression. The study was designed to collect three types of resources (direct costs, indirect costs, and patient out-of-pocket expenses) in order to provide a real-world cost representation of NSCLC management. The cost analysis included surviving patients in order to collect information via a patient survey about healthcare resources from providers other than their main NSCLC treatment center (for example local hospital emergency care and general practitioner visits), indirect costs (lost productivity for patients and caregivers), patient out-of-pocket expenses (non-reimbursed transportation and childcare) and health-related quality of life (QoL) using the EQ-5D questionnaire. The study also included patients who were deceased in order to research the period of care up until the time of death.

Detailed information about demographic and disease characteristics, disease progression, adjuvant treatment, and resource utilization was extracted from patients' medical records by their physicians or site staff using a custom electronic data collection form. Information was collected from diagnosis until death, or until the last entry in the record. The patient survey was administered to patients still living at the time of the study. Patient surveys were completed from July 2013 through January 2014. The recall period of the patient survey was limited to 3 months to minimize recall bias, but included exceptional events such as hospitalizations and changes in employment status due to their NSCLC, which the patient would be expected to recall with more reliability and which represent substantial costs. Physicians did not send the survey to patients if they felt that this was inappropriate for that patient. Informed consent was collected only from living patients who

participated in the patient survey according to country-specific procedures.

2.3. Analysis

Descriptive summaries of results were generated by country and no statistical comparisons were performed. Costs were estimated from the healthcare provider and societal perspectives in euros (€) (and pounds sterling, £, for the UK). Monetary values for resource use were identified from published country-specific recognized sources (reference year 2013/inflation-adjusted to 2013). UK-specific costs were converted to euros using an exchange rate of £1 = €1.22 (2013).

Costs were summarized for each country for four disease phases: 1) the adjuvant treatment period defined as the period from the date of surgical resection until the date adjuvant treatment ended; 2) the disease-free post-adjuvant (or no adjuvant) period, defined as the period from the date of surgical resection until the date of first disease progression (death or end of follow-up, whichever came first) in patients who did not receive adjuvant treatment, and as the period from the date adjuvant treatment ended until the date of first disease progression (death or end of follow-up, whichever came first) in patients who had received adjuvant treatment; 3) the period of locoregional recurrence defined as the period from the date of first disease progression until the date of detection of metastatic disease (death or end of follow-up, whichever came first) and; 4) distant metastatic and terminal disease, defined as the period from date of first distant metastasis until the date of death (or end of follow-up) in patients who did not experience a time of locoregional recurrence only, and the period from the date of detection of metastatic disease until the date of death (or end of follow-up) in patients who did experience locoregional recurrence adjuvant treatment period.

The duration of follow-up was the date of diagnosis until the end of data collection or date of death. Resource utilization recorded in the medical record abstraction form was analyzed over the duration of follow-up. Resource utilization recorded in the patient survey for the past 3 months was also reported. The following were estimated separately for each of the disease phases and overall across all disease phases:

- NSCLC-direct costs - treatments, adverse events, hospital and emergency visits, diagnostics, hospice and other costs, and reimbursed transportation.
- Additional community care direct costs - medical care visits outside of the participating physician's office, and hospitalizations in a hospital other than the NSCLC center.
- Indirect costs - cost of lost work days for patients or caregivers, and costs associated with a change in job status due to NSCLC.
- Out-of-pocket expenses - cost of childcare, and non-reimbursed transportation costs incurred by the patient or their family/friends.

For each patient, monthly costs were estimated by dividing his/her total NSCLC-care costs accumulated during the disease phase by the duration of follow-up (or recall) within the disease phase. Missing values were assumed to be the mean of the non-missing cost data within each disease phase period. Analyses were performed using the software SAS.

2.4. Estimation of direct costs from resource utilization data

Information on physician visits, hospitalizations, adjuvant treatments, radiotherapy, post-progression systemic therapy, toxicity management, emergency room visits, rehabilitation, diagnostics, hospice care and reimbursed transportation costs was collected from the medical records. Not all patients included in the medical record abstraction completed the patient survey, therefore the calculation of total direct costs was made separately for data collected from medical record abstraction (NSCLC direct costs) and from the patient survey (community care direct costs).

2.5. Estimation of lost productivity costs

The cost of lost work days for patients until death or the end of follow-up (whichever came first) and caregivers in work was estimated from the number of work days lost that were reported in the patient survey and the national average salary (from national statistics). The cost associated with changes in job status (e.g. permanently disabled, early retirement) due to NSCLC was estimated using the friction cost method [11].

Because disability benefits were obtained only from living patients who completed the survey and not from all patients for whom a medical record abstraction form was completed, they were not included in the total direct costs but were reported separately to avoid bias due to missing data. Disability benefits were excluded from total indirect cost estimates in the UK on the basis that these were transfer payments. For France, disability benefits are paid by the health insurance company and were therefore included in the total direct costs (health insurance perspective). For Germany, disability benefits are not paid for the first 6 weeks. Costs thereafter were included in the total direct costs (health insurance perspective).

2.6. Estimation of out-of-pocket expenses

Out-of-pocket expenses were estimated based on the patient survey 3-month recall period. Childcare costs were estimated from the number of days of childcare due to NSCLC and the unit daily cost for childcare in each country. Transportation costs were estimated using the number of visits to the main NSCLC treatment center from the medical record abstraction, the usual method of transportation and journey time collected in the patient survey, and cost estimates for each transportation method. When available, journey costs used national data (e.g., statutory mileage *Approved Mileage Allowance Payments* rates) or local data examples (e.g., local taxi and public transport rates).

2.7. Estimation of national cost-of-illness

The national cost-of-illness due to Stage IB-/IIIA NSCLC (direct costs, indirect costs, and out-of-pocket expenses) was computed based on mean annual per-patient costs (12 × mean monthly costs) from the current study multiplied by the number of prevalent cases of resected Stage IB-/IIIA NSCLC in each country.

The annual incidence of all lung cancers in the study countries was obtained from the 2012 EUCAN (European Cancer Observatory) registry [12]. Of all incident lung cancers, 85% were estimated to be NSCLC [13–15]. 39% of incident NSCLC were estimated to present as stages IB-IIIA, and 67% of these were estimated to undergo complete surgical resection [16,17]. Annual incidence counts of resected Stage IB-IIIA NSCLC were calculated as the product of these terms (annual incidence count for all lung cancers in a given country × 0.85 × 0.37 × 0.67).

Prevalence counts in each country were estimated as the annual incidence count multiplied by the average survival time (approximately 4 years) for patients with resected Stage IB-IIIA NSCLC based on data reported by the International Adjuvant Lung Cancer Trial Collaborative Group [18]. Annual per-person costs were obtained by multiplying average monthly costs by 12, and national total costs were calculated by multiplying annual per-person costs by the estimated prevalence counts.

