IQWiG Reports – Commission No. V18-03

Relationship between volume of services and quality of treatment outcome for surgical treatment of lung carcinoma[1]

Extract

[1] Translation of Chapters 1 to 7 of the rapid report V18-03 *Zusammenhang zwischen Leistungsmenge und Qualität des Behandlungsergebnisses bei der chirurgischen Behandlung des Lungenkarzinoms* (Version 1.0; Status: 8 October 2019 [German original], 20 December 2019 [English translation]). Please note: This document was translated by an external translator and is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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This rapid report was prepared in collaboration with an external expert and underwent an external review.

The responsibility for the contents of the report lies solely with IQWiG.

According to §139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received". The Institute received the completed *Form for disclosure of potential conflicts of interest* from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Appendix C of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

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Key statement

Research question

The aim of this investigation is to

present and assess the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of lung carcinoma (research question 1a),

present and assess the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of other malignant tumours in the lung (research question 1b), and

present studies that investigate the effects of a minimum number of cases specifically introduced into the healthcare system on the quality of treatment outcome for the surgical treatment of lung carcinoma and other malignant tumours in the lung (research question 2).

Whenever this process reveals any data on a correlation between volume of services and quality of treatment outcome for palliative surgery cases, such data will be presented as supplementary information.

Conclusion

In total, 23 observational studies could be included to investigate the correlation between the volume of services provided and the quality of treatment outcome in the surgical treatment of lung carcinoma; 19 of these studies contained usable data. The informative value of results was low in all studies.

For overall survival, treatment-related mortality, and in-hospital death, a positive correlation between the volume of services provided and the quality of treatment outcome could mostly be shown. Thus, a higher mortality rate is to be assumed with a lower volume of services. Across studies, the available data only showed an inconsistent correlation between the volume of services and the quality of treatment outcome for 30- and 90-day mortality, since different conclusions on this outcome were drawn in the studies.

For outcomes additionally identified (length of hospital stay and re-admission), for which only few usable results were available, it was not possible to derive a correlation between the volume of services per hospital and the quality of treatment outcome.

No (usable) data were reported for the outcome category “morbidity” (comprising disease-free survival, serious, life-threatening or fatal infections, and other serious treatment-related complications) and health-related quality of life, so that no conclusion can be drawn here on the correlation between the volume of services and the quality of treatment outcome.

No relevant studies could be identified to investigate the correlation between the volume of services and the quality of treatment outcome with regard to surgical treatment of other

malignant tumours in the lung. No meaningful studies could be identified for the investigation of the effects of minimum case numbers specifically introduced into health care on the quality of treatment outcome with regard to the surgical treatment of lung carcinoma or other malignant tumours in the lung.

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List of abbreviations

Abbreviation	Meaning
CIHI	Canadian Institute for Health Information
DRG	Diagnosis-related group
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HTA	Health Technology Assessment
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
NSCLC	Non-small cell lung cancer
RCT	Randomized controlled trial
PRDB	Ontario Registered Persons Database
SCLC	Small cell lung cancer
SEER	Surveillance, Epidemiology, and End Results Program
SGB	Sozialgesetzbuch (Social Code Book)
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TREND	Transparent Reporting of Evaluations with Nonrandomized Designs

1 Background

Relationship between volume of services and quality of treatment outcome

As early as in 1979, Luft et al. examined the relationship between volume of services and quality of treatment outcome for 12 surgical procedures of different levels of complexity [1]. Their investigations showed that, for complex surgical procedures, there is a correlation between a hospital's volume of services and the quality of treatment outcome. In the following years, various studies showed a similar correlation for many medical services in different healthcare systems, with the volume of services being investigated per hospital and per physician [2–5].

The legal mandate of the Federal Joint Committee (G-BA) regarding minimum volume rules [6] is based upon the idea that there is a specific connection between the probability of treatment success and the experience of the parties principally involved in rendering the service [6]. As part of quality assurance of registered hospitals, the G-BA therefore defines a catalogue of plannable services for which the quality of treatment outcomes is dependent on the volume of services provided. This dependency is to be assessed on the basis of appropriate studies [7]. In December 2003, the G-BA for the first time set forth minimum volumes which are binding in Germany in accordance with §137a (3), Sentence 1, No. 2 Social Code Book V (SBG V).

These minimum volume rules are binding for hospitals approved in accordance with §108 SBG V and specify the cases in which a hospital may render services governed by said rules [8]. However, some exceptions apply. For instance, minimum volumes generally do not apply in cases of emergency, and state authorities responsible for hospital planning can define exceptions for services where the implementation of minimum volume rules might jeopardize the nationwide provision of care to the population.

No binding minimum volumes are currently in place for surgical procedures performed to treat lung cancer [7].

Lung carcinoma

Most lung cancers are epithelial tumours that develop from squamous or glandular epithelium (adenocarcinoma) [9].

Lung carcinoma is also referred to as bronchial carcinoma since this malignant tumour arises from the bronchial epithelium [10, 11]. It is classified into the following main histological types [12]:

- Small cell lung cancer (SCLC; approx. 15%)
- Non-small cell lung cancer (NSCLC; approx. 85%):
  - squamous cell carcinoma: spindle cell variant (40%)

  - adenocarcinoma (50%): acinar, papillary, bronchioloalveolar, solid with mucus formation
  - large-cell carcinoma (10%): giant-cell carcinoma, clear cell carcinoma
- Other types of carcinoma: adenosquamous carcinoma, bronchial gland carcinoma, carcinoid (≤ 1%)

The above-mentioned main histological types can be broken down further into numerous subtypes [13].

Other malignant tumours in the lung

Malignant lymphomas and sarcomas are cancerous tumours that can arise as primary thoracic tumours or as lung metastases [14]. Metastases to the lung often also develop in connection with carcinomas of the colon, rectum, kidney, breast, prostate, and oropharynx [15].

Diffuse malignant pleural mesothelioma originates in the mesothelial or submesothelial cells of the pleura, peritoneum, or pericardium. More than 80% of mesotheliomas originate in the pleura. Mesothelioma is rarer than lung carcinoma and develops mostly in men (80% of cases).

Risk factors and epidemiological data

In 2014, 53 840 patients in Germany were diagnosed with lung cancer, and, at 64% of cases, more men than women were affected. In the same year, 45 084 patients diagnosed with lung cancer died. The estimates for 2018 are similar, with the percentage of women increasing slightly [17]. Throughout Europe, approx. 353 000 patients died of lung cancer in 2012 [18]. The 5-year survival rate is below 20% [19, 20], in part because lung cancer produces symptoms only at a late point and is therefore often already in an advanced stage at the time of diagnosis. About 50% of all patients with lung cancer have distant metastases at diagnosis [21]. Hence, according to cancer statistics, lung cancer is the most common cause of death in men and the second most common in women [22]. Smoking is still the main cause of lung cancer. The risk is 24 times higher in active smokers than in non-smokers and remains 7.5 times higher in former smokers when compared to non-smokers [23]. In total, 85% of deaths from lung cancer are due to smoking [24].

Surgical treatment of lung carcinoma

The choice of therapy largely depends on the histological findings of the tumour [10]. Of particular relevance is the differentiation between small cell and non-small cell lung cancer [10, 21]. In the treatment of lung carcinoma, surgery is a local treatment modality that can be preceded by neoadjuvant chemotherapy, radiation therapy, or a combination of both (chemoradiotherapy) or followed by them as adjuvant therapy [21]. In general, treatment options depend on the results of the molecular pathological diagnostics and the patient's general condition, cardiovascular and pulmonary factors, age-related comorbidities, etc. [25, 26].

For non-small cell lung cancer (NSCLC) in stages I through IIA, surgery alone is recommended, and in stages IIB through IIIB, surgery plus neoadjuvant or adjuvant chemotherapy or trimodal therapy (surgery and chemotherapy plus adjuvant radiation therapy of the mediastinum) is recommended [27].

Only about 5% of patients with small cell lung cancer (SCLC) are in an early tumour stage of T1-2 N0-1 at diagnosis [28]. In this context, "T" refers to the size and extent of the primary tumour and "N" to the condition of the lymph nodes near the tumour in accordance with the TNM classification system (T = tumour, N = node, M = metastasis). In this stage, surgical procedures are a treatment option (with preoperative exclusion of mediastinal lymph node involvement); however, for this small group of patients, the S3 guideline provides only a moderately strong recommendation for surgery since a lack of prospective randomized studies precludes the reliable assessment of the value of surgery [27, 29].

The standard surgical treatment of lung carcinoma is anatomic resection in the form of lobectomy (removal of a pulmonary lobe) or pneumonectomy (removal of one lung) with systematic lymphadenectomy. In central tumours, lobectomies can also be performed in the form of sleeve resection at the bronchus and/or pulmonary artery to avoid pneumonectomy in many cases. Smaller tumours can also be anatomically resected at the segment level, but due to a lack of study data, it is currently unclear whether segmental resection is equivalent to lobectomy from an oncological perspective [27]. Lobectomies and segmentectomies can be performed as either open or minimally invasive procedures, the latter being associated with less pain and a better quality of life postoperatively [30]. The surgical treatment of lung carcinoma by means of non-anatomic resection is considered obsolete [31].

Surgical treatment of other malignant tumours in the lung

No curative treatment of pleural mesothelioma is currently available. Multimodal treatment strategies are used, which represent a supposedly curative treatment approach. This may also culminate in the decision to perform surgery. In these situations, the goal remains complete macroscopic tumour removal, although complete tumour removal is usually impossible in mesothelioma [16].

For the surgical treatment of mesothelioma, 2 methods are available: pleurectomy/decortication and extrapleural pleuropneumonectomy. Pleurectomy/decortication [16] is a lung-sparing procedure involving the resection of the visceral and parietal pleura. Extrapleural pleuropneumectomy, in contrast, involves the radical resection of all contents of one side of the thorax, including the pleura, lung, diaphragm, and pericardium [16, 32].

Even in case of metastases within the lung, surgical procedures can be used with curative intent, provided that the metastases are limited to the lung. Likewise, in case of recurrent metastatic development isolated in the lung, repeat surgery can be performed [15].

Palliative surgery

If metastases have spread throughout the lung or the lung is inoperable for technical or functional reasons, any surgery at best serves palliative purposes [15]. In these cases, surgery is intended to relieve tumour-related symptoms. For example, it is possible to surgically treat pathological fractures caused by bone metastases and unstable vertebral fractures or to relieve spinal compression [26].

2 Research question

The aim of this investigation is to

- present and assess the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of lung carcinoma (research question 1a),
- present and assess the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of other malignant tumours in the lung (research question 1b), and
- present studies that investigate the effects of a minimum number of cases specifically introduced into the healthcare system on the quality of treatment outcome for the surgical treatment of lung carcinoma and other malignant tumours in the lung (research question 2).

Whenever this process reveals any data on a correlation between volume of services and quality of treatment outcome for palliative surgery cases, such data will be presented as supplementary information.

3 Course of the project

On 16 August 2018, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) with a systematic literature search and evaluation of the evidence on the correlation between volume of services and quality of treatment outcome in the surgical treatment of lung carcinoma.

On the basis of the project outline, a rapid report was generated and additionally subjected to an external review. This report was sent to the G-BA and published 4 weeks later on the IQWiG website.

4 Methods

Due to differences between the research questions, different methods were used in some cases.

4.1 Criteria for study inclusion in the investigation

4.1.1 Population

The assessment included studies with the following patients, broken down by research question:

- Research question 1a: patients with lung carcinoma who were surgically treated
- Research question 1b: patients with other malignant tumours in the lung who were surgically treated
- Research question 2: patients with lung carcinoma or other malignant tumours in the lung who were surgically treated

4.1.2 Volume of services

The volume of services was defined as the number of surgical procedures performed to treat lung carcinoma and/or other malignant tumours of the lung per hospital, per physician, or per hospital-physician combination within a defined time period.

4.1.3 Outcomes

For the investigation, the following outcomes were examined:

- Mortality, such as
  - overall survival
  - treatment-related mortality
  - 30-day and 90-day mortality
  - in-hospital death
- Morbidity, such as
  - disease-free survival,
  - adverse effects of therapy such as
    - serious, life-threatening, or fatal infections
    - further serious treatment-related complications, if any
- Health-related quality of life, including activities of daily living and dependence on help from others

If usable data were found on other outcomes, they were permitted to be included as well.

4.1.4 Study types

Observational studies (e.g. cohort studies or case control studies) or adequately controlled interventional studies were suitable for answering research questions 1a, 1b, and 2.

For adequately controlled interventional studies, the intervention to be examined was the specification of a minimum number of cases. Possible comparator groups were groups with a different or no specified volume.

4.1.5 Adjustment

In the surgical treatment of lung carcinoma or other malignant tumours in the lung, the quality of treatment outcome is materially influenced by individual risk factors such as tumour stage at initial diagnosis, patient age, lung function, cardiovascular risk, and prior patient treatment. Further indication-specific risk factors are also possible.

Therefore, control of relevant confounders (risk adjustment) was a prerequisite for study inclusion. Control was assumed to exist if the study analysis involved suitable statistical methods to adjust for relevant confounders in an effort to address the problem of potential structural inequalities (unfair comparisons) between hospitals or treatment providers (physicians, nurses, etc.) with high and low volumes of services.

Likewise, cluster effects (e.g. greater similarity of outcomes in patients within the same hospital versus patients from different hospitals due to hospital-specific characteristics) had to have been taken into consideration by means of adequate statistical methods.

4.1.6 Study duration

There were no restrictions regarding the study duration.

4.1.7 Publication period

In accordance with the commission, studies with a publication date of January 2000 or later were included in the study.

4.1.8 Transferability

To ensure the transferability of study results to the German healthcare system, studies from European countries as well as the USA, Canada, Australia, and New Zealand were eligible for inclusion.

For international studies, at least 80% of the data had to come from the above countries.

4.1.9 Tabular presentation of the criteria for study inclusion

The tables below list the criteria that had to be met by studies included in the assessment.