3. Results

Data were extracted for 831 patients from 39 centers (Fig. 1). Of these patients, 526 were invited to participate in the patient survey of which 306 were completed (104 in France, 127 in Germany and 75 in

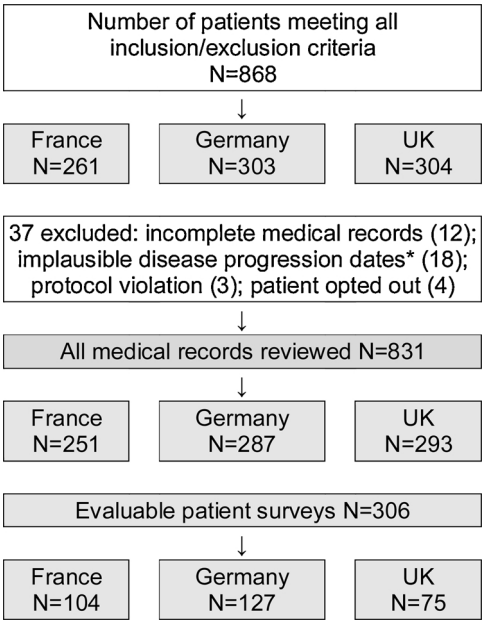

Fig. 1. Patient disposition.
NSCLC: non-small cell lung cancer, UK: United Kingdom.
*12 patients had a progression date that was before/during adjuvant treatment which continued unchanged after disease progression, 2 had a surgical resection date during/after adjuvant treatment, 4 reported a start of adjuvant treatment date that was > 100 days post surgery.

the UK), with an overall response rate of 58% (306/526). The median follow-up period for all patients was 26 months; 30 months in France, 24 months in Germany and 25 months in the UK.

Of 831 patients, 62% (513/831) were male, although the proportion ranged from 70.9% in France to 61.0% in Germany and 54.6% in the UK. Overall, 67% (557/831) were aged > 65 years at diagnosis and there were 20–30% of patients in each disease stage. Adenocarcinomas were the most prevalent (53%) followed by squamous cell carcinoma (38%), large cell tumors (2%) and other/unspecified (6%). Overall, 7.7% of patients had participated in clinical trials of post-recurrence treatment. Clinical and disease characteristics and clinical outcomes of patients are described in Chouaid et al. (back-to-back publication in this journal issue).

3.1. Quality of life

The mean (95% confidence interval [CI]) health utility weight estimates based on the EQ-5D index for the subset of patients providing a patient survey were 0.72 (0.68–0.75) for patients who were disease-free (n = 238, ranging from 0.71 in Germany to 0.73 in France), 0.62 (0.51–0.74) for patients with locoregional recurrence (n = 19, ranging from 0.58 in Germany to 0.66 in France) and 0.67 (0.55–0.78) for patients with distant metastasis and/or terminal disease (n = 32 ranging from 0.59 in the UK to 0.73 in France and Germany). A higher EQ-5D score indicates better QoL.

3.2. Direct costs

50% of patients were hospitalized during the adjuvant treatment period for reasons other than adjuvant treatment administration, and 19% were hospitalized for events related to adjuvant therapy (Fig. 2). The percentage of patients who were hospitalized, and the duration of hospitalization, was the highest in distant metastatic and terminal disease phase in all countries (Fig. 2). Overall resource consumption, in terms of the number of episodes of use of each resource was the highest

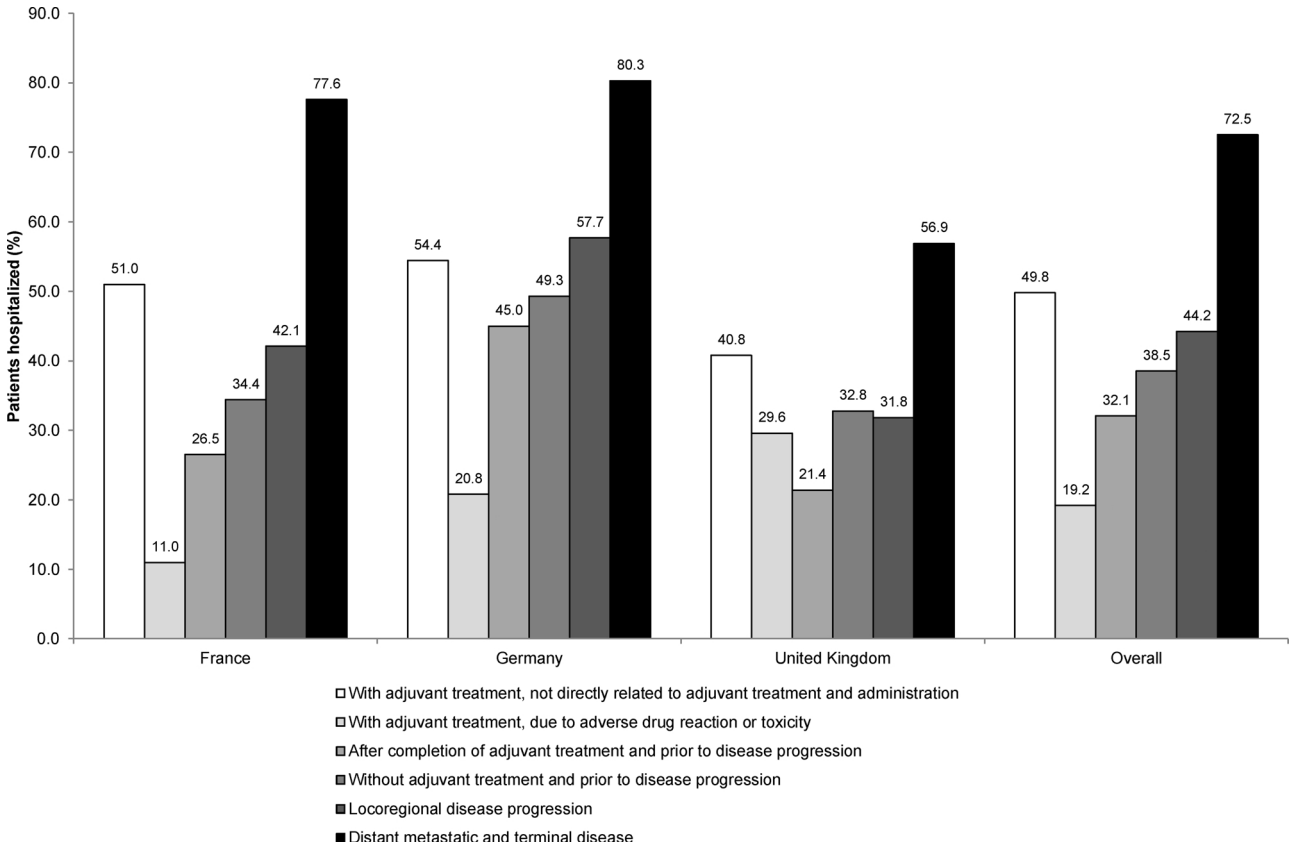

Fig. 2. Percentage of patients hospitalized by disease phase (from medical record abstraction).

during the disease-free, distant metastatic and terminal disease phases (Table 1).

Resource use was similar between countries except for generally higher use of diagnostic tests in France and Germany than the UK; higher use of radiotherapy in France during all disease stages; greater use of chemotherapy during disease progression in France (see companion publication) and longer duration of hospitalization in France compared to Germany and the UK during disease progression (Appendix A Tables A1 and A2). For example, during the period of locoregional progression, the mean number of radiotherapy courses was 25.1 in France versus 3.5 in Germany and 1.2 in the UK; 65.8% of patients received systemic chemotherapy in France compared to 42.3% in Germany and 31.8% in the UK (see companion publication); and the overall length of hospital inpatient stay was 19.3 days in France, 14.7 days in Germany and 14.0 days in the UK. Similar trends were observed during the phase of distant metastatic and terminal disease (Appendix A Table A2).

Additional resource consumption was also identified by the patient survey including visits to or by healthcare professionals such as nurses and general practitioners, visits to emergency departments, counseling and periods spent in hospice or nursing home care (Appendix A Table A3). Overall, 23.9% (74/306) of patients reported being hospitalized outside of their main treatment center, with a mean length of stay of 13.9 days. Hospice stays were recorded by 17.3% of patients in France (18/104), with a mean length of stay of 28.9 days.

The mean total direct cost per patient over the entire medical-record follow-up period was €19,057 (95% Confidence Interval [CI:] 16,770–21,429) in France, €14,185 (95% CI: 12,544–15,876) in Germany, and €8377 (95% CI: 7310–9518) (£6,866, 95% CI: 5992–7802) in the UK (Fig. 3). The largest cost drivers were treatment costs in France and, to a lesser extent, in the UK (€12,375 and 3694, respectively), and hospitalization and emergency department costs in Germany (€7706). The total mean per-patient costs associated with management of adverse events during adjuvant treatment were €1063 in France, €1282 in Germany, and €894 (£733) in the UK.

In France and Germany, monthly direct costs per patient (the total

Table 1
Adjuvant treatment and resource use associated with resected Stage IB-IIIA NSCLC by disease phase for the major direct resource categories (from medical record abstraction).

Variable	Disease Phase				
	Adjuvant Treatment N = 402	Disease-free post-adjuvant N = 402	Disease-free no adjuvant N = 204	Locoregional recurrence N = 86	Distant metastatic and terminal disease N = 200
Patients that received adjuvant treatment (N = 831)					
None	N = 429 (51.6%)				
Cisplatin/vinorelbine	N = 258 (SD 64.2%), mean duration (wks) 9.4/10.3, planned cumulative dose 323.2 mg/m^2 (SD 134.3)/173.2 mg/m^2 (SD 139.8)				
Carboplatin/vinorelbine	N = 39 (9.7%), mean duration (wks) 9.0/9.3, planned cumulative dose 19.2 mg/m^2 (SD 4.1)/297.1 mg/m^2 (SD 258.3)				
Cisplatin/gemcitabine	N = 19 (4.7%), mean duration (wks) 8.0/ 9.1, planned cumulative dose 273.5 mg/m^2 (SD 68.9)/4595.0 mg/m^2 (SD 1384.9)				
Other[a]	N = 86 (10.3%)				

Resource use	Related to adjuvant treatment, mean number of episodes (SD)	Unrelated to treatment, mean number of episodes (SD)	Mean number of episodes (SD)
Oncologist visits	2.3 (2.0)	4.9 (3.9)	5.3 (4.1)
Surgeon visits	1.0 (-)	1.3 (0.9)	2.6 (2.2)
Pulmonologist/respiratory physician	1.4 (0.8)	5.1 (4.1)	4.6 (3.5)
Palliative care physician (G & UK)	0	8.0 (-)	0
Other specialist visits	1.1 (0.4)	1.6 (3.2)	3.2 (3.3)
Nurse visits (UK)	1.8 (1.5)	2.7 (1.6)	1.6 (0.8)
Hospitalizations	1.5 (1.0)	2.5 (2.1)	1.8 (1.4)
Duration of hospitalization (days)	7.3 (7.1)	10.0 (10.4)	12.3 (15.2)
Patient hotel/hospice stays (UK)	2.0 (1.0)	4.0 (3.0)	–
Home hospital visits (G & F)	–	–	–
ED visits	1.2 (0.5)	1.4 (0.8)	1.2 (0.6)
CT scans	1.1 (0.3)	1.6 (1.2)	3.5 (2.3)
MRI	1.0 (0.0)	1.1 (0.3)	1.4 (1.1)
PET scans	0	1.3 (0.5)	1.2 (0.4)
PET-CT combination	0	1.1 (0.3)	2.4 (2.2)
Ultrasound	1.0 (0.0)	1.3 (0.7)	2.5 (2.4)
Gamma-knife procedure	0	0	1.0 (-)
Nuclear medicine scans	–	–	1.4 (0.8)
Counseling sessions	1.7 (1.2)	1.4 (0.8)	–
Ambulance transports	1.6 (0.9)	1.8 (1.3)	1.7 (1.8)
Other paid transport services	2.0 (1.4)	6.9 (6.9)	6.9 (8.0)
Radiotherapy courses	–	11.0 (17.1)	9.8 (12.1)
Radiotherapy fractions	–	39.8 (14.6)	44.2 (15.6)
Brachytherapy	–	–	–
Laser surgery	–	–	–
Photodynamic therapy	–	–	–

NSCLC: non-small cell lung cancer, N: number of patients, SD: standard deviation, ED: emergency department, PET: positron emission tomography, CT: computer tomography, MRI: magnetic resonance imaging, wks: weeks, UK: United Kingdom, G: Germany only, F: France only, UK: UK only.

[a] Includes: Carboplatin, Cisplatin, Docetaxel, Gemcitabine, Paclitaxel, Pemetrexed, Carboplatin + either Etoposide, Gemcitabine, Paclitaxel, Pemetrexed or Other, Cisplatin + either Docetaxel, Etoposide, Paclitaxel, Pemetrexed, Vinblastine, or Other, Gemcitabine + Vinorelbine, Carboplatin + Docetaxel + Vinorelbine, Carboplatin + Etoposide + Other, Carboplatin + Paclitaxel + Vinorelbine, Cisplatin + Etoposide + Gemcitabine, Cisplatin + Gemcitabine + Vinorelbine, Cisplatin + Paclitaxel + Vinorelbine.