Table 1: Overview of inclusion and exclusion criteria of studies for research questions 1a and 1b

Inclusion criteria	
I1.1	Patients with ▪ lung carcinoma (research question 1a) or ▪ other malignant tumours in the lung (research question 1b) who were surgically treated (also see Section 4.1.1)
I1.2	Investigation of the correlation between the volume of services and the quality of treatment outcome (also see Section 4.1.2)
I1.3	Outcomes as formulated in Section 4.1.3
I1.4	Observational study as formulated in Section 4.1.4
I1.5	Adjustment as formulated in Section 4.1.5
I1.6	Publication date of January 2000 or later
I1.7	Full publication available[a]
I1.8	Studies which are transferable to the German healthcare system (also see Section 4.1.8)
Exclusion criterion	
E1.1	Multiple publications without relevant additional information

a: In this context, a study report in accordance with ICH E3 [33] or a report about the study which met the criteria of the STROBE statement [34] and allowed an assessment of the study was considered a full publication, so long as the information on both the study methods and study results provided in these documents was not confidential.

ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

Table 2: Overview of inclusion and exclusion criteria of studies for research question 2

Inclusion criteria	
I2.1	Patients with lung carcinoma or other malignant tumours in the lung who were surgically treated (research question 2) (also see Section 4.1.1)
I2.2	Study intervention: use of a minimum number of cases (also see Section 4.1.4)
I2.3	Comparator intervention: use of a different or no minimum number of cases (also see Section 4.1.4)
I2.4	Outcomes as formulated in Section 4.1.3
I2.5	Controlled intervention study as formulated in Sections 4.1.4 and 4.1.5
I2.6	Publication date of January 2000 or later
I2.7	Full publication available[a]
I2.8	Studies which are transferable to the German healthcare system (also see Section 4.1.8)
Exclusion criterion	
E2.1	Multiple publications without relevant additional information

a: In this context, full publication also refers to any study report in accordance with ICH E3 [33] or a study-related report which has met the criteria of the TREND statement [35] and allowed an assessment of the study, so long as the information on both the study methods and study results provided in these documents was not confidential.

ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; TREND: Transparent Reporting of Evaluations with Nonrandomized Designs

4.1.10 Inclusion of studies which do not fully meet the above criteria

In accordance with IQWiG General Methods Version 5.0, Chapter 9 [36], for the inclusion criteria I1.1/I2.1 (population), I1.2 (volume of services), I2.2 (experimental intervention, with respect to the study's intervention group), I2.3 (comparator intervention, with respect to the study' comparator group), and I1.8/I2.8 (transferability), it sufficed if at least 80% of included patients fulfilled these criteria. For such studies, subgroup analyses, if any, on patients who fulfilled the inclusion criteria were used. Studies in which the inclusion criteria I1.1/I2.1 and I1.2/I2.2, and I2.3 as well as I1.8/I2.8 were fulfilled by fewer than 80% of patients were included only if subgroup analyses were available for patients who did fulfil the inclusion criteria.

4.2 Comprehensive information retrieval

4.2.1 Sources of information

For the comprehensive information retrieval, a systematic search was conducted for relevant studies or documents in accordance with IQWiG General Methods Version 5.0, Chapter 8 [36]. The following primary and further information sources as well as search techniques were selected:

Primary information sources

- Bibliographic databases
  - MEDLINE
  - Embase
  - Cochrane Central Register of Controlled Trials
  - Cochrane Database of Systematic Reviews
  - Health Technology Assessment (HTA) Database

Further information sources and search techniques

- Use of further search techniques
  - screening of reference lists of systematic reviews found
- Requests to authors

4.2.2 Selection of relevant studies

Selection of relevant studies or documents from the results of the bibliographic search

In a first step, the titles and, if available, abstracts of the hits retrieved in the bibliographic databases were screened for potential relevance in terms of the inclusion criteria (see Table 1 and Table 2). In a second step, any documents considered potentially relevant were checked for relevance based on their full texts. Both steps were performed by 2 persons independently of each other. Any discrepancies were resolved by discussion between them.

Selection of relevant studies or documents from further information sources

Search results from additionally considered information sources were screened for studies by 1 reviewer. The studies found were then checked for relevance. The whole process was then checked by a second reviewer. Any discrepancies in one of the listed selection steps were resolved by discussion between the 2 reviewers.

4.3 Information synthesis and analysis

4.3.1 Presentation of the individual studies

All information needed for the investigation was extracted from the documents regarding the included studies and entered into standardized tables. Any discrepancies found in connection with the comparison of information from different documents or from multiple data points within the same document, provided such discrepancies had the potential of considerably influencing the interpretation of results, are presented in the results section of the report.

Results were typically omitted from the investigation whenever they were based on fewer than 70% of the patients to be included in the analysis, that is, whenever more than 30% of patients were excluded from analysis.

Results were also omitted from the investigation whenever the percentage of patients excluded from analysis differed by more than 15% between groups.

Whenever the studies' authors used several statistical models and justified their choice of a preferred model for their underlying data, the statistical model preferred by the authors was used, provided the model fulfilled the conditions defined in Section 4.1.5. Whenever several models were appropriate for the underlying data, the simpler model was used, taking into account Section 4.1.5.

4.3.2 Assessment of the informative value of results

The informative value of the results from the included observational studies was assessed on the basis of quality criteria developed especially for studies assessing volume-outcome correlations [37–40]. In terms of the informative value of results, the assessment considered the way the risk adjustment was performed, i.e. the risk factors taken into account and the sources used (administrative databases, clinical databases, medical records). Likewise, the quality of the statistical models used to examine the correlation between volume of services and outcome was assessed; said quality depends on the form in which the volume attribute was entered into the analysis (continuous versus categorical data), on the consideration of cluster effects (see Section 4.1.5), and on the examination of model quality [41]. The completeness of reporting (e.g. description of analysed data and reporting of point estimates, confidence intervals, and p-values) was likewise considered an aspect affecting the informative value of results. On the basis of the entirety of these quality criteria, the observational studies were categorized by quality into those with high versus low informative value.

4.3.3 Assessment of the risk of bias

The risk of bias of the results of the included controlled interventional studies was assessed in accordance with IQWIG General Methods Version 5.0, Chapter 9 [36].

4.3.4 Subgroup attributes

If the studies provided separate analyses of patients with different histological tumour findings, a separate assessment by histological findings was performed as well, where appropriate (e.g. differentiation between SCLC and NSCLC).

4.3.5 Summary assessment of information

The results on the outcomes reported in the studies were comparatively described in the report.

Results from continuous modelling were preferred over results from categorical modelling and included in the report. This is because categorical analysis is associated with a loss of information (e.g. the linearity assumption is violated within the individual categories) and might deliver less reliable results than continuous analysis [40]. However, if the studies presented results exclusively for categorical analysis or only the results from categorical analysis were usable, the summary assessment relied on categorical analyses.

Where possible, beyond the comparison of results from the individual studies, suitable meta-analytical methods were to be used, and subgroup analyses were to be performed whenever appropriate [36]. A final summary assessment of the information was performed in any case.

5 Results

5.1 Comprehensive information retrieval

5.1.1 Primary information sources

Figure 1 shows the results of the systematic literature search in the bibliographic databases and the study selection in accordance with the criteria for study inclusion. The search strategies for the search in bibliographic databases is found in Appendix A. The most recent search was conducted on 8 February 2019.

The references of the hits screened at full-text level but excluded are found in Section 9.3 of the full report, with the respective reason for exclusion.

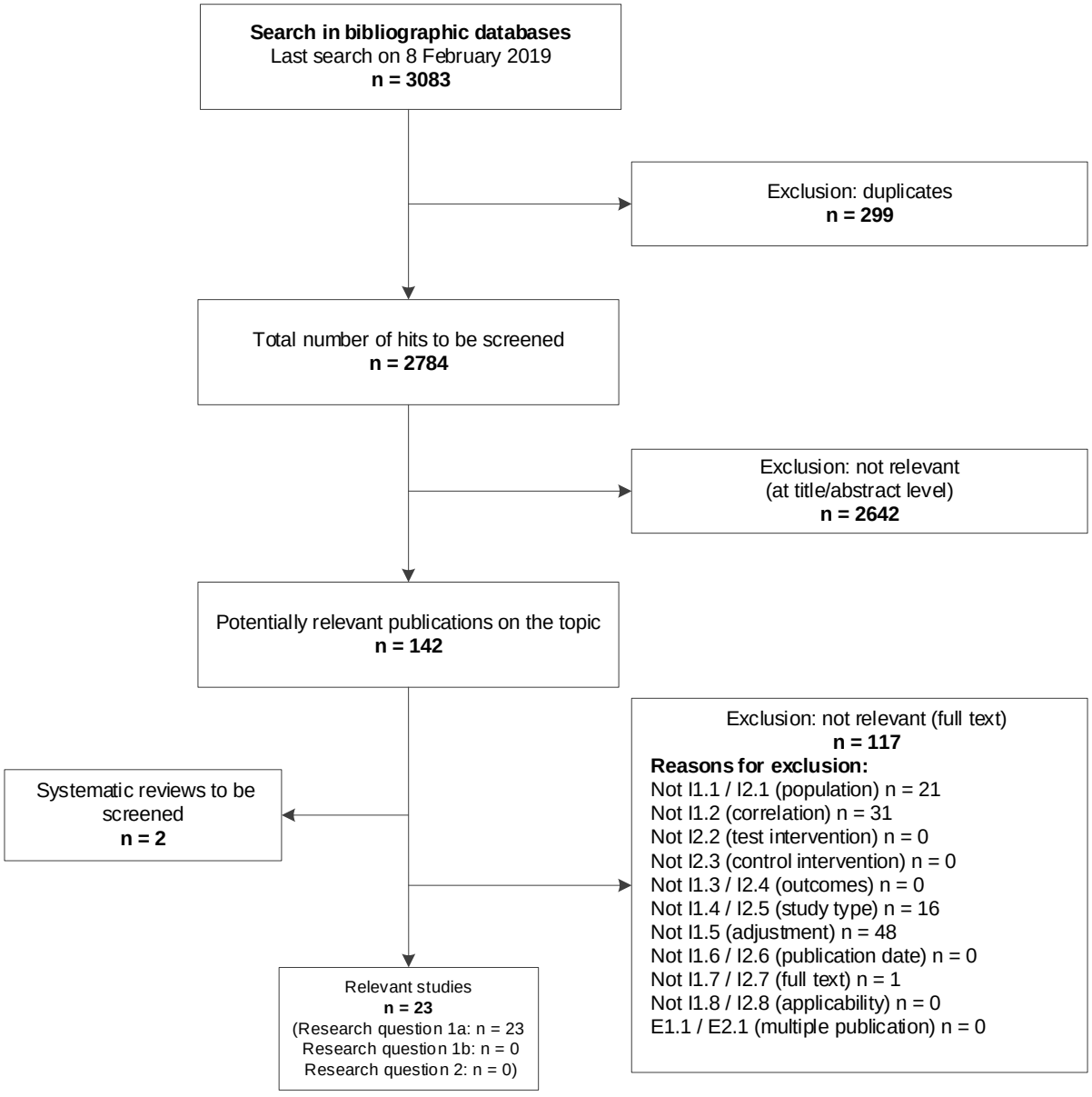

Figure 1: Result of the bibliographic search and study selection

5.1.2 Further information sources and search techniques

Relevant studies or documents found through further information sources and search techniques are presented below unless they were already found through primary information sources.

5.1.2.1 Use of further search techniques

As part of the information retrieval, 2 systematic reviews were found – the corresponding references are provided in Section 9.2 of the full report. The lists of references of these systematic reviews were screened.

No relevant studies or documents not already identified in other search steps were found.

5.1.2.2 Requests to authors

No requests to authors to obtain additional information on relevant studies were necessary since such information was not expected to have a relevant impact on the assessment.

5.2 Resulting study pool

Through the various search steps, a total of 23 relevant studies (23 documents) were found for research question 1a (see also Table 3). The corresponding references are found in Section 9.1 of the full report. No reliable studies were found to answer research question 1b or research question 2.

Table 3: Study pool for research question 1a

Study	Full publication (in professional journals)
Avritscher 2014	Yes [42]
Bilimoria 2008	Yes [43]
Birkmeyer 2002	Yes [44]
Birkmeyer 2003	Yes [45]
Birkmeyer 2006	Yes [46]
Birkmeyer 2007	Yes [47]
Finlayson 2003	Yes [48]
Harrison 2018	Yes [49]
Hollenbeck 2007a	Yes [50]
Hollenbeck 2007b	Yes [51]
Kim 2016	Yes [52]
Kozower 2011	Yes [53]
Learn 2010	Yes [54]
Lüchtenborg 2013	Yes [55]
Møller 2016	Yes [56]
Nimptsch 2017	Yes [57]
Pezzi 2014	Yes [58]
Sahni 2016	Yes [59]
Simunovic 2006	Yes [60]
Smith 2017	Yes [61]
Stukenborg 2004	Yes [62]
Urbach 2004	Yes [63]
Wakeam 2015	Yes [64]

5.3 Characteristics of the studies included in the assessment

The characteristics of the studies included for research question 1a are presented in Table 4 and summarized below.

Table 4: Characteristics of the studies included for research question 1a

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Avritscher 2014/ retrospective observational study (data from the Texas Hospital Inpatient Discharge Public Use Data File)	USA/1 January 2002 – 30 November 2006/ investigation of the correlation between hospital VoS and serious postoperative infections	▪ Residents of Texas, USA ▪ Age: ≥ 18 years ▪ Resection of a lung, oesophageal, gastric, pancreatic, colon, or rectal carcinoma in a Texan hospital ▪ No emergency surgery ▪ No serious infection at admission ▪ No HIV infection ▪ No alcohol or drug abuse	Lung carcinoma (not further specified)	Lung resection (not further specified)	9891[c]	For all indications, the classification into hospitals with low, moderate, or high VoS was done specifically on the basis of the actual number of cases in the observation period.
Bilimoria 2008/ retrospective observational study (NCDB data)	USA/1994–1999/ investigation of the correlation between hospital VoS and perioperative mortality or 5-year survival rate	▪ Age ≥ 18 years at diagnosis ▪ Resection of a primary colon, oesophageal, gastric, liver, lung, pancreatic, or rectal carcinoma ▪ No tumours of atypical histology (e.g. lymphomas, sarcomas, or metastases to the liver) ▪ No stage IV cancer	Nonmetastatic primary lung carcinoma	▪ Lobectomy ▪ Pneumonectomy	40 754[c]	Threshold of > 83 annual interventions for hospitals with high VoS and < 21 annually for low VoS.

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Birkmeyer 2002/ retrospective observational study (data from the Centers for Medicare and Medicaid Services [incl. MEDPAR])	USA/1994–1999/ investigation of the correlation between hospital VoS and operative mortality	▪ Age: 65–99 years ▪ Resection of a primary lung, colon, gastric, oesophageal, pancreatic, kidney, bladder carcinoma ▪ Performance of cardiovascular surgery	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	85 973[d]	Thresholds for the number of lung resections per hospital and year: ▪ Very low VOS: < 9 ▪ Low VOS: 9–17 ▪ Moderate VOS: 18–27 ▪ High VOS: 28–46 ▪ Very high VOS: > 46
Birkmeyer 2003/ retrospective observational study (data from the Centers for Medicare and Medicaid Services [incl. MEDPAR])	USA/1998–1999/ investigation of the correlation between physician or hospital VoS and operative mortality	▪ Age: 65–99 years ▪ Resection of a primary lung, pancreatic, oesophageal, or bladder carcinoma (or performance of cardiovascular surgery) with unambiguous reference to an ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Lung resection (not further specified)	24 092[c]	Thresholds for the number of lung resections per **physician** and year: ▪ Low VOS: < 7 ▪ Moderate VOS: 7-17 ▪ High VOS: > 17 Thresholds for the number of lung resections per **hospital** and year: ▪ Low VOS: < 17 ▪ Moderate VOS: 17–35.5 ▪ High VOS: > 35.5
Birkmeyer 2006/ retrospective observational study (national Medicare claims data and data from the SEER database)	USA/2000–2002/ investigation of the correlation between hospital VoS, process of care, and operative mortality	▪ Age: 65–99 years ▪ Resection of primary lung, oesophageal, gastric, liver, or pancreatic carcinoma with unambiguous reference to an ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Anatomic resections (segmentectomy, lobectomy, pneumonectomy)	49 280[d]	Hospitals with low versus high VoS were categorized into quintiles.

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Birkmeyer 2007/ retrospective observational study (U.S. national Medicare claims data and data from the SEER database)	USA/1992–1999 (follow-up until 2002)/ investigation of the correlation between hospital VoS and 5-year survival rate	▪ Age: 65–99 years ▪ Resection of primary lung, bladder, colon, oesophageal, pancreatic, or gastric carcinoma	Lung carcinoma (not further specified)	Anatomic resections (segmentectomy, lobectomy, pneumonectomy)	12 967[d]	Range of lung resections per hospital and year: ▪ Low VOS: 0.3–11.4 ▪ Moderate VOS: 11.4–24.9 ▪ High VOS: 25.2–313.2
Finlayson 2003/ retrospective observational study (NIS data)	USA/1995–1997/ investigation of the correlation between hospital VoS and operative mortality (before hospital discharge)	Execution of lobectomy, pneumonectomy, colectomy, gastrectomy, oesophagectomy, pancreatectomy, nephrectomy, or cystectomy for carcinoma removal	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	21 890[c]	Mean number of lung resections per hospital and year: ▪ Low VOS: < 19 ▪ Moderate VOS: 19–37 ▪ High VOS: > 37
Harrison 2018/ retrospective observational study (SID and HCUP data)	USA/2009–2011/ investigation of the correlation between hospital VoS and mortality before hospital discharge, hospital length of stay, and postoperative complications	▪ Age: ≥ 18 years ▪ Performance of lobectomy, pneumonectomy, or oesophagectomy, with confirmed diagnosis of lung or oesophageal carcinoma	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	20 138[c]	Thresholds for the number of lung resections (lobectomies + pneumonectomies) per hospital and year: ▪ Low VOS: < 40 ▪ High VOS: ≥ 40
Hollenbeck 2007a/ retrospective observational study (U.S. national Medicare claims data and data from the SEER database)	USA/1994–1999/ investigation of the correlation between hospital VoS and operative mortality depending on the origin of the data (SEER vs. Medicare database)	▪ Age: 65–99 years ▪ Resection of lung, oesophageal, bladder, or colon carcinoma with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	8183[c]	For all indications, the classification into hospitals with low, moderate, or high VoS was done specifically on the basis of the actual number of cases in the observation period.

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Hollenbeck 2007b/ retrospective observational study (HCUPNIS data)	USA/1993–2003/ investigation of the correlation between hospital VoS and operative mortality up to hospital discharge or hospital length of stay	▪ Resection of a lung, prostate, bladder, pancreatic, oesophageal, or liver carcinoma with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	90 088[c, e]	For all indications, the categorization of hospitals into low VoS (lowest deciles) and high VoS (highest deciles) was done specifically on the basis of the actual number of cases in the observation period.
Kim 2016/ retrospective observational study (discharge data of participating hospitals and AHA surveys)	USA/2000–2011/ investigation of the correlation between hospital VoS and mortality up to hospital discharge	▪ Age: ≥ 21 years ▪ No referral to another hospital ▪ Resection of a lung, colon, oesophageal, pancreatic, or rectal carcinoma	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	59 491[c]	No differentiation between hospitals with low vs. high VoS. Reported were the maximum volume in the years 2000 and 2011 and the mean and SD for the entire observation period. Further, quartiles were reported (pneumonectomy/lobectomy): ▪ 1st quantile: 2/7 ▪ 2nd quantile: 3/18 ▪ 3rd quantile: 5/34 ▪ 4th quantile: 8/47

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Kozower 2011/ retrospective observational study (HCUPNIS discharge data)	USA/2007/investigation of the correlation between hospital VoS and mortality	▪ Resection of lung carcinoma with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Lung resection (not further specified)	7911[f]	Hospitals categorized by VoS on the basis of the actual number of annual cases: ▪ 1st quintile: 1–2 ▪ 2nd quintile: 3–6 ▪ 3rd quintile: 7–12 ▪ 4th quintile: 13–23 ▪ 5th quintile: ≥ 24
Learn 2010/ retrospective observational study (HCUPNIS discharge data)	USA/1997-2006/ investigation of the correlation between hospital VoS and mortality before hospital discharge	▪ Age: ≥ 18 years ▪ Resection of lung, pancreatic, oesophageal, or gastric carcinoma with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Anatomic resections (segmentectomy, lobectomy, pneumonectomy)	62 716[c]	Thresholds for the number of lung resections per hospital and year: ▪ Low VOS: 1–16 ▪ Moderate VOS: 17–33 ▪ High VOS: > 33
Lüchtenborg 2013/ retrospective observational study (NCDR data supported by cause of death statistics from NHS and HES data)	UK/2004-2008/ investigation of the correlation between hospital VoS and survival 0 through 30 days.	▪ Resection of non-small cell lung cancer	Non-small cell lung cancer	▪ Lobectomy (68%) ▪ Wedge resection (19%) ▪ Pneumonectomy (12%) ▪ Sleeve resection (1%)	12 862[c]	Hospitals categorized by VoS on the basis of the actual number of annual cases: ▪ 1st quintile: < 70 ▪ 2nd quintile: 70–99 ▪ 3rd quintile: 100–129 ▪ 4th quintile: 130–149 ▪ 5th quintile: ≥ 150

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Møller 2016/ retrospective observational study (data from NCDR and discharge data as well as data from the U.K. National Cancer Registration and U.K. National Lung Cancer Audit datasets)	UK/2006–2010/ investigation of the correlation between hospital VoS and hospital length of stay, mortality, and rehospitalization after 30 or 90 days	Resection of non-small cell lung cancer	Non-small cell lung cancer	▪ Lobectomy (85%) ▪ Pneumonectomy (10%) ▪ Other pulmonary resection (5%)	15 738[d, c]	Hospitals categorized by VoS on the basis of the actual number of annual cases: ▪ 1st quintile: 1–75 ▪ 2nd quintile: 77–112 ▪ 3rd quintile: 114–155 ▪ 4th quintile: 156–186 ▪ 5th quintile: 189–287
Nimptsch 2017/ retrospective observational study (DRG data from the German Federal and State Statistical Offices)	Germany/2009–2014/ investigation of the correlation between hospital VoS and mortality before hospital discharge	▪ Age: ≥ 20 years ▪ Administration of one of the 25 most common inpatient treatments (including resection of lung carcinoma)	Lung carcinoma (not further specified)	Lung resection (not further specified)	73 983[c]	Hospitals categorized by VoS on the basis of the actual number of cases per year (median): ▪ Very low VOS: 5 ▪ Low VOS: 49 ▪ Moderate VOS: 89 ▪ High VOS: 137 ▪ Very high VOS: 272
Pezzi 2014/ retrospective observational study (NCDB data)	USA/2007–2011/ investigation of the correlation between hospital VoS and death within 30 days after surgery or death between postoperative days 31 and 90	▪ Age: ≥ 18 years ▪ Resection of lung carcinoma (except wedge resection)	Lung carcinoma (not further specified)	▪ (Bi-)Lobectomy (93.4%) ▪ Pneumonectomy (6.6%)	124 418[g]	Thresholds for the number of lung resections per hospital and year: ▪ Category 1: 0–9 ▪ Category 2: 10–19 ▪ Category 3: 20–29 ▪ Category 4: 30–39 ▪ Category 5: 40–89 ▪ Category 6: ≥ 90

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Sahni 2016/ retrospective observational study (U.S. national Medicare data [incl. MEDPAR])	USA/2008–2013/ investigation of the correlation between physician VoS and mortality 30 days after hospital admission	▪ Age: ≥ 66 years ▪ Physicians with appropriate expertise ▪ Resection of a lung, bladder, pancreatic, or oesophageal carcinoma (or performance of cardiovascular surgery) with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Lung resection (not further specified)	85 966[c]	Physician categorization by VoS was done on the basis of the actual number of annual surgeries: ▪ Lowest quarter: 1.6 ▪ 2nd quarter: 5.1 ▪ 3rd quarter: 10.4 ▪ Top quarter: 32.6
Simunovic 2006/ retrospective observational study (data from the Ontario Cancer Registry, CIHI, and RPDB)	Canada/1990–2000/ investigation of the correlation between hospital VoS and mortality before hospital discharge	▪ Patients with an initial diagnosis of cancer of the lung, breast, colon, oesophagus, or liver ▪ Resection of lung, breast, colon, oesophageal, or liver carcinoma	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	2698[c]	Hospitals categorized by VoS on the basis of the actual number of surgeries in 3 years: ▪ Low VoS: ≤ 32 ▪ Low to moderate VoS: 33–85 ▪ Moderate to high VoS: 86–130 ▪ High VOS: ≥ 131

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Smith 2017/ retrospective observational study (U.S. national Medicare claims data and data from the SEER database)	USA/2000–2010/ investigation of the correlation between physician VoS and mortality within 30 days after surgery and adverse events	▪ Age: ≥ 65 years ▪ Resection of non-small cell lung cancer in stage I ▪ Tumour size ≤ 5 cm	Non-small cell lung cancer stage I	▪ Lobectomy (67%) ▪ Segmentectomy (5%) ▪ Wedge resection (28%) via VATS	2295[c]	Physicians categorized by VoS (low, moderate, high) on the basis of the actual number of surgeries per year. The respective thresholds were not reported.
Stukenborg 2004/ retrospective observational study (discharge data of California hospitals)	USA/1996–1999/ investigation of the correlation between hospital VoS (average annual VoS and VoS in the 12 months before surgery) and mortality before hospital discharge	Resection of lung carcinoma with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	Lung resection (not further specified)	14 456[c]	Hospitals categorized by VoS on the basis of the actual annual number of surgeries within the prior 12 months / on the basis of the average annual VoS: ▪ Minimum: 0/0.3 ▪ 0.1 percentile: 6.0/5.8 ▪ 0.25 percentile: 12.0/13.0 ▪ 0.5 percentile: 21.0/21.0 ▪ 0.75 percentile: 32.0/32.3 ▪ 0.9 percentile: 48.0/47.8 ▪ Maximum: 125.0/100.8

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

Study / study design[a] (data source)	Recruitment country/follow-up period[b]/study objective	Inclusion and exclusion criteria	Tumour type	Surgical intervention	Total number of units	Definition of VoS
Urbach 2004/ retrospective observational study (data from the Ontario health database)	Canada/1994–1999/ investigation of the correlation between hospital VoS and mortality within 30 days after surgery	Performance of lobectomy or pneumonectomy for lung carcinoma, oesophagectomy, resection of colon or rectal carcinoma, pancreatectomy, or surgical treatment of an aneurysm of the abdominal aorta	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Pneumonectomy	5156[c]	Threshold for categorizing hospitals as high vs. low VoS (corresponds to the median number of lung resections performed per hospital and year): 45.0
Wakeam 2015/ retrospective observational study (NIS data)	USA/2007–2011/ investigation of the correlation between hospital VoS and mortality before hospital discharge	▪ Age: ≥ 18 years ▪ Performance of lobectomy, segmentectomy, or pneumonectomy with unambiguous ICD-9 code for the surgical indication	Lung carcinoma (not further specified)	▪ Lobectomy ▪ Segmentectomy ▪ Pneumonectomy	37 740[h]	Thresholds for the number of lung resections per hospital and year: ▪ Low VoS: < 21 ▪ Moderate VOS: 21–40 ▪ High VOS: 40–78 ▪ Very high VOS: > 78

(continued)

Table 4: Characteristics of the studies included for research question 1a (continued)

a: If a data source was specified in a study, e.g. a secondary data analysis/registry study, the data source is entered here.
b: In secondary data analyses/registry studies, for instance, the follow-up duration is to be understood as the data collection period.
c: Number of lung resections performed.
d: IQWiG's own calculation: number of patients with lung carcinoma.
e: In the results, data are reported only on pneumonectomy.
f: Three of these patients were not included in the analysis due to an unclear discharge status.
g: This number represents the amount of lung resections. From this total, 30-day mortality was investigated in 121 099 patients, 90-day mortality in 118 290 patients, and related 90-day mortality in 114 905 patients.
h: Among these, about 83.6% due to lung or bronchial carcinoma (IQWiG's own calculation).