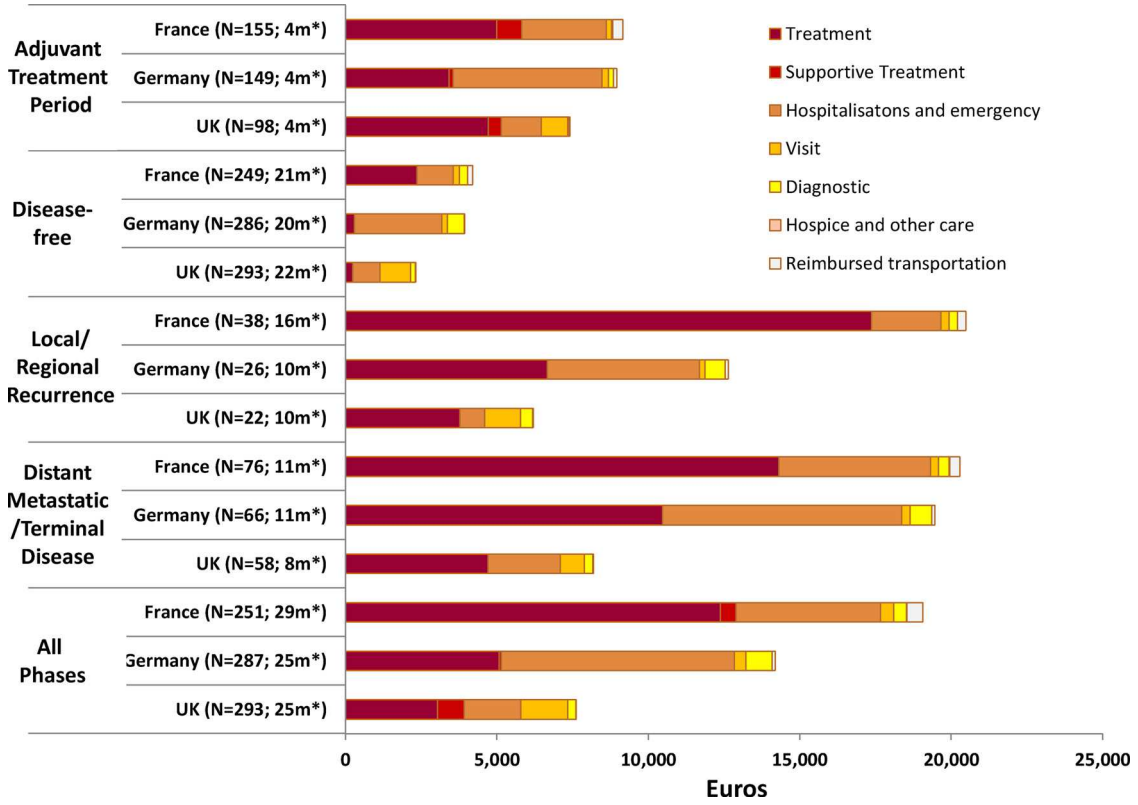

Fig. 3. Direct costs (per patient) associated with NSCLC over the follow-up period by country for the major direct resource category (medical record abstraction). Country (n = x), y = number of patients and mean duration of follow-up for the specified phase and country.
Treatment costs = systemic therapy, radiotherapy, gamma knife procedures, brachytherapy, laser surgery, photodynamic therapy, and embolization, and are obtained by adding up the treatments during the adjuvant treatment period during the no-recurrence period and systemic therapy and chemotherapy received during later phases along with the associated administration costs.
Supportive treatment costs = Supportive treatment during the adjuvant treatment period including pegfilgrastim, filgrastim, erythropoietin, and aprepitant.
Visit costs = Visits to specialists (oncologist, pulmonologist/respiratory specialist, palliative care physician, surgeon, other), nurse visits, and counseling.
Diagnostic costs = X-rays, PET, CT, PET-CT scans, MRI, nuclear.
Hospice and other care costs = Home/hospital medical care in the home.
Reimbursed transport costs = Ambulance and other transportation to the primary NSCLC-care clinic, or other transports paid by health services.
NSCLC: non-small cell lung cancer, n: number of patients, UK: United Kingdom, MRI: magnetic resonance imaging, PET: positron emission tomography, CT: CT: computed tomography.

direct costs divided by the number of months the patient spent in the different disease phases) were the highest during the distant metastasis/terminal illness phase (€15,562 based on 76 patients in France and €6047 based on 66 patients in Germany), followed by the adjuvant treatment period (€2361 based on 155 patients in France and €2278 based on 149 patients in Germany) (Table 2). In the UK, the largest monthly direct costs per patient were for the adjuvant treatment period (€2490 based on 98 patients) followed by the distant metastasis or terminal illness phase (€2162 based on 58 patients).

3.3. Indirect costs and out-of-pocket expenses

One half (51.5%, 428/831) of patients were of working age (aged < 65 years) at diagnosis and, approximately 10% of patients overall (30/302, data missing for 4 patients) reported being on long-term (> 3 months) sick leave, disability leave, permanently disabled or a leave of absence from their job. Overall, 24.7% (70/283, data was missing for 23 patients) stated that their employment status changed as a result of their lung cancer; 16% of patients (15/97, 7 with missing data) in France, 36% (44/122, 5 with missing data) in Germany, and 17% (11/64, 11 with missing data) in the UK. Of 50/302 patients (16.6%) across all countries who were employed full-time or part-time at the time of the survey, 19 (38%) reported missing a median of 2 weeks of work (mean 32.0 days) in the last 3 months.

Overall, 8% (25/306) of patients received disability benefits for a mean of 17 weeks. To provide a cost estimate for the disability benefits, the duration of benefits was combined with country-specific unit costs. In the UK, the overall cost was €105 (£86) per patient; however, due to the method by which disability costs are paid in France and Germany, disability costs were bundled with additional community-care direct costs in these countries. Total community-care direct costs were €3423 per patient in France, €1265 per patient in Germany, and €794 (£651) per patient in the UK. Mean total indirect costs per patient were estimated as €696 for France, €2476 for Germany, and €1414 (£1159) for the UK (Table 2).

3.4. National cost-of-illness

The annual incidence estimate for completely resected stage IB-IIIA NSCLC was 8895 in France, 11,287 in Germany, and 8970 in the UK (Table 3). The corresponding national prevalence count estimates were 35,580 in France, 45,148 in Germany, and 35,880 in the UK. The final prevalence estimates, when combined with the annual per-person costs for direct, indirect and patient out-of-pocket expenses, provided annual cost estimates for stage IB-IIIA NSCLC of approximately €478.4 million in France, €574.6 million in Germany and €325.8 million (£267.1 million) in the UK (Table 3). The annual indirect national cost estimates were approximately €35.7 million in France, €111.5 million in

Table 2
Costs per patient (mean, 95% CI) and monthly costs associated with NSCLC for the overall follow-up period, by country and disease phase.

Variable	Data source	Disease Phase				Overall
		Adjuvant treatment[a]	Disease-free (post/no adjuvant)	Locoregional recurrence	Distant metastatic and terminal disease	
Per-patient costs (mean, 95% CI)						
France, €						
Direct costs	Medical records	9151 (7991–10,446)	4199 (3321–5146)	20,475 (15,698–25,565)	20,280 (16,550–24,362)	19,057 (16,770–21,429)
Out-of-pocket expenses	Medical records	0	0	0	0	0
Community care direct costs	Patient survey	1702 (867–2696)	2331 (1417–3382)	48 (0–112)	547 (168–990)	3423 (2,367–4,608)
Indirect costs	Patient survey	184 (0–475)	522 (207–905)	109 (0–339)	336 (0–1120)	696 (292–1172)
Germany, €						
Direct costs	Medical records	8955 (7728–10,287)	3930 (3379–4512)	12,638 (8979–16,461)	19,460 (15,581–23,700)	14,185 (12,544–15,876)
Out-of-pocket expenses	Medical records	55 (44–68)	59 (50–70)	56 (31–94)	146 (75–249)	126 (100–158)
Community care direct costs	Patient survey	589 (189–1068)	521 (312–776)	1632 (49–5145)	1876 (381–4006)	1265 (772–1842)
Indirect costs	Patient survey	1106 (473–1835)	1718 (1067–2423)	0	554 (0–1813)	2476 (1716–3289)
UK, €						
Direct costs	Medical records	9032 (7692–10,777)	2815 (2,416-3,262)	7565 (5115–10,286)	9969 (7952–12,048)	8377 (7310–9518)
Out-of-pocket expenses	Medical records	95 (87–104)	74 (66–84)	112 (74–154)	87 (67–107)	132 (120–145)
Community care direct costs	Patient survey	162 (0–425)	565 (271–909)	506 (0–2028)	2197 (0–4231)	794 (415–1231)
Indirect costs	Patient survey	1249 (281–2500)	755 (203–1476)	0	3395 (0–10,951)	1414 (620–2336)
Per-patient monthly costs (mean, 95% CI)						
France, €						
Direct costs	Medical records	2361 (2065–2706)	342 (252–445)	1846 (1326–2433)	15,562 (2453–41,277)	780 (679–888)
Out-of-pocket expenses	Medical records	0	0	0	0	0
Community care direct costs	Patient survey	413 (216–645)	214 (93–381)	16 (0–37)	145 (31–278)	257 (133–426)
Indirect costs	Patient survey	25 (0–76)	77 (9–173)	36 (0–113)	20 (0–61)	84 (14–183)
Germany, €						
Direct costs	Medical records	2278 (2006–2563)	408 (317–511)	1542 (1056–2086)	6047 (2259–11,669)	757 (648–870)
Out-of-pocket expenses	Medical records	15 (12–18)	5 (4-6)	6 (4–10)	28 (14–45)	6 (5–8)
Community care direct costs	Patient survey	192 (55–362)	56 (37–79)	93 (16–237)	168 (74–280)	92 (64–123)
Indirect costs	Patient survey	366 (130–665)	178 (89–287)	0	40 (0–118)	206 (116–316)
UK, €						
Direct costs	Medical records	2490 (2163–2863)	368 (245–519)	847 (655–1032)	2162 (1631–2757)	492 (405–587)
Out-of-pocket expenses	Medical records	27 (24–29)	6 (5–7)	12 (9–15)	15 (11–17)	7 (6–7)
Community care direct costs	Patient survey	49 (0–132)	46 (24–79)	48 (0–190)	750 (0–1459)	71 (35–120)
Indirect costs	Patient survey	372 (81–749)	94 (18–220)	0	1132 (0–3650)	184 (40–389)

NSCLC: non-small cell lung cancer, CI: confidence interval (95 percentile bootstrapped CI using 10,000 samples), SD: standard deviation, UK: United Kingdom.
[a]Costs in the adjuvant treatment phase are the mean among patients who received adjuvant treatment, not the mean among all patients in the cohort (some patients did not receive adjuvant treatment).
Total NSCLC-care direct costs include treatment costs, supportive treatment costs, hospitalizations and emergency costs, visit costs, diagnostic costs, hospice and other care costs, and reimbursed transportation costs (medical record abstraction).
Missing costs are imputed from patients with available data.
Total out-of-pocket expenses are determined by adding up the non-reimbursed transportation costs associated with treatment visits and visits to specialists (medical record abstraction).

Germany, and €79.4 (£65.1) million in the UK. Annual out-of-pocket expense estimates were reported for Germany (approximately €3.4 million for non-reimbursed transportation) and the UK (€2.9 million [£2.4] for non-reimbursed transportation and €1.08 million [£887,649] for childcare) only. In France, annual out-of-pocket expense estimates were assumed to be zero where cancer care (including medical transportation) was fully covered by the national health insurance under the status of long-term illness.

4. Discussion

To our knowledge, this is the first study to comprehensively describe the burden of illness in patients with completely resected stage IB-IIIA NSCLC. This study assessed healthcare utilization and costs among patients with resected stage IB-IIIA NSCLC diagnosed in France, Germany and the UK between 2009 and 2012. A combination of medical-record data abstraction and a patient survey allowed us to capture information about resource use from a wide range of service providers, and to estimate the financial burden for patients, caregivers and their employers. Uniquely, our study estimated the cost of adverse events associated with adjuvant treatment, as well as indirect costs that are often absent in many cost-of-illness studies.

In each country, the monthly mean per-patient direct costs were higher after disease recurrence (locoregional or distant metastasis/terminal disease phases) than during the disease-free period. Costs during the adjuvant treatment phase were also substantial, driven largely by the costs of drugs and hospitalizations/emergency department visits.

The overall costs of treating resected Stage IB-IIIA NSCLC, and the monthly distribution of costs over each disease phase varied considerably in each country. These contrasts reflect differences in patterns of resource consumption in each country, with less use of radiotherapy or chemotherapy after disease progression, as well as fewer investigations and shorter hospitalizations in the UK, compared, in particular, with France. Some of this variability will also reflect differing unit costs, differing distribution of direct/indirect/out-of-pocket expenses in each country and different coverage of some expenses by the local healthcare system. For example, out-of-pocket expenses to the patient in France are low due to the high coverage of these costs by the national health insurance.