AHA: American Hospital Association; CIHI: Canadian Institute for Health Information; DRG: diagnosis-related Group; HCUP(NIS): Healthcare Cost and Utilization Project (Nationwide Inpatient Sample, U.S.A.); HES: Hospital Episode Statistic (U.K.); HIV: human immunodeficiency virus; ICD: International Classification of Diseases; IQWIG: Institute for Quality and Efficiency in Health Care; MEDPAR: Medicare Provider Analysis and Review files; NCDB/NCDR: National Cancer Data Base/Repository (U.S.A.); NCI: National Cancer Institutes (U.S.A); NIS: National Inpatient Sample (U.S.A.); RPDB: Ontario Registered Persons Database; SD: standard deviation; SEER: Surveillance Epidemiology and End Results Program (U.S.A); SID: State Inpatient Databases (U.S.A.); VATS: video-assisted thoracoscopy; VoS: volume of services; vs.: versus

5.3.1 Study design and data source

All 23 included studies were retrospective observational studies.

Three studies used administrative data from the U.S. Centers for Medicare and Medicaid Services [44, 45, 59]. Medicare is the U.S. national insurance system which covers older people (65 years and older), people with disabilities, and people with dialysis-dependent kidney failure. In 2017, 17.2% of the U.S. population were covered by Medicare [65]. Another 4 studies used Medicare data linked with the registry of the U.S. Surveillance Epidemiology and End Results Program (SEER) [46, 47, 50, 61]. These linked data include both data from the U.S. SEER registry, which collects clinical data on demographics and causes of death in cancer patients, and the aforementioned Medicare data from the start of coverage until death. Five studies [49, 51, 53, 54, 64] used databases of the U.S. Healthcare Cost and Utilization Project (National [Nationwide] Inpatient Sample, State Inpatient Database). These databases include comprehensive information on inpatient care.

Avritscher 2014 used data from the Texas Hospital Inpatient Discharge Public Use Data File. Nimptsch 2017 used diagnosis-related group (DRG) statistics from the German federal and state statistical offices. The Bilimoria 2008 and Pezzi 2014 studies analysed data from the U.S. National Cancer Database. The investigations of the Lüchtenborg 2013 and Møller 2016 studies were based on data from national cancer databases, linked with cause of death statistics from the National Health Service (U.K.) and hospital statistics as well as data from the national registry and National Lung Cancer Audit (UK) dataset. The authors of the Simunovic 2006 study used data from the National Cancer Registry in Ontario, the database of the Canadian Institute for Health Information (CIHI), and the Ontario Registered Persons Database (RPDB).

In the Kim 2016 study, discharge data from the hospitals participating in the study and surveys of the American Heart Association (AHA) were analysed for the investigation. A similar approach was used by the authors of Stukenborg 2004, who used discharge data of California hospitals for their analysis. The Urbach 2004 study analysed data from the Ontario health database.

5.3.2 Recruitment country, follow-up period, and study objective

Out of the 23 studies, 18 were conducted in the USA [42–54, 58, 59, 61, 62, 64], 2 in Canada [60, 63], 2 in the UK [55, 56], and 1 in Germany [57].

The studies' follow-up periods ranged from approximately 1 year [53] to 12 years [52]. The oldest data are from 1990 [60].

The objectives of 22 studies comprised, at minimum, the investigation of the correlation between volume of services and mortality or survival rates. One study [42] investigated exclusively the correlation between volume of services and severe postoperative infections.

The authors of the Hollenbeck 2007a study additionally looked at any differences in the correlation between volume of services and quality of treatment outcome based on the origin of the data (SEER vs. Medicare data). Aside from the correlation between volume of services and mortality or survival rates, some studies investigated the effects on other outcomes, such as length of stay, rehospitalization [56], and adverse events [49, 61].

5.3.3 Key inclusion and exclusion criteria of the studies

Specific information regarding the age restrictions specified for the study population was provided by 15 studies. The reported data ranged from ≥ 18 years [42, 43, 49, 54, 58, 64], ≥ 20 years [57], ≥ 21 years [52], > 65 years [61], and 65 through 99 years [44–47, 50] and ≥ 66 years [59].

Out of the 23 included studies, 7 focused exclusively on the resection of lung carcinoma [53, 55, 56, 58, 61, 62, 64]. The remaining 16 studies included lung carcinoma as well as cancers of other organ systems, such as the pancreas, colon, oesophagus, liver, and/or stomach.

5.3.4 Data on tumour type

On the study level, only 4 studies provided detailed information on the included tumour types [43, 55, 56, 61]. The remaining 19 studies referred to lung carcinoma in general, without providing any further detail. On the study population level, further information on tumour type/stage was available. This information is found in Table 18 of the full report and in Section 5.3.7.

5.3.5 Surgical interventions

Six studies reported “lung resection” in general as the surgical intervention, without providing any further detail [42, 45–47, 53, 54, 57, 59, 62]. Three studies [46, 47, 54] mentioned “major lung resection”, which generally means anatomic resection (segmentectomy, lobectomy, pneumonectomy). In 10 studies [43, 44, 48–52, 58, 60, 63], the resection procedures of lobectomy and pneumonectomy were included. The remaining studies focused on lobectomy, pneumonectomy, and wedge resection [55, 61], segmental resection [64], sleeve resection [55], and other pulmonary resections (not further specified) [56].

5.3.6 Volume of services

Three studies reported specific thresholds for categorizing hospitals and/or physicians as high or low volume of services [43, 49, 63]. Two further studies [44, 64] reported the thresholds used to categorize hospitals as having very low and/or low, moderate, high, and very high volume of services. Likewise, the Birkmeyer 2003, Birkmeyer 2007, Finlayson 2003, and Learn 2010 studies state the lung resection thresholds or ranges used to categorize hospitals and physicians as having a low, moderate, and high volume of services. The Simunovic 2006 study classified hospitals as having a low, low to moderate, moderate to high, or high volume of services, and reported specific thresholds. While the authors of the Avritscher 2014, Birkmeyer 2006, Hollenbeck 2007a/b, and Smith 2017 studies pointed out that the volumes of

services per hospital or physician were classified as low, moderate, and high depending on the number of cases per follow-up period, they did not report any specific thresholds.

In Pezzi 2014, 6 categories were used to represent the specific thresholds for the annual number of lung resections per hospital.

In 6 studies, hospitals or physicians were categorized by ascending volume of services into quantiles/percentiles [52, 59, 62] or quintiles [53, 55, 56]. The Nimptsch 2017 study reported the medians to allow hospitals to be broken down into those with very low, low, moderate, high, and very high volume of services.

5.3.7 Data on the study population

The key characteristics of the study populations for research question 1a are presented in Appendix B, Table 18 of the full report and summarized in 5.3 below.

The 23 included studies analysed differing numbers of patients and/or lung resections, ranging from 2295 to 124 418. Information on the age of the study population was explicitly provided in 15 studies (see Section 5.3). In the studies which did not report any explicit data on age but used data from the Medicare database (see Section 5.3.1), it was generally possible to derive the age of the study population (between 65 and 99 years of age). In 18 studies, the composition of the study population was additionally broken down by sex.

Only 7 studies provided data on tumour type and/or stage. The analysis of the Bilimoria 2008 study focused on patients with nonmetastatic primary lung carcinoma in stages 1 through 3. Birkmeyer 2007 and Pezzi 2014 included patients with lung carcinoma of any stage (0 through 4). Smith 2017 focused exclusively on tumour stages 1 and 2. Tumour type was considered in addition to tumour stage/status [61] by Møller 2016 and Smith 2017. All histological subtypes of non-small cell cancer (squamous cell carcinoma, adenocarcinoma, large cell carcinoma) and small cell lung cancer were included. Kim 2016 reported the percentage of patients with lymph node involvement and metastases.

Information on patient comorbidities were reported in 14 studies. Furthermore, 4 studies analysed treatments such as adjuvant chemotherapy, adjuvant radiotherapy, neoadjuvant therapy, and mediastinal lymphadenectomy [43, 47, 58, 61].

5.4 Assessment of the informative value of results

Table 5 presents the informative value of results. For all 23 included studies, the informative value of results was rated as low.

All studies described the procedures used to account for cluster effects. Only Hollenbeck 2007b referred to the SUDAAN software (statistical software for the analysis of correlated data) without describing the exact procedure. Therefore, this aspect was assessed as “unclear” in the assessment of the informative value of results. While the authors of the Harrison 2018 study

took cluster effects into account during their investigations, they presented only the results, without accounting for cluster effects; no justification for this approach was provided. In addition, the study's authors did not report to what extent the results of the two analyses diverged.

Only Birkmeyer 2003 adjusted for risk factors on all 3 levels. In 8 studies, the authors adjusted for risk factors on both patient and hospital levels. In the Smith 2017 study, the authors took into account both the risk factors on the patient level and the factors on the physician level. In all studies, the authors adjusted for risk factors on the patient level. The analyses of these studies included primarily data on age, sex, ethnicity, and comorbidities (primary diseases and/or comorbidities). Few studies considered data on the severity of disease, the histological findings, lymph node involvement, tumour stage, and tumour size. Likewise, few studies took into account accompanying treatments such as adjuvant/neoadjuvant chemotherapy or radiation therapy in their analyses. On the hospital level, the studies' analyses mainly took into account the factors of academic status, legal form, and rural versus urban location, and, on the physician level, the factor of specialization.

Table 6 and Table 7 show an overview of the relevant risk factors accounted for in the studies on the levels of patients, physicians, and hospitals.

Seven studies reported information on model quality checks. All studies except for Kim 2016 checked model quality using the C-index/C-statistics. In the supplement to Kim 2016, the authors reported R^2 for the results from regression analyses. Only 1 of the studies provided information on the validation of the employed statistical models.

In 3 studies (Kim 2016, Learn 2010, Stukenborg 2004), the authors analysed the volume of services exclusively continuously.

The authors of 8 studies (Birkmeyer 2002, Birkmeyer 2003, Finlayson 2003, Kozower 2011, Nimptsch 2017, Sahni 2016, Urbach 2004, Wakeam 2015) reported that the volume of services was analysed both continuously and categorically. In 4 out of these 8 studies (Birkmeyer 2002, Finlayson 2003, Nimptsch 2017, Urbach 2004), only the results from categorical analyses were listed in order to simplify presentation (justification provided by the authors) or it was possible to derive the results of the continuous analysis only from the running text or figures. Other than that, some of the studies that relied on continuous analyses supplied complete data on points estimators (odds ratio), precision (confidence interval), and the p-value. The remaining 12 studies conducted exclusively categorical analysis. In these studies, point estimates (odds ratio, hazard ratio) and confidence intervals were reported throughout, albeit with the p-values also being omitted in a few cases.

Table 5: Informative value of results

	High quality of individual data	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment on all levels	Adequate handling of missing data	Information on a check of model quality	Model validation	Information on point estimate, including precision	Adequate reporting of relevant aspects	Further aspects	Informative value of results
Avritscher 2014	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	Yes	Yes	None	Low
Bilimoria 2008	Yes	Unclear	Categorical	Unclear	Yes	Yes	No[a, b]	Unclear	No	Unclear	Yes	Yes	Voluntary nature of hospital participation n.s.	Low
Birkmeyer 2002	Unclear	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[a, b]	Unclear	Yes	Unclear	In part	No	Voluntary nature of hospital participation unclear	Low
Birkmeyer 2003	Yes	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	Yes	Unclear	No	Unclear	Yes	Yes	▪ Regarding the presentation of the investigated interventions, discrepancy found between the methods part and results part ▪ Three approaches on the comorbidities index were investigated	Low
Birkmeyer 2006	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	In part	No	None	Low

(continued)

Table 5: Informative value of results (continued)

	High quality of individual data	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment on all levels	Adequate handling of missing data	Information on a check of model quality	Model validation	Information on point estimate, including precision	Adequate reporting of relevant aspects	Further aspects	Informative value of results
Birkmeyer 2006	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	In part	No	None	Low
Birkmeyer 2007	No	Unclear	Categorical	Yes	Yes	Yes	No[a, b]	Unclear	No	Unclear	In part	Yes	None	Low
Finlayson 2003	No	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[a, b]	Unclear	No	Unclear	In part	Yes	None	Low
Harrison 2018	No	Unclear	Categorical	Yes	Yes	Yes	No[a, b]	Unclear	No	Unclear	Yes	No[c]	Voluntary nature of hospital participation unclear	Low
Hollenbeck 2007a	No	Unclear	Categorical	Yes	Yes	Yes	No[a, b]	Unclear	No	Unclear	In part	Yes	None	Low
Hollenbeck 2007b	No	Unclear	Categorical	Yes	Yes	Unclear	No[a, b]	Unclear	Yes	Unclear	In part	Yes	None	Low
Kim 2016	Unclear	Unclear	Continuous	Unclear	Yes	Yes	No[b]	Unclear	Yes	Unclear	In part	Yes	▪ Investigation of the volume outcome was not a primary study objective ▪ Voluntary nature of hospital participation unclear	Low

(continued)

Table 5: Informative value of results (continued)