Table 3
National total cost-of-illness estimates.

Variable	France	Germany	UK
Epidemiological data	N	N	N
Annual incident cases[a]	13,275	16,845	13,387
Complete surgical resection n (%)[b]	8895	11,287	8970
Estimated prevalence counts of cases with complete surgical resection[c]	35,580	45,148	35,880
Cost	€	€	€
Annual costs per person[d]			
Direct costs (medical record abstraction)	9356	9082	5902
Additional community care costs (patient survey)	3085	1099	855
Indirect costs (patient survey)	1,004	2,470	2,212
Out-of-pocket expenses per person			
Non-reimbursable travel (medical record abstraction)	N/A	75	81
Childcare (patient survey)	0	0	29
Annual national costs[e]			
Direct costs (medical record abstraction)	332,891,172	410,025,654	211,780,864
Additional community care costs (patient survey)	109,748,612	49,624,540	30,694,718
Indirect costs (patient survey)	35,732,330	111,528,429	79,385,280
Non-reimbursable travel (medical record abstraction)	N/A	3,396,523	2,897,169
Childcare (patient survey)	0	0	1,082,932

NSCLC: non-small cell lung cancer, N: number of patients, N/A: not applicable, UK: United Kingdom.

[a] Country-specific incidences in 2012 were obtained from the European Cancer Observatory (EUCAN) [11]. 85% of incidence cancers were estimated to be NSCLC [12–14].

[b] Among patients with stage IB-IIIA NSCLC, 39% of incident NSCLC were estimated to present as stages IB-IIIA, and 67% of these were estimated to undergo complete surgical resection [15,16]. The annual incidence counts of patients with newly diagnosed stage IB-IIIA NSCLC with complete surgical resection was obtained by multiplying counts in row 1 by 0.67. Values were rounded to the next higher integer.

[c] Prevalence counts were obtained by multiplying incidence counts in row 2 by the median survival time of patients with stage IB-IIIA NSCLC and complete surgical resection, taken as 4 years from [17]. Values were rounded to the next higher integer.

[d] Per-person-costs were obtained by multiplying the average monthly costs by 12.

[e] National total costs were obtained by multiplying the per-person costs by the estimated prevalence of counts of stage IB-IIIA NSCLC patients with complete surgical resection.

Costs for patients receiving adjuvant treatment were similar across all three countries (range €8955–€9151 during the treatment period). However, total overall direct costs were lower in the UK (€8377) compared to France and Germany (€19,057 and €14,185 respectively). This was largely due to a lower proportion of patients receiving adjuvant therapy (33.4% in the UK versus 61.8% in France and 51.9% in Germany) and lower costs after disease progression in the UK.

While we did not identify any study describing the overall costs of care associated with resected NSCLC, there are published data that describe the cost of care of advanced (Stage IIIB and IV) NSCLC. The total per-patient cost of care of advanced (Stage IIIB and IV) NSCLC in Spain was estimated between €11,301 and €32,754 (from the start of active anti-cancer therapies until death), varying according to the number of treatments received (2009 prices) [19]. In the United States, the cost of treating advanced NSCLC increased substantially during disease progression, and the authors concluded that disease progression was a significant clinical event in terms of cost implications [20]. One Mexican study that included all lung cancer types and early disease stages, estimated that the annual cost per patient of Stage I disease was $13,456, Stage II disease $35,648 and Stage III disease $106,186 (2013 prices) [21]. Chemotherapy treatments exceeded other costs during Stages II and III. None of these studies considered the contribution of indirect costs and costs of adverse events to the overall burden of illness, and several used modeling approaches based on expert panels and published data to determine time to disease progression.

We collected real-world information from a large cohort of patients with NSCLC. This approach provides advantages to previous studies because it provides a comprehensive view of the resource use and clinical outcomes of patients with NSCLC. Our wide-range approach collected information about diagnostic tests performed, visits and treatment by nurses and home hospital staff, and information on the direct costs of community care via the patient survey. Furthermore, we collected data using a combination of practicing-physician-led characterization of medical practice through medical record review, and patient-reported data collected via a patient survey. This combination of data sources allowed for timely collection of a wide range of direct and indirect costs, including costs accrued outside of the main NSCLC center of care, and is therefore more likely to represent the true economic burden of illness incurred by the participating patients. The patient survey was able to collect data from local hospital care or emergency department visits, but these data may not have been fully captured since we relied on patient recall and a limited recall period of 3 months. Recall bias and uncertainty around the accuracy of the information collected through the patient survey is a potential limitation of our study.

QoL measures suggested a higher utility score during the period of distant metastasis and/or terminal disease than in the period of locoregional recurrence. However, there were few patients who provided QoL data during these stages, resulting in wide 95% CIs.

While we selected sites to achieve variation in geographic location, size, and type of center, the study data are not guaranteed to be representative of all sites and physicians treating patients with stage IB-IIIA NSCLC across each country, potentially leading to inaccuracies in our national cost-of-illness estimates. Furthermore the limited sample size may also be a source of imprecision. No external validation of data from the medical record abstractions was possible because of the need to protect patient confidentiality. As is the case with all studies that rely on existing medical records, availability of information in records varied by physician practice and by country, and reflects differences in practice patterns, recording practices, and medical norms.

5. Conclusions

Our study provides real-world data describing country-specific costs associated with the treatment of Stage IB-IIIA NSCLC. Treatment of Stage IB-IIIA NSCLC is associated with large annual national costs in all three countries of which a majority is incurred during disease progression. The study findings can assist decision-makers to understand cost patterns associated with the management of NSCLC, and can be used for assessing the benefits and costs of new NSCLC treatments.

Ethics approval and consent to participate

This study was approved by the RTI Health Solutions Institutional Review Board and the following Ethics Committees:

United Kingdom

- The National Research Ethics Service Committee Yorkshire and the Humber-Sheffield.

Germany:

- Landesärztekammer Hessen.

France:

- Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé (CCTIRS).
- Commission Nationale de l'Informatique et des Libertés (CNIL).

Informed consent was collected from living patients who participated in the patient survey following country-specific procedures. Consent was obtained by the patient's clinical care team. Living patients who did not participate in the patient survey, but only had their medical records abstracted, were not asked to provide informed consent. Families of deceased patients were not contacted during the study, and no informed consent was collected for the inclusion of data from the medical records of deceased patients. In addition, no attempt was made to collect patient survey data from family members of deceased patients.

Data anonymization process

No patient-identifying information was collected during the study or accessed by study personnel. Only members of a patient's clinical care team who entered the patient's data without any identifying information, were aware of each patient's identity. Each study center assigned a unique patient-identifying number, which was linked to the patient's name only at the clinical site. RTI Health Solutions and Kantar Health study staff received information identified by this number. Only the physician and the physician's staff providing medical services were able to link the patient number back to the patient. All data was handled in strictest confidence in conformity with national and international data protection regulations.

Competing interests

Andreas S. discloses honoraria for advisory boards and lectures from Roche, Boehringer Ingelheim, Pfizer, and the GSK group of companies.

In the past 5 years, Chouaid C. received fees for attending scientific meetings, speaking, organizing research or consulting from AstraZeneca, Boehringer Ingelheim, Hoffman La Roche, Sanofi Aventis, Eli Lilly, Novartis, Amgen, BMS, MSD, and the GSK group of companies.

Danson S. reports grants, personal fees, and nonfinancial support from the GSK group of companies during the conduct of the study, grants and nonfinancial support from the GSK group of companies, Eli Lilly, Bristol Myers Squibb, Boehringer Ingelheim, AstraZeneca, Onco-NX, Incanthera, Genta, Abraxane, Daiichi-Sankyo and Morphotek outside the submitted work; and familial relationship (brother-in-law) with an employee of the GSK group of companies.

Obukohwo S. is an employee of the GSK group of companies.

Benjamin L., Ehness R., Dramard-Goasdoue M. and Barth J. were employees of the GSK group of companies; and Benjamin L. and Ehness R. hold shares and/or restricted shares in the GSK group of companies.

Hoffmann H. reports no conflict of interest.

Potter V. reports receiving fees from the GSK group of companies regarding the set-up of this study in the UK.

Barlesi F. reports no conflict of interest.

Price M., Wolowacz S., Chirila C., Hollis K., Sweeney C. and Kaye J. A. report funding from the GSK group of companies to their employer, RTI Health Solutions, during the conduct of the study.

Kontoudis I. was an employee of the GSK group of companies at the time of the study.

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Authors' contributions

All authors were involved in the conception and/or the design of the study.

HH, SA, LB, CoC, ChC, SD, KH, IK, VP, MP, CS and SW participated in the collection or generation of the study data.

SA, LB, CoC, ChC, SD, KH, IK, VP, MP, CS and SW performed the study.

SA, CoC, ChC, SD, KH, IK, MP, CS, SW contributed to the analysis tools.

SA, FB, LB, CoC, ChC, SD, MHDG, KH, JAK, IK, MP, CS, SW were involved in the analyses and/or the interpretation of the data.

BS was involved in the implementation of the study design.

KH led the design and initiation of the project and served as project supervisor.

ChC was lead statistician of the project, wrote the analysis plan, supervised, programmed, and reviewed the SAS output tables, reviewed and provided input for the reporting of the results.

All authors read, reviewed and approved the present manuscript.

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Appendix A

Table A1
Resource use associated with resected Stage IB-IIIA NSCLC during the adjuvant treatment period and disease-free periods, by country, for the major direct resource categories (from medical record abstraction).

	France	Germany	UK
Adjuvant treatment period: unrelated to adjuvant treatment, mean number of episodes (SD)	**N = 155**	**N = 149**	**N = 98**
Oncologist visits	2.8 (2.9)	6.9 (4.9)	4.5 (2.0)
Surgeon visits	1.3 (0.9)	1.3 (0.5)	1.5 (0.9)
Pulmonologist/respiratory physician	5.5 (4.3)	6.0 (3.4)	1.4 (0.7)
Other specialist visits	1.4 (0.9)	2.8 (6.7)	1.1 (0.3)
Hospitalizations	2.5 (1.5)	3.0 (2.8)	1.7 (1.0)
Duration of hospitalization (number of days)	8.4 (11.0)	13.3 (10.9)	6.3 (4.4)
ED visits	1.5 (1.0)	1.3 (0.6)	1.1 (0.4)
CT scans	1.8 (1.6)	1.5 (0.9)	1.6 (1.0)
MRI	1.0 (0)	1.2 (0.4)	0
PET scans	1.4 (0.6)	1.3 (0.5)	1.0 (-)
Ultrasound	1.8 (0.8)	1.3 (0.6)	1.1 (0.4)
Counseling sessions	1.4 (0.6)	1.4 (0.9)	1.0 (-)
Ambulance transports	1.7 (1.2)	1.4 (0.7)	3.3 (2.3)
Other paid transport services	7.9 (6.9)	4.8 (7.5)	2.0 (-)
Radiotherapy courses	23.8 (21.9)	1.8 (2.5)	7.3 (11.0)
Radiotherapy fractions	46.8 (12.7)	33.8 (11.4)	20.0 (0.0)
Adjuvant treatment period: related to treatment, mean number of episodes (SD)	**N = 155**	**N = 149**	**N = 98**
Oncologist visits	1.3 (0.8)	3.0 (2.3)	1.4 (0.9)
Pulmonologist/respiratory physician	1.5 (1.0)	1.2 (0.5)	1.0 (-)
Other specialist visits	1.2 (0.4)	1.0 (0.0)	0
Hospitalizations	1.3 (0.8)	1.9 (1.3)	1.3 (0.5)
Duration of hospitalization (number of days)	3.9 (3.5)	12.1 (9.2)	5.3 (3.5)
ED visits	1.1 (0.4)	1.3 (0.7)	1.0 (0.0)
Ambulance transports	3.0 (-)	1.3 (0.5)	0
Disease-free period post-adjuvant treatment, mean number of episodes (SD)	**N = 155**	**N = 149**	**N = 98**
Oncologist visits	4.8 (3.4)	6.7 (4.5)	4.1 (3.9)
Surgeon visits	1.9 (1.5)	2.5 (3.3)	3.1 (2.0)
Pulmonologist/respiratory physician	5.5 (3.8)	3.3 (2.5)	3.3 (2.3)
Other specialist visits	3.3 (3.7)	3.4 (2.9)	2.8 (2.6)
Hospitalizations	1.5 (0.9)	2.2 (1.7)	1.5 (0.8)
Duration of hospitalization (number of days)	10.3 (10.9)	13.1 (14.4)	13.9 (23.4)
ED visits	1.1 (0.4)	1.2 (0.8)	1.4 (0.7)
CT scans	3.8 (2.3)	3.9 (2.3)	2.0 (1.1)
MRI	1.2 (0.4)	1.7 (1.4)	1.0 (0.0)
PET scans	1.2 (0.5)	1.2 (0.4)	1.0 (0.0)
Ultrasound	1.2 (0.4)	3.0 (2.7)	1.8 (1.2)
Nuclear medicine studies	1.2 (0.4)	1.6 (1.0)	1.3 (0.5)
Ambulance transports	3.3 (3.2)	1.0 (0.0)	1.3 (0.5)
Radiotherapy courses	22.8 (9.5)	1.6 (1.6)	1.0 (0.0)
Radiotherapy fractions	54.3 (12.6)	30.5 (7.6)	55.0 (0.0)
Disease-free period no adjuvant treatment, mean number of episodes (SD)	**N = 96**	**N = 138**	**N = 195**
Oncologist visits	5.2 (2.8)	6.2 (5.4)	2.9 (2.8)
Surgeon visits	1.6 (1.2)	2.9 (2.8)	4.1 (2.9)
Pulmonologist/respiratory physician	4.8 (3.9)	3.4 (2.9)	4.0 (3.3)
Other specialist visits	4.1 (4.5)	2.8 (2.2)	4.3 (5.0)
Hospitalizations	1.9 (1.7)	1.9 (1.4)	1.8 (1.3)
Duration of hospitalization (number of days)	24.5 (26.8)	21.5 (30.4)	11.2 (11.9)
ED visits	1.5 (0.6)	1.6 (0.8)	1.7 (1.0)
CT scans	3.7 (2.2)	3.6 (2.1)	1.8 (1.1)
MRI	1.1 (0.3)	1.7 (1.4)	1.1 (0.3)
PET scans	1.0 (0.0)	1.0 (-)	1.2 (0.6)
PET-CT scans	1.2 (0.6)	1.0 (0.0)	1.3 (0.6)
Ultrasound	1.5 (1.1)	3.6 (3.0)	1.5 (0.8)
Nuclear medicine studies	1.0 (0.0)	1.5 (1.0)	1.0 (0.0)
Radiotherapy courses	24.5 (6.8)	1.0 (0.0)	3.9 (7.1)
Radiotherapy fractions	49.4 (12.5)	28.4 (14.8)	25.9 (18.4)