	High quality of individual data	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment on all levels	Adequate handling of missing data	Information on a check of model quality	Model validation	Information on point estimate, including precision	Adequate reporting of relevant aspects	Further aspects	Informative value of results
Kozower 2011	No	No	▪ Continuous ▪ Categorical	No	Yes	Yes	No[a, b]	Unclear	Yes	Unclear	In part	Yes	None	Low
Learn 2010	No	Unclear	Continuous	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	Yes	Yes	Voluntary participation of hospitals	Low
Lüchtenborg 2013	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[a, b]	Unclear	Yes	Unclear	Yes	Yes	Hospital participation likely voluntary; but not explicitly stated	Low
Møller 2016	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	Yes	No	▪ Hospital participation likely voluntary; but not explicitly stated ▪ Not all outcomes were subjected to an adjusted analysis.	Low
Nimptsch 2017	Yes	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[a, b]	Unclear	No	Unclear	In part	Yes	None	Low

(continued)

Table 5: Informative value of results (continued)

	High quality of individual data	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment on all levels	Adequate handling of missing data	Information on a check of model quality	Model validation	Information on point estimate, including precision	Adequate reporting of relevant aspects	Further aspects	Informative value of results
Pezzi 2014	Yes	Yes	Categorical	Yes	Yes	Yes	No[b]	No	No	Unclear	Yes	Yes	Hospital participation likely voluntary; but not explicitly stated	Low
Sahni 2016	Yes	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	In part	Yes	None	Low
Simunovic 2006	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	Yes	Yes	None	Low
Smith 2017	No	Unclear	Categorical	Yes	Yes	Yes	No[a]	Unclear	No	Unclear	In part	Yes	None	Low
Stukenborg 2004	Unclear	Unclear	Continuous	Yes	Yes	Yes	No[a,b]	Unclear	Yes	Yes	In part	Yes	Voluntary nature of hospital participation unclear	Low
Urbach 2004	Unclear	No	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[a,b]	Unclear	No	Unclear	In part	Yes	Voluntary nature of hospital participation unclear	Low
Wakeam 2015	No	Yes	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[a, b]	Unclear	Yes	Unclear	In part	Yes	▪ Underlying data include only 20% of U.S. hospitals ▪ Discrepant data on outcomes	Low

a: No risk adjustment on the hospital level.
b: No risk adjustment on the physician level.
c: Representation of results without taking into account cluster effects.
n.s.: not specified

Table 6: Risk factors at the patient level for which an adjustment was performed

Study	Level of risk adjustment																									
	Patient																									
	Age	Sex	Ethnicity	Residence	Socioeconomic status[a]	Type of insurance	Comorbidities	Marital status	Prior cancer diseases	Year of diagnosis	Disease severity	Lymph node involvement	Period between hospital admission and surgery	Presence of metastases	Inpatient complications occurring at the same time	Type of surgical procedure	Year of surgery	Expansion of the surgical area	Tumour stage	Tumour size	Histological finding	Urgency of hospital admission	Referral from another hospital	Type of cancer	Concomitant treatments	Performance Status	Weekday of surgery
Avritscher 2014	X	X	X	-	X	-	X	-	-	-	-	X	-	X	X	X	-	-	-	-	-	-	-	-	-	-	-
Bilimoria 2008	X	X	X	-	X	-	X	-	-	X	-	-	-	-	-	X	-	-	X	-	-	-	-	-	X	-	-
Birkmeyer 2002	X	X	X	-	X	-	X	-	-	-	-	-	-	-	-	-	X	-	-	-	-	X	-	-	-	-	-
Birkmeyer 2003	X	X	X	-	X	-	X	-	-	-	-	-	-	-	-	-	X	-	-	-	-	X	-	-	-	-	-
Birkmeyer 2006	X	X	X	-	-	-	X	-	-	-	-	-	-	-	-	-	X	-	-	-	-	X	-	X	-	-	-
Birkmeyer 2007	X	X	X	-	X	-	X	-	-	-	-	-	-	-	-	-	X	-	X	-	X	X	-	-	X	-	-
Finlayson 2003	X	X	X	-	X	-	X	-	-	-	-	-	-	-	-	-	X	-	-	-	-	X	-	-	-	-	-
Harrison 2018	X	X	X	X	X	X	X	-	-	-	-	-	-	-	-	X	X	-	-	-	-	-	-	-	-	-	-
Hollenbeck 2007a	X	X	X	-	-	-	X	-	-	-	X	-	-	-	-	-	-	-	X	-	-	X	-	-	-	-	-
Hollenbeck 2007b	X	X	X	-	-	X	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	X	-	-	-	-	-

(continued)

Table 6: Risk factors at the patient level for which an adjustment was performed (continued)

Study	Level of risk adjustment																									
	Patient																									
	Age	Sex	Ethnicity	Residence	Socioeconomic status	Type of insurance	Comorbidities	Marital status	Prior cancer diseases	Year of diagnosis	Disease severity	Lymph node involvement	Period between hospital admission and surgery	Presence of metastases	Inpatient complications occurring at the same time	Type of surgical procedure	Year of surgery	Expansion of the surgical area	Tumour stage	Tumour size	Histological finding	Urgency of hospital admission[a]	Referral from another hospital	Type of cancer	Concomitant treatments	Performance Status	Weekday of surgery
Kim 2016	X	X	X	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-	X	-	-	X	-	-	-	-	-
Kozower 2011	X	X	-	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Learn 2010	X	X	-	-	-	-	X	-	-	-	-	-	-	-	-	-	X	-	-	-	-	-	-	-	-	-	-
Lüchtenborg 2013	X	X	-	-	X	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Møller 2016	X	-	X	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-	X	-	X	-	-	-	-	X	-
Nimptsch 2017	X	X	-	-	-	-	X	-	-	-	-	-	-	X	-	-	X	X	-	-	-	-	-	-	-	-	-
Pezzi 2014	X	X	X	-	X	X	X	-	X	X	-	-	-	-	-	X	-	-	X	-	-	-	-	-	X	-	-
Sahni 2016	X	X	X	-	-	-	X	-	-	-	-	-	X	-	-	X	X	-	-	-	-	-	-	-	-	-	X
Simunovic 2006	X	X	-	-	X	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Smith 2017	X	X	X	-	X	-	X	X	-	-	X	-	-	X	-	-	-	-	X	X	X	-	-	-	-	-	-

(continued)

Table 6: Risk factors at the patient level for which an adjustment was performed (continued)

Study	Level of risk adjustment																										
	Patient																										
	Age	Sex	Ethnicity	Residence	Socioeconomic status	Type of insurance	Comorbidities	Marital status	Prior cancer diseases	Year of diagnosis	Disease severity	Lymph node involvement	Period between hospital admission and surgery	Presence of metastases	Inpatient complications occurring at the same time	Type of surgical procedure	Year of surgery	Expansion of the surgical area	Tumour stage	Tumour size	Histological finding	Urgency of hospital admission[a]	Referral from another hospital	Type of cancer	Concomitant treatments	Performance Status	Weekday of surgery
Pezzi 2014	X	X	X	-	X	X	X	-	X	X	-	-	-	-	-	X	-	-	X	-	-	-	-	-	X	-	-
Sahni 2016	X	X	X	-	-	-	X	-	-	-	-	-	X	-	-	X	X	-	-	-	-	-	-	-	-	-	X
Simunovic 2006	X	X	-	-	X	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Smith 2017	X	X	X	-	X	-	X	X	-	-	X	-	-	X	-	-	-	-	X	X	X	-	-	-	-	-	-
Stukenborg 2004	X	X	X	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	X	X	-	-	-	-
Urbach 2004	X	X	-	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Wakeam 2015	X	X	X	-	X	X	X	-	-	-	-	-	-	-	-	X	-	-	-	-	-	-	-	-	-	-	-

a: Also comprises income.
-: Studies contain no data on this factor.

Table 7: Risk factors at the physician and hospital level for which an adjustment was performed

Study	Level of risk adjustment													
	Physician			Hospital										
	Volume of services[a]	Private practice	Physician specialization	Academic status	Affiliation to a medical faculty	Number of registered nurses per bed	Availability of a wound care service	Infection protection (isolation rooms)	Legal form of the hospital (for-profit, not-for-profit)	Rural vs. urban hospital care	Volume of services[a]/geographical resection rate	Processes of health care	Operating costs	Physicians employed full time
Avritscher 2014	-	-	-	X		X	X	X	X	X	-	-	-	-
Bilimoria 2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Birkmeyer 2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Birkmeyer 2003	X	-	-	X	-	-	-	-	X	X	X	-	-	-
Birkmeyer 2006	-	-	-	X	-	-	-	-	X	-	-	X	-	-
Birkmeyer 2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Finlayson 2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harrison 2018	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hollenbeck 2007a	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hollenbeck 2007b	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kim 2016	-	-	-	X	-	-	-	-	X	X	-	-	X	X
Kozower 2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Learn 2010	-	-	-	X	-	-	-	-	-	X	-	-	-	-
Lüchtenborg 2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Møller 2016	-	-	-	-	-	-	-	-	-	-	X	-	-	-
Nimptsch 2017	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pezzi 2014	-	-	-	-	-	-	-	-	-	X	-	-	-	-
Sahni 2016	-	-	X	X	-	-	-	-	-	-	-	-	-	-
Simunovic 2006	-	-	-	X	-	-	-	-	-	X	-	-	-	-
Smith 2017	-	X	X	-	-	-	-	-	-	-	-	-	-	-
Stukenborg 2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urbach 2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Wakeam 2015	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a: In general, all analyses considered the VoS as a key factor; in Birkmeyer 2003, however, adjustments were made specifically for the VoS per physician and hospital.

-: The studies contain no data on this factor.

VoS: volume of services

5.5 Overview of the outcomes relevant for the assessment

There were no usable results in the studies Avritscher 2014, Harrison 2018, Smith 2017 and Wakeam 2015. The reasons for this can be found in Section 5.6.

Data on relevant outcomes were extracted from the 19 remaining studies. Table 8 presents an overview of the available data on the relevant outcomes from the included studies.

19 of the 23 included studies reported results regarding the relationship between volume of services and quality of treatment outcome for the outcome category “mortality”. 4 of the 22 studies [43,47,55,60] contained results on overall survival. 6 of the 22 studies contained results on the outcome “treatment-related mortality” [43,47,55,60]. The studies Lüchtenborg 2013, Møller 2016, Pezzi 2014, Sahni 2016 and Urbach 2004 contained usable results on the outcome “30- and 90-day mortality”. 7 studies [48,52-54,57,60,62] contained information on the outcome “in-hospital death”.

2 studies [51,56] contained information on the additionally identified outcomes “length of hospital stay” and “re-admission”. The included studies contained no usable data on the outcomes “disease-free survival”, “serious, life-threatening, or fatal infections” and “further serious treatment-related complications”. The included studies contained no data on the outcome “health-related quality of life” including activities of daily living and dependence on help from others.

Table 8: Matrix of the relevant outcomes

Study	Outcomes									
	Mortality				Morbidity			QoL	Further outcomes	
	Overall survival	Treatment-related mortality	30- and 90-day mortality	In-hospital death	Disease-free survival	Serious, life-threatening, or fatal infections	Further serious treatment-related complica-tions	Health-related quality of life	Length of hospital stay	Re-admission
Avritscher 2014	-	-	-	-	-	○	-	-	-	-
Bilimoria 2008	●	●	-	-	-	-	-	-	-	-
Birkmeyer 2002	-	●	-	-	-	-	-	-	-	-
Birkmeyer 2003	-	●	-	-	-	-	-	-	-	-
Birkmeyer 2006	-	●	-	-	-	-	-	-	-	-
Birkmeyer 2007	●	-	-	-	-	-	-	-	-	-
Finlayson 2003	-	-	-	●	-	-	-	-	-	-
Harrison 2018	-	-	-	○	-	○	○	-	○	-
Hollenbeck 2007a	-	●	-	-	-	-	-	-	-	-
Hollenbeck 2007b	-	●	-	-	-	-	-	-	●	-
Kim 2016	-	-	-	●	-	-	-	-	-	-

(continued)

Table 8: Matrix of the relevant outcomes (continued)

Study	Outcomes									
	Mortality				Morbidity			QoL	Further outcomes	
	Overall survival	Treatment-related mortality	30- and 90-day mortality	In-hospital death	Disease-free survival	Serious, life-threatening, or fatal infections	Further serious treatment-related complications	Health-related quality of life	Length of hospital stay	Re-admission
Kozower 2011	-	-	-	●	-	-	-	-	-	-
Learn 2010	-	-	-	●	-	-	-	-	-	-
Lüchtenborg 2013	●	-	●	-	-	-	-	-	-	-
Møller 2016	-	-	●	-	-	-	-	-	○	●
Nimptsch 2017	-	-	-	●	-	-	-	-	-	-
Pezzi 2014	-	-	●	-	-	-	-	-	-	-
Sahni 2016	-	-	●	-	-	-	-	-	-	-
Simunovic 2006	●	-	-	●	-	-	-	-	-	-
Smith 2017	○	-	○	-	-	○	○	-	○	○
Stukenborg 2004	-	-	-	●	-	-	-	-	-	-
Urbach 2004	-	-	●	-	-	-	-	-	-	-
Wakeam 2015	-	-	-	○	-	-	-	-	-	-

● Data were reported and were usable.
○ Data were reported, but were not usable for the investigation.
- No data were reported (no further information). / The outcome was not recorded.
QoL: health-related quality of life

5.6 Results on relevant outcomes

The results on the outcomes relevant for the report are presented below. The studies Avritscher 2014, Harrison 2018, Smith 2017 and Wakeam 2015 were rated as relevant, but did not contain any usable results for the presentation and assessment of the relationship between volume of services and quality of treatment outcome:

- The authors of the Avritscher 2014 study reported results on the outcome "serious postoperative infections", but no usable results could be obtained from the study, as they were not specifically reported for lung resections.
- The authors of the Harrison 2018 study presented results on relevant outcomes only from analyses that did not take cluster effects into account. However, the authors did not provide a justification or an explanation as to how the results would change if cluster effects were taken into account.
- In the Smith 2017 study, the rates presented and the associated unadjusted odds ratios were not comprehensible. Besides, it remained unclear to which comparison the presented point estimates referred. Thus, also the results of the adjusted analyses were overall not considered usable.
- The Wakeam 2015 study presented the relationship between volume of services and quality of treatment outcome only for subgroup characteristics, such as preoperative risk and age, and hence only for the corresponding subgroups and not across all characteristics. The subgroups were not subgroups as specified in Section 4.3.4.