NSCLC: non-small cell lung cancer, N: number of patients, SD: standard deviation, ED: emergency department, PET: positron emission tomography, CT: computer tomography, MRI: magnetic resonance imaging, UK: United Kingdom, G: Germany only, F: France only, UK: UK only.

Table A2
Resource use associated with resected Stage IB-IIIA NSCLC during the periods of locoregional recurrence and distant metastases or terminal disease, by country, for the major direct resource categories (from medical record abstraction).

	France	Germany	UK
Locoregional recurrence, mean number of episodes (SD)	**N = 38**	**N = 26**	**N = 22**
Received systemic treatment (number, %)	25 (65.8)	11 (42.3)	15 (68.2)
Oncologist visits	4.0 (3.2)	6.9 (7.2)	6.9 (5.1)
Surgeon visits	2.0 (1.6)	1.3 (0.6)	2.0 (1.7)
Pulmonologist/respiratory physician	8.1 (8.0)	4.6 (3.8)	2.6 (2.2)
Other specialist visits	3.1 (2.1)	1.9 (1.4)	2.5 (1.3)
Hospitalizations	2.1 (1.0)	2.3 (2.5)	1.3 (0.5)
Duration of hospitalization (number of days)	19.3 (14.5)	14.7 (11.9)	14.0 (20.7)
ED visits	1.7 (0.7)	2.0 (1.2)	1.3 (0.6)
CT scans	3.6 (2.9)	2.8 (1.6)	2.2 (1.1)
MRI	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)
PET scans	1.3. (0.5)	1.0 (0.0)	1.0 (0.0)
PET-CT scans	2.0 (1.1)	1.0 (0.0)	1.0 (-)
Ultrasound	1.0 (0.0)	1.8 (0.8)	1.0 (-)
Nuclear medicine studies	1.2 (0.5)	1.0 (0.0)	1.0 (-)
Radiotherapy courses	25.1 (13.6)	3.5 (8.1)	1.2 (0.4)
Radiotherapy fractions	57.4 (12.6)	29.0 (15.0)	14.5 (6.7)
Distant metastatic and terminal disease, mean number of episodes (SD)	**N = 76**	**N = 66**	**N = 58**
Received systemic treatment (number, %)	51 (67.1)	28 (42.4)	18 (31.0)
Oncologist visits	5.6 (4.6)	11.3 (15.9)	5.3 (5.1)
Surgeon visits	2.0 (1.4)	1.1 (0.5)	1.3 (0.6)
Pulmonologist/respiratory physician	6.5 (7.7)	3.6 (2.7)	1.0 (0.0)
Other specialist visits	3.8 (4.3)	4.6 (7.6)	1.3 (0.7)
Hospitalizations	2.0 (1.4)	2.7 (2.5)	1.8 (1.2)
Duration of hospitalization (number of days)	23.5 (22.6)	21.5 (19.7)	15.2 (14.4)
ED visits	1.5 (1.0)	1.9 (1.2)	1.4 (0.7)
CT scans	3.5 (2.7)	3.9 (3.0)	2.3 (2.0)
MRI	2.4 (3.1)	2.7 (2.0)	1.2 (0.4)
PET scans	1.1 (0.4)	1.0 (0.0)	2.0 (-)
PET-CT scans	1.7 (1.2)	1.0 (0.0)	1.0 (0.0)
Ultrasound	1.6 (1.1)	2.5 (1.7)	1.3 (0.5)
Nuclear medicine studies	1.7 (1.5)	1.4 (1.0)	1.0 (0.0)
Radiotherapy courses	10.2 (4.4)	2.0 (2.1)	1.5 (0.9)
Radiotherapy fractions	34.6 (11.9)	30.3 (27.2)	9.8 (7.8)

NSCLC: non-small cell lung cancer, N: number of patients, SD: standard deviation, ED: emergency department, PET: positron emission tomography, CT: computer tomography, MRI: magnetic resonance imaging, UK: United Kingdom.

Table A3
Resource use associated with resected Stage IB-IIIA NSCLC in all patients from the patient survey.

Variable, mean number of episodes (SD) (past 3 months)	Overall N = 306
General practitioner visits at home	2.1 (1.2)
General practitioner visits in the clinic	2.4 (2.2)
Hospital doctor/specialist visits outside of the main treatment center	1.7 (1.5)
Nurse visits at home	33.6 (31.3)
Nurse visits in clinic or hospital	2.6 (2.4)
Emergency department visits	1.4 (0.7)
Counseling or psychological support visits	3.1 (3.1)
Number of hospital inpatient stays	1.5 (0.9)
Duration of hospital stays (days)	13.9 (14.5)
Number of hospice/nursing home stays	1.1 (0.2)
Duration of hospice/nursing home stays	28.9 (19.0)
Days of missed work	32.0 (33.9)
Days of work missed by family member or unpaid caregiver	14.7 (26.6)
Weeks of disability benefits	17.4 (22.0)
Days of childcare	5.0 (-)

N: number of patients, SD: standard deviation, NSCLC: non-small cell lung cancer.

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