5.6.1 Mortality

5.6.1.1 Results on the outcome "overall survival"

4 of 23 included studies contained usable results on the outcome "overall survival" (see Table 9).

The studies Bilimoria 2008, Birkmeyer 2007 and Simunovic 2006 showed statistically significant differences in favour of hospitals with high volumes of services in comparison with hospitals with low volumes of services for the outcome "overall survival".

The authors of the Bilimoria 2008 study reported the point and interval estimates for the comparison of < 21 lung resections versus > 83 lung resections both for the 5-year survival (HR [95% CI]: 1.09 [1.04; 1.14]) and for the conditional 5-year survival (HR [95% CI]: 1.06 [1.01; 1.12]). The authors of the Birkmeyer 2007 study compared hospitals performing 0.3 to 11.4 lung resections per year with hospitals performing 25.2 to 313.2 lung resections per year (HR [95% CI]: 0.84 [0.79; 0.90]). In the Simunovic 2006 study, for all comparisons with the reference category (hospitals with the highest volumes of services of ≥ 131 lung resections for the period of 3 years), the authors presented statistically significant differences in favour of the reference category for long-term survival.

The Lüchtenborg 2013 study reported partly statistically significant differences in favour of a higher volume of services per hospital and year.

The authors of the Lüchtenborg 2013 study divided the volumes of services per hospital and year into quintiles. The first quintile included hospitals with the lowest volumes of services (< 70 lung resections per year) and the fifth quintile hospitals with the highest volumes of services (≥ 150 lung resections per year). The authors of the study reported statistically significant differences in favour of the respective hospitals with the higher volumes of services in comparison with hospitals with the lowest volumes of services only for the volumes of services of 70 to 99 and ≥ 150 lung resections. The authors did not report any p-values for the individual comparisons, but provided a p-value for the trend ($p < 0.01$).

Across studies, there was a positive correlation between the volume of services per hospital and the quality of treatment outcome for the outcome “overall survival”, with a low informative value of results.

Table 9: Results – overall survival

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Bilimoria 2008	**5-year survival:** calculation in months from the time point of surgery until death or last contact with the patient (median follow-up: 29 months)	Total: 40 754[a]	VoS per hospital and year:		
		ND	Hospitals with low VoS: < 21	ND (32.7)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.09 [1.04; 1.14]; < 0.001
		ND	Hospitals with medium VoS[c]	ND (34.8)	
		ND	Hospitals with high VoS: > 83	ND (36.0)	
	Conditional 5-year survival: time point of surgery until death or last contact with the patient who is still alive 60 days after surgery (patients with event for perioperative mortality are excluded)	ND	Hospitals with low VoS: < 21	ND (35.0)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.06 [1.01; 1.12]; 0.018
		ND	Hospitals with medium VoS[c]	ND (37.1)	
		ND	Hospitals with high VoS: > 83	ND (38.1)	
Birkmeyer 2007	**5-year survival:** vital status 5 years after surgery or at end of follow-up (31 December 2002)	Total: 12 967[d]	VoS per hospital and year:		
		4325	Hospitals with low VoS: 0.3–11.4[e]	1622[d] (37.5)	**Hospitals with high VoS vs. hospitals with low VoS:** 0.84 [0.79; 0.90]; < 0.05
		4418	Hospitals with medium VoS: 11.4–24.9[e]	ND	
		4224	Hospitals with high VoS: 25.2–313.2[e]	1837[d] (43.5)	
Lüchtenborg 2013	Survival time from time point of surgery until death or end of study (31 December 2009)	Total: 12 862	VoS per hospital and year:		**p-value for trend: < 0.01**
		2582	1.quintile: < 70	ND	Reference category
		2662	2nd quintile: 70–99	ND	0.86 [0.77; 0.97]; ND
		2378	3rd quintile: 100–129	ND	0.90 [0.79; 1.02]; ND
		2651	4th quintile: 130–149	ND	0.89 [0.78; 1.02]; ND
		2589	5th quintile: ≥ 150	ND	0.78 [0.67; 0.90]; ND

(continued)

Table 9: Results – overall survival (continued)

Study	Definition of the outcome	N	Information on volume of services (number of lung resections)	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Simunovic 2006	**Long-term survival:** from the time point of hospital admission until death or end of follow-up (31 December 2000) without patients with event for in-hospital death	Total: 2698	VoS per hospital for the period of 3 years:		
		653	Hospitals with low VoS: ≤ 32	ND	1.3 [1.1; 1.6][b]; < 0.01
		730	Hospitals with low to medium VoS: 33–85	ND	1.4 [1.2; 1.6][b]; < 0.001
		644	Hospitals with medium to high VoS: 86–130	ND	1.2 [1.0; 1.4][b]; 0.02
		671	Hospitals with high VoS: ≥ 131	ND	Reference category

a: Number of lung resections performed.
b: Values > 1 indicate an advantage for hospitals with high VoS.
c: Contains second, third and fourth quintiles.
d: IQWiG's own calculation.
e: Range/year.
CI: confidence interval; N: number of included patients; n: number of patients with event; ND: no data; OS: overall survival; VoS: volume of services; vs.: versus

5.6.1.2 Results on the outcome "treatment-related mortality"

6 of 23 included studies contained usable results on the outcome "treatment-related mortality" (see Table 10 and Table 11).

The studies Bilimoria 2008, Hollenbeck 2007a and Hollenbeck 2007b showed statistically significant differences in favour of hospitals with high volumes of services in comparison with hospitals with low volumes of services for the outcome "treatment-related mortality".

The authors of the Bilimoria 2008 study reported the point and interval estimators for the comparison of < 21 lung resections versus > 83 lung resections per hospital and year (HR [95% CI]: 1.31 [1.14; 1.51]). The authors of the Hollenbeck 2007a study did not provide any specific numbers of lung resections for the individual categories of volumes of service. In addition, they performed separate analyses based on Medicare data (OR [95% CI]: 1.48 [1.13; 1.94]) and SEER-Medicare data (OR [95% CI]: 1.32 [1.03; 1.71]). The volume of services was considered per hospital and for the observation period of the study. In the Hollenbeck 2007b study, the volume of services was divided into deciles, and the lowest decile (mean: 3.6 lung resections, SD: 2.2) was compared with the highest decile (mean: 116.3 lung resections, SD: 68.6) (OR [95% CI]: 1.4 [1.2; 1.7]). The volume of services was considered per hospital and for the observation period of the study.

The studies Birkmeyer 2002 and Birkmeyer 2003 only partially reported statistically significant differences in favour of hospitals with higher volumes of services.

The Birkmeyer 2002 study presented results for the outcome "treatment-related mortality" separately for the interventions lobectomy and pneumonectomy per hospital and year. With the exception of the category of 9 to 17 lung resections, comparisons with hospitals with very low volumes of services (< 9 lung resections per year) produced statistically significant results in favour of the respective hospitals with higher volumes of services for lobectomy. For pneumonectomy, only the comparison of hospitals of the reference category with hospitals with very high volumes of services (> 46 lung resections per year) produced a statistically significant result.

The Birkmeyer 2003 study reported point estimates separately for the volumes of services of physicians and hospitals per year. A statistically significant difference in favour of very high volumes of services was shown for the hospitals (OR [95% CI]: 1.22 [1.04; 1.44]), whereas this was not the case at the physician level (OR [95% CI]: 1.16 [0.99; 1.36]; not significant).

For the Birkmeyer 2006 study, significance was unclear with regard to the volume of services per hospital and year.

The authors of the Birkmeyer 2006 study divided the volumes of services per hospital into quintiles, with the first quintile comprising hospitals with low volumes of services and the fifth quintile comprising hospitals with high volumes of services. The authors did not provide any specific numbers on the proportions. The study showed a difference in favour of hospitals with high volumes of services, the significance of which cannot be determined (OR [95% CI]: 1.18 [1.00; 1.38]).

Across studies, there was a positive correlation between the volume of services per hospital or physician and the quality of treatment outcome for the outcome "treatment-related mortality", with a low informative value of results.

Table 10: Results part 1 – treatment-related mortality (survival time data)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Bilimoria 2008	**Perioperative mortality:** death within 60 days after surgery	Total: 40 754[a]	VoS per hospital and year:		
		ND	Hospitals with low VoS: < 21	ND (6.4)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.31 [1.14; 1.51]; < 0.001
		ND	Hospitals with medium VoS[c]	ND (6.1)	
		ND	Hospitals with high VoS: > 83	ND (5.5)	

a: Number of lung resections performed.
b: Values > 1 indicate an advantage for hospitals with high VoS.
c: Contains second, third and fourth quintiles.
CI: confidence interval; N: number of included patients; n: number of patients with event; ND: no data; VoS: volume of services; vs.: versus

Table 11: Results part 2 – treatment-related mortality (binary data)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Birkmeyer 2002	**Operative mortality:** death before hospital discharge or within 30 days after surgery	**Lobectomy** Total: 75 563[a]	Categories formed on the basis of the overall number of lung resections (lobectomy + pneumonectomy) per hospital and year:	**Lobectomy**	
		14 816	Hospitals with very low VoS: < 9	948[a] (6.4)	Reference category
		15 731	Hospitals with low VoS: 9–17	928[a] (5.9)	0.94 [0.85; 1.04]; ND
		14 759	Hospitals with medium VoS: 18–27	812[a] (5.5)	0.89 [0.80; 0.99]; ND
		15 469	Hospitals with high VoS: 28–46	820[a] (5.3)	0.87 [0.78; 0.97]; ND
		14 788	Hospitals with very high VoS: > 46	621[a] (4.2)	0.70 [0.60; 0.81]; ND
	Operative mortality: death before hospital discharge or within 30 days after surgery	**Pneumonectomy** Total: 10 410[a]	Categories formed on the basis of the overall number of lung resections (lobectomy + pneumonectomy) per hospital and year:	**Pneumonectomy**	
		1969	Hospitals with very low VoS: < 9	335[a] (17.0)	Reference category
		2098	Hospitals with low VoS: 9–17	323[a] (15.4)	0.91 [0.76; 1.08]; ND
		2072	Hospitals with medium VoS: 18–27	325[a] (15.7)	0.93 [0.78; 1.11]; ND
		2088	Hospitals with high VoS: 28–46	313[a] (15.0)	0.91 [0.76; 1.08]; ND
		2183	Hospitals with very high VoS: > 46	231[a] (10.6)	0.62 [0.50; 0.77]; ND

(continued)

Table 11: Results part 2 – treatment-related mortality (binary data) (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Birkmeyer 2003	**Operative mortality:** death before hospital discharge or within 30 days after surgery	Total: 24 092	VoS per physician and year:		
		7668[a]	Physician with low VoS: < 7	ND	**Change from physician with low VoS to physician with high VoS[b]:** 1.16 [0.99; 1.36]; NS
		8360[a]	Physician with moderate VoS: 7–17	ND	
		8064[a]	Physician with high VoS: > 17	ND	
		Total: 24 092	VoS per hospital and year:		
		8270[a]	Hospitals with low VoS: < 17	ND	**Change from hospital with low VoS to hospital with high VoS[b]:** 1.22 [1.04; 1.44]; ND
		7769[a]	Hospitals with medium VoS: 17–35.5	ND	
		8053[a]	Hospitals with high VoS: > 35.5	ND	
Birkmeyer 2006	**Operative mortality:** death before hospital discharge or within 30 days after surgery	Total: 49 280[a]			
		9838[a]	1st quintile (low VoS)	ND	**Hospitals with low VoS vs. hospitals with high VoS (1st quintile vs. 5th quintile)[b]:** 1.18 [1.00; 1.38]; ND
		10 420[a]	2nd quintile	ND	
		10 399[a]	3rd quintile	ND	
		10 116[a]	4th quintile	ND	
		8507[a]	5th quintile (high VoS)	ND	

(continued)

Table 11: Results part 2 – treatment-related mortality (binary data) (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Hollenbeck 2007a	**Operative mortality:** death within 30 days after surgery or before hospital discharge	**Medicare**			
		Total: 8183	VoS was formed on the basis of the Medicare database per hospital and over the 6-year observation period		
		3396[a]	Hospitals with low VoS	224[a] (6.6)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.48 [1.13; 1.94]; ND
		2513[a]	Hospitals with medium VoS	ND	
		2274[a]	Hospitals with high VoS	109[a] (4.8)	
		SEER-Medicare			
		Total: 8183	VoS was formed on the basis of the SEER-Medicare database		
		2735[a]	Hospitals with low VoS	167[a] (6.1)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.32 [1.03; 1.71]; ND
		2723[a]	Hospitals with medium VoS	ND	
		2725[a]	Hospitals with high VoS	125[a] (4.6)	
Hollenbeck 2007b	**Operative mortality:** death during surgery or before hospital discharge after surgery	Total: 90 088[c, d]	Mean value of the lung resections performed per hospital during the 11-year observation period		
		ND	Hospitals with low VoS (lowest decile): mean (SD): 3.6 (2.2)	ND (4.9)	**Hospitals with low VoS vs. hospitals with high VoS[b]:** 1.4 [1.2; 1.7]; ND
		ND	Hospitals with high VoS (highest decile): mean (SD): 116.3 (68.6)	ND (2.7)	

a: IQWiG's own calculation.
b: Values > 1 indicate an advantage for hospitals with high VoS.
c: Number of performed lung resections (lobectomy + pneumonectomy).
d: Data only on pneumonectomy are reported within the results.

CI: confidence interval; N: number of included patients; n: number of patients with event; ND: no data; NS: not statistically significant; SD: standard deviation; SEER: Surveillance, Epidemiology, and End Results; VoS: volume of services; vs.: versus

5.6.1.3 Results on the outcome "30- and 90-day mortality"

5 of the 23 included studies reported usable results on the outcome "30- and 90-day mortality" (see Table 12 and Table 13). None of the studies indicated a specific cause of death within this period, so that the outcome designation "(30- and 90-day) lethality" could not be used with sufficient certainty, and the term "mortality" was therefore used.

The authors of the Urbach 2014 study showed a statistically significant difference for the outcome "30-day mortality" after lung resection in favour of hospitals with high volumes of services (≥ 45 lung resections per year) in comparison with hospitals with low volumes of services (< 45 lung resections per year) (OR [95% CI]: 0.64 [0.44; 0.94]).

The studies Lüchtenborg 2013, Møller 2016 and Pezzi 2014 reported partly statistically significant results. Significant differences were only shown for individual comparisons between the categories of volumes of services or did not apply to both outcomes.

The Lüchtenborg 2013 study divided the volumes of services per hospital and year into quintiles. A statistically significant difference was determined for 30-day mortality for the comparison of hospitals with the lowest volumes of services (< 70 lung resections; first quintile) and hospitals with the highest volumes of services (≥ 150 lung resections; fifth quintile). A reduction by 42% was shown in 30-day mortality (HR [95% CI]: 0.58 [0.38; 0.89]). The comparisons between the hospitals with the lowest volumes of services and the other quintiles (second to fourth quintiles) showed no statistically significant differences. Similarly, the Møller 2016 study showed a statistically significant result for 90-day mortality in favour of the hospitals with the highest volumes of services only for the comparison of hospitals with low volumes of services per year (1 to 75 lung resections; first quintile) versus hospitals with volumes of services between 189 and 287 lung resections per year (fifth quintile) (OR [95% CI]: 0.67 [0.46; 0.96]). For the remaining quintiles and for 30-day mortality, the authors did not report statistically significant results for any of the comparisons with the reference category. The situation is similar with the results of the comparison of hospitals with low volumes of services (1 to 75 lung resections) versus hospitals with the highest volumes of services (189 to 287 lung resections) (OR [95% CI]: 0.50 [0.25; 1.01]).

The Pezzi 2014 study reported results for death within 30 days and for death between 31 and 90 days after a lung resection, in each case as overall numbers and separately for resection procedure (lobectomy/pneumonectomy) per hospital and year. For the comparison of hospitals with the highest volumes of services (≥ 90 lung resections) versus hospitals with volumes of services of < 10, 10 to 29 as well as 30 to 89 lung resections, the authors reported statistically significant differences for the outcome "30-day mortality" in favour of hospitals with higher volumes of services regardless of the resection procedure. Specifically for lobectomy and pneumonectomy, all comparisons also showed statistically significant differences for 30-day mortality in favour of hospitals with high volumes of services. For the (conditional) 90-day mortality, statistically significant differences (lung resections overall and lobectomy) were shown in favour of the hospitals with the highest volumes of services only for the comparison

of hospitals with the highest volumes of services versus hospitals with volumes of services < 10. The remaining comparisons are not statistically significant or the statistical significance cannot be determined.

The Sahni 2016 study reported no statistically significant difference between the increase in the volume of services per physician per year and death within 30 days of hospital admission.

Across studies, there was no consistent correlation between the volume of services and the quality of treatment outcome for the outcome "30- and (conditional) 90-day mortality", with a low informative value of results. This was also shown within the studies with respect to the comparisons of the categories.

Table 12: Results part 1 – 30- and 90-day mortality (survival time data)

Study	**Definition of outcome**	**N**	**Information on volume of services (number of lung resections)**	**Mortality raw n (%)**	**Adjusted hazard ratio [95% CI]; p-value**
Lüchtenborg 2013	**Perisurgical period:** survival time within the period of 0 to 30 days after surgery	Total: 12 862	VoS per hospital and year:		**Follow-up (0–30 days):**
		2582	1.quintile: < 70	ND	Reference category
		2662	2nd quintile: 70–99	ND	0.81 [0.58; 1.13]; ND
		2378	3rd quintile: 100–129	ND	0.75 [0.52; 1.08]; ND
		2651	4th quintile: 130–149	ND	0.91 [0.64; 1.31]; ND
		2589	5th quintile: ≥ 150	ND	0.58 [0.38; 0.89]; ND
CI: confidence interval; N: number of included patients; n: number of patients with event; ND: no data; VoS: volume of services; vs.: versus					

Table 13: Results part 2 – 30- and 90-day mortality (binary data)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p value
Møller 2016	Death within **30 days** after surgery	Total: 15 738	VoS per hospital and year::	**30-day mortality**	
		3190	1st quintile: 1–75	33 (1.0)	Reference category
		3230	2nd quintile: 77–112	42 (1.3)	1.26 [0.75; 2.11]; ND
		3026	3rd quintile: 114–155	24 (0.8)	0.77 [0.43; 1.38]; ND
		3189	4th quintile: 156–186	29 (0.9)	0.84 [0.47; 1.50]; ND
		3103	5th quintile: 189–287	17 (0.5)	0.50 [0.25; 1.01]; ND
	Death within **90 days** after surgery	Total: 15 738	VoS per hospital and year:	**90-day mortality**	
		3190	1st quintile: 1–75	98 (3.1)	Reference category
		3230	2nd quintile: 77–112	111 (3.4)	1.15 [0.85; 1.56]; ND
		3026	3rd quintile: 114–155	72 (2.4)	0.79 [0.56; 1.11]; ND
		3189	4th quintile: 156–186	95 (3.0)	0.95 [0.68; 1.31]; ND
		3103	5th quintile: 189–287	67 (2.2)	0.67 [0.46; 0.96]; ND

(continued)

Table 13: Results part 2 – 30- and 90-day mortality (binary data) (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Pezzi 2014[a]	**30-day mortality (lobectomy + pneumonectomy)**				
	30-day mortality after surgery	Total: 121 099	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		10 860	Category 1: < 10	404 (3.7)	2.1 [1.7; 2.6][b]; ND
		43 409	Category 2: 10–29	1363 (3.1)	1.7 [1.4; 2.1][b]; ND
		53 155	Category 3: 30–89	1384 (2.6)	1.4 [1.1; 1.7][b]; ND
		13 675	Category 4: ≥ 90	238 (1.7)	Reference category
	30-day mortality (pneumonectomy)				
	30-day mortality after surgery	Total: 7949	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		ND	Category 1: < 10	ND (10.9)	2.2 [1.5; 3.2][b]; ND
		ND	Category 2: 10–29	ND (9.1)	1.7 [1.3; 2.4][b]; ND
		ND	Category 3: 30–89	ND (8.1)	1.5 [1.1; 2.1][b]; ND
		ND	Category 4: ≥ 90	ND (5.4)	Reference category
	30-day mortality (lobectomy)				
	30-day mortality after surgery	Total: 113 150	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		ND	Category 1: < 10	ND (3.2)	2.0 [1.6; 2.6][b]; ND
		ND	Category 2: 10–29	ND (2.7)	1.6 [1.3; 2.0][b]; ND
		ND	Category 3: 30–89	ND (2.2)	1.3 [1.1; 1.6][b]; ND
		ND	Category 4: ≥ 90	ND (1.5)	Reference category

(continued)

Table 13: Results part 2 – 30- and 90-day mortality (binary data) (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Pezzi 2014[a] (continued)	**Conditional 90-day mortality (lobectomy + pneumonectomy)**				
	Death between 31st and 90th day after surgery	Total: 114 905	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		10 278	Category 1: < 10	303 (2.9)	1.3 [1.1; 1.6][b]; ND
		41 035	Category 2: 10–29	1146 (2.8)	1.2 [1.0; 1.4][b]; ND
		50 615	Category 3: 30–89	1238 (2.4)	1.0 [0.9; 1.2][b]; ND
		12 977	Category 4: ≥ 90	281 (2.2)	Reference category
	Conditional 90-day mortality (pneumonectomy)				
	Death between 31st and 90th day after surgery	Total: 7106	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		ND	Category 1: < 10	ND (6.8)	1.2 [0.8; 2.0][b]; ND
		ND	Category 2: 10–29	ND (6.9)	1.2 [0.8; 1.7][b]; ND
		ND	Category 3: 30–89	ND (5.9)	1.1 [0.9; 1.3][b]; ND
		ND	Category 4: ≥ 90	ND (5.8)	Reference category
	Conditional 90-day mortality (lobectomy)				
	Death between 31st and 90th day after surgery	Total: 107 799	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:		
		ND	Category 1: < 10	ND (2.7)	1.3 [1.1; 1.7][b]; ND
		ND	Category 2: 10–29	ND (2.5)	1.2 [1.0; 1.5][b]; ND
		ND	Category 3: 30–89	ND (2.2)	1.1 [0.9; 1.3][b]; ND
		ND	Category 4: ≥ 90	ND (1.9)	Reference category

(continued)

Table 13: Results part 2 – 30- and 90-day mortality (binary data) (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Sahni 2016	Death within 30 days after hospital admission	Total: 85 966[c]	VoS per physician per year: ▪ Physician with VoS in lowest quarter: 1.6 ▪ Physician with VoS in second quarter: 5.1 ▪ Physician with VoS in third quarter: 10.4 ▪ Physician with VoS in highest quarter:: 32.6	ND	Increase in annual VoS of treating physician by presumably 1 resection; Relative risk: 1.00 [ND]; 0.34
Urbach 2004	Death within 30 days after surgery	Total: 5156 2597 2559	VoS per hospital and year: Hospital with low VoS: < 45 Hospital with high VoS: ≥ 45	 126 (4.9) 89 (3.5)	 0.64 [0.44; 0.94]; < 0.05

a: The results on 90-day mortality are presented only graphically in the Pezzi 2014 study. Deriving the results from the graph is prone to errors. For this reason, the results are not presented in the report.
b: Values > 1 indicate an advantage for hospitals with a high volume of services.
c: Number of lung resections performed.
CI: confidence interval; N: Number of evaluated patients; n: Number of patients with an event; ND: no data; VoS: volume of services

5.6.1.4 Results on the outcome "in-hospital death"

In 7 of the 23 studies included, usable results were reported on the outcome "in-hospital death" (see Table 14).

In the Kim 2016, Learn 2010, Nimptsch 2017 and Stukenborg 2004 studies, statistically significant differences could be shown in favour of hospitals with a high volume of services versus hospitals with a low volume of services for in-hospital death.

The authors of the Kim 2016 study presented the regression coefficients with associated standard errors separately for lobectomy and pneumonectomy. From this, the respective results (OR [95% CI]) could be calculated (lobectomy: 0.996 [0.99; 0.999] and pneumonectomy: 0.98 [0.96; 0.99]). The volume of services (maximum volume) per hospital and for the years 2000 and 2011 as well as for the entire observation period is reported. In the Learn 2010 study, the estimates were given independently of the resection procedure (OR [95% CI]: 0.996 [0.994; 0.998]). The respective point estimates of both studies (presumably) refer to the increase of the annual volume of services by 1 case. In the Nimptsch 2017 study, the volume of services categories were formed on the basis of the medians of the annual volume of services per hospital. Both the point and interval estimates for the increase of the annual volume of services by 50 (OR [95% CI]: 0.88 [0.86; 0.91]) and the regression coefficient with the p-value for the increase by 1 case (resulting OR; p-value: 0.998; < 0.001) were reported. The authors of the Stukenborg 2004 study divided the volume of services into percentiles and presented the results for an increase in the volume of services from 10 to 30 lung resections per hospital and year (OR [95% CI]: 0.84 [0.76; 0.94]).

In the Simunovic 2006 study, statistically significant differences in favour of a higher volume of services were only partially reported. Only for the comparison of the reference category (hospitals with ≥ 131 lung resections) with hospitals with a low to medium volume of services (33 to 85 lung resections) could the authors of the study show a statistically significant difference for in-hospital death (OR [95% CI]: 2.8 [1.20; 6.30]). The volume of services per hospital was considered for a period of 3 years.

In the Finlayson 2003 and Kozower 2011 studies, there were no statistically significant differences between the volume of services provided by hospitals and the quality of treatment outcome with regard to in-hospital death. Here the authors of the Finlayson 2003 study reported point and interval estimates separately by resection procedure (lobectomy, pneumonectomy). In both studies, the volume of services per hospital and year was considered.

Across studies, a predominantly positive correlation between the number of lung resections per hospital and the quality of treatment outcome was found for in-hospital death, with a low informative value of results. The statistically significant differences were mainly based on the preferred continuous analyses of the volume of services. For the different resection procedures, different conclusions were drawn with regard to the correlation between the volume of services and the quality of treatment outcome.

Table 14: Results – in-hospital death

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Finlayson 2003	**Operative mortality:** Death before hospital discharge	Total: 21 890[a]	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:	**Pneumonectomy:**	
		7380[a]	Hospital with low VoS: < 19	ND (10.6)	**Hospital with high VoS vs. hospital with low VoS** 0.83 [0.58; 1.20][b]; ND
		7499[a]	Hospital with medium VoS: 19–37	ND (10.1)	
		7011[a]	Hospital with high VoS: > 37	ND (8.9)	
		Total: 21 890[a]	Categories based on the total number of lung resections (lobectomy + pneumonectomy) per hospital and year:	**Lobectomy:**	
		7380[a]	Hospital with low VoS: < 19	ND (4.3)	**Hospital with high VoS vs. hospital with low VoS** 0.86 [0.69; 1.06][b]; ND
		7499[a]	Hospital with medium VoS: 19–37	ND (2.9)	
		7011[a]	Hospital with high VoS: > 37	ND (3.5)	
Kim 2016	In-hospital death	**Pneumonectomy:**			
		5043	▪ 50% quantile: 2 ▪ 75% quantile: 3 ▪ 90% quantile: 5 ▪ 95% quantile: 8 M (SD): 2.02 (0.94)	ND	Increase of annual VoS of the treating hospital presumably by 1 case[c]: 0.98 [0.96; 0.99]; < 0.05
		Lobectomy:			
		54 448	▪ 50 % quantile: 7 ▪ 75% quantile: 18 ▪ 90% quantile: 34 ▪ 95% quantile: 47 M (SD): 11.51 (4.22)	ND	Increase of annual VoS of the treating hospital presumably by 1 case[c]: 0.996 [0.99; 0.999]; < 0.001
Kozower 2011	In-hospital death	7908	1st quintile: 1–2 2nd quintile: 3–6 3rd quintile: 7–12 4th quintile: 13–23 5th quintile: ≥ 24	ND	Increase of annual VoS of the treating hospital presumably by 1 case[d] 1.01 [1.00; 1.02]; 0.25

(continued)

Table 14: Results – in-hospital death (continued)

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Mortality raw n (%)	Adjusted odds ratio [95% CI]; p-value
Learn 2010	**In-hospital mortality:** Death during hospital stay due to lung resection	62 628[e]	Generation of VoS is based on the number of lung resections 1997–1999 ▪ Hospital with low VoS: 1–16 ▪ Hospital with medium VoS: 17–33 ▪ Hospital with high VoS: > 33	ND	Increase of annual VoS of the treating hospital presumably by 1 case 0.996 [0.994; 0.998]; < 0.001[f]
Nimptsch 2017	Death before discharge from hospital	Total: 73 983[g]	Median annual VoS (IQR)		Increase of annual VoS by 50 cases: 0.88 [0.86; 0.91][i]; ND Increase of annual VoS by 1 case: 0.998[j] [ND]; < 0.001
		14 655	Hospital with very low VoS: 5 (2–14)	660 (4.5)[h]	
		14 766	Hospital with low VoS: 49 (43–59)	458 (3.1)[h]	
		14 626	Hospital with medium VoS: 89 (79–98)	453 (3.1)[h]	
		14 872	Hospital with high VS: 137 (122–160)	357 (2.4)[h]	
		15 064	Hospital with very high VS: 272 (208–313)	241 (1.6)[h]	
Simunovic 2006	From time point of admission for surgery	Total: 2698	VoS per hospital for period of 3 years:		
		653	Hospital with low VoS: ≤ 32	38[g] (5.8)	2.2 [0.80; 5.60][k]; 0.11
		730	Hospital with low to medium VoS: 33–85	43[g] (5.9)	2.8 [1.20; 6.30][k]; 0.01
		644	Hospital with medium to high VoS: 86–130	24[g] (3.7)	1.4 [0.60; 3.50][k]; 0.46
		671	Hospital with high VoS: ≥ 131	16[g] (2.4)	Reference category
Stukenborg 2004	Mortality before discharge from hospital	14 456	▪ Minimum VoS: 0.3 ▪ 0.1 percentile: 5.8 ▪ 0.25 percentile: 13.0 ▪ 0.5 percentile: 21.0 ▪ 0.75 percentile: 32.3 ▪ 0.9 percentile: 47.8 ▪ Maximum VoS: 100.8 M: 25.1	ND	Increase in annual VoS per hospital from 10 to 30 cases: 0.84 [0.76; 0.94]; ND

(continued)

Table 14: Results – in-hospital death (continued)

a: Number of lung resections performed (lobectomy + pneumonectomy).
b: Read from Figure 1 of the Finlayson 2003 study on the adjusted odds ratio; applies to an increase in the annual VoS of the treating hospital from lower to higher VoS.
c: IQWiG's own calculation from information on regression coefficient and standard error; presumably valid if the annual VoS of the treating hospital increases by 1 case.
d: Unclear to which change in the annual VoS of the treating hospital the odds ratio refers. The linearity between VoS and treatment outcome is questionable. No significant differences could be shown with the other models (spline regression and categorical analysis) either.
e: Discrepant data, when the number is calculated for the individual categories separately by study years, 62,713 patients were calculated.
f: Applies if the annual VoS of the treating hospital increases by 1 case.
g: IQWiG's own calculation.
h: Read from Figure 1 of the Nimptsch 2017 study.
i: Read from Figure 2 of the Nimptsch 2017 study on the adjusted odds ratio; applies when the annual VoS of the treating hospital increases by 50 cases.
j: IQWiG's own calculation from information on the regression coefficient.
k: Values > 1 indicate an advantage for hospitals with high VoS.
IQR: interquartile range; M: mean value; N: number of patients included; n: number of patients with event; ND: no data; SD: standard deviation, VoS: volume of services

5.6.2 Morbidity

5.6.2.1 Results on the outcome “disease-free survival”

None of the studies included reported data on disease-free survival.

5.6.2.2 Results on the outcome “adverse effects of treatment”

Only the Avritscher 2014, Harrison 2018 and Smith 2017 studies reported results on serious, life-threatening or fatal infections. However, no usable results could be obtained from these studies.

The authors of the Harrison 2018 and Smith 2017 studies reported results on serious treatment-related complications. However, no usable results could be obtained from these studies.

5.6.3 Health-related quality of life including activities of daily living and dependence on the help of others

None of the studies included reported data on this outcome.

5.6.4 Results on further outcomes

5.6.4.1 Length of hospital stay

4 out of 23 included studies examined the length of hospital stay (see Table 15). However, no usable results could be obtained from 3 studies. Usable results were only available for the study Hollenbeck 2007b. Patients who underwent surgery in hospitals with a low volume of services were more likely to stay longer (beyond the 90th percentile of the respective study year) than patients in hospitals with a high volume of services (OR [95% CI]: 1.3 [1.0; 1.6]). However, no conclusion could be drawn regarding the significance of the observed difference, as the authors did not provide any specific information on the p-value. The volume of services per hospital was examined for the observation period.

In the Møller 2016 study, only mean values for the length of hospital stay were reported within the categories of volumes of services per hospital and year.

Across studies, there was no correlation between the volume of services per hospital and the quality of treatment outcome for length of hospital stay, with a low informative value of results.

Table 15: Results – length of hospital stay

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Length of hospital stay (%)	Adjusted odds ratio [95% CI]; p-value
Hollenbeck 2007b	**Extended length of hospital stay:** Patients whose hospital stay was longer then the 90th percentile within each study year	Total: 90 088[a, d] ND ND	VoS per hospital and over the 11-year observation period: Hospital with low VoS (lowest decile): M (SD): 3.6 (2.2) Hospital with high VoS (highest decile): M (SD): 116.3 (68.6)	 13.7 7.8	**Hospital with low VoS vs. hospital with high VoS (lowest decile vs. highest decile)[b]:** 1.3 [1.0; 1.6]; ND
Møller 2016	From time point of surgery	Total: 15 738 3190 3230 3026 3189 3103	VoS per hospital and year: 1st quintile: 1–75 2nd quintile: 77–112 3rd quintile: 114–155 4th quintile: 156–186 5th quintile: 189–287	Days (M): 9.60 9.82 9.88 9.61 9.33 9.35	No usable results[c]

a: Number of lung resections performed (lobectomy + pneumonectomy).
b: Values > 1 indicate an advantage for hospitals with high VoS.
c: No point estimate reported from adjusted analysis.
d: Within the results, data are reported only on pneumonectomy.
CI: confidence interval; M: mean value; N: number of included patients; ND: no data; VoS: volume of services

5.6.4.2 Re-admission

2 of the 23 studies included reported results on re-admission (see Table 16). However, no usable results could be obtained from 1 of these studies.

The Møller 2016 study reported statistically significant differences in favour of the higher quintiles for re-admission within 30 days, apart from the comparison of the reference category (1 to 75 lung resections per hospital and year) with the third quintile (114 to 155 lung resections per hospital and year).

For re-admission within 90 days, the picture was exactly the opposite of re-admission within 30 days. Only the comparison between the reference category and the third quintile (114 to 155 lung resections) showed a statistically significant result (OR [95% CI]: 0.85 [0.73; 0.98]).

Across studies, for re-admission, there was no correlation between the volume of services per hospital and the quality of treatment outcome due to the inconsistent results in view of the different operationalizations of re-admission and the data situation in 1 study; the informative value of results was low.

Table 16: Results – re-admission

Study	Definition of outcome	N	Information on volume of services (number of lung resections)	Re-admission raw n (%)	Adjusted odds ratio [95% CI]; p-value
Møller 2016	Re-admission to hospital (regardless of the reason for admission) within **30 days** of discharge after lung resection	**30 days**			
		Total: 15 738	VoS pro hospital and year:	3106 (20)	
		3190	1st quintile: 1–75	680 (22)	Reference category
		3230	2nd quintile: 77–112	607 (19)	0.86 [0.75; 0.99]; ND
		3026	3rd quintile: 114–155	610 (20)	0.90 [0.77; 1.04]; ND
		3189	4th quintile: 156–186	610 (19)	0.85 [0.73; 0.99]; ND
		3103	5th quintile: 189–287	599 (19)	0.82 [0.69; 0.97]; ND
	Re-admission to hospital (regardless of the reason for admission) within **90 days** of discharge after lung resection	**90 days**			
		Total: 15 738	VoS per hospital and year:	6855 (45)	
		3190	1st quintile: 1–75	1450 (47)	Reference category
		3230	2nd quintile: 77–112	1465 (47)	0.90 [0.79; 1.02][a]; ND
		3026	3rd quintile: 114–155	1301 (44)	0.85 [0.73; 0.98][a]; ND
		3189	4th quintile: 156–186	1314 (42)	0.88 [0.76; 1.03][a]; ND
		3103	5th quintile: 189–287	1325 (44)	0.93 [0.78; 1.10][a]; ND

CI: confidence interval; N: number of included patients; n: number of patients with events, ND: no data

5.6.5 Meta-analyses

A meta-analytical summary of the results was not performed for any of the reported outcomes, as the definition of the volume of services differed markedly between the studies. In addition, the studies considered different adjustment factors in their analyses. Furthermore, the operationalization of outcomes differed greatly between the studies.

5.6.6 Subgroup characteristics and other effect modifiers

Separate results for patients with different histological findings for the tumour were not reported in any of the included studies.

5.7 Summarizing assessment of results

A total of 23 studies were identified that investigated the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of lung carcinoma (research question 1a).

For the outcome category “mortality”, data were available on 4 outcomes. With regard to overall survival and treatment-related mortality, a (predominantly) positive correlation could be shown between the volume of services provided per hospital and per physician and the quality of treatment outcome, with a low informative value of results. With regard to in-hospital death, the studies identified a predominantly positive correlation between the volume of

services provided and the quality of treatment outcome, which considered lung resections as a whole. The studies that considered the correlation between the volume of services provided and the quality of treatment outcome separately according to the resection procedure, produced different results overall. A consistent correlation could not be derived for 30-day and 90-day mortality, as the studies came to different conclusions. None of the studies indicated a specific cause of death within this period, so that the outcome definition (30- and 90-day) lethality could not be used with sufficient certainty and therefore the term “mortality” was used.

No correlation between the volume of services provided and the quality of treatment outcome could be derived for length of hospital stay and re-admission, for which only a few usable results with a low informative value were available from a few studies.

No (usable) data were reported for the outcome category “morbidity” (which comprised disease-free survival, serious, life-threatening or fatal infections, and other serious treatment-related complications) and for health-related quality of life, including activities of daily living and dependence on the help of others. Thus, for these outcomes, no conclusion can be drawn on the correlation between the volume of services provided and the quality of treatment outcome.

It was not possible to draw a conclusion on the effects of minimum case numbers (introduced into the health care for the surgery of lung carcinoma and other lung cancers) on the quality of treatment outcome, as no meaningful studies were identified.

Table 17 summarizes the results of the included studies on the relevant outcomes.

Table 17: Overview of the observed differences in the results on the outcomes analysed and the correlation between the volume of services and the relevant outcomes

Intervention	Outcomes									
	Mortality				Morbidity			Quality of life	Further outcomes	
	Overall survival	Treatment-related mortality	30- and 90-day mortality	In-hospital death	Disease-free survival	Serious, life-threatening or fatal infections	Further serious treatment-related compli-cations	Health-related quality of life	Length of hospital stay	Re-admission
Differences in the results on outcomes after lung resection (low vs. high VoS)										
Lung resection	(↑)	(↑)	(↔)	(↑)	-	-	-	-	(↔)	(↔)
Lobectomy	-	(↑)	(↔)	(↔)	-	-	-	-	-	-
Pneumonec-tomy	-	(↔)[a]	(↔)	(↔)	-	-	-	-	-	-
Correlation between VoS and quality of treatment outcome										
	Positive correlation between the VoS per hospital and per physician and the quality of treatment outcome		No consistent correlation can be derived between the VoS and the quality of treatment outcome	Positive correlation between the VoS per hospital and the quality of treatment outcome	No conclusion possible			No conclusion possible	No correlation can be derived between the VoS and the quality of treatment outcome	

(↑): 1 or more studies with a low informative value show a statistically significant difference in the outcome in favour of hospitals and / or physicians with high VoS. Studies with non-statistically significant differences point in the same direction or do not call the association into question.
(↔): 1 or more studies with a low informative value and non-statistically significant effects or equally statistically significant and non-significant results.
- No (usable) data reported in the included studies.
a: Only 1 significant effect reported for 1 comparison.
VoS: volume of services

6 Discussion

The aim of this rapid report was to present and evaluate a possible correlation between the volume of services provided and the quality of treatment outcome in the surgical treatment of lung carcinoma or other malignant tumours in the lung. Further aims were the presentation of the effects of minimum case numbers specifically introduced into health care on the quality of treatment outcome. The background of the commissioning by the G BA was the initiation of a consultation procedure to determine a minimum volume for surgery of lung carcinoma.

A total of 23 studies were identified that investigated the correlation between the volume of services and the quality of treatment outcome in the surgical treatment of lung carcinoma (research question 1a). No studies could be identified for research question 1b. With regard to research question 2, no meaningful studies could be identified that investigated the effect of minimum case numbers specifically introduced into health care on the quality of treatment outcome. In 4 studies, no usable results could be identified for the evaluation of the correlation between the volume of services and the treatment outcome. The 23 included studies contained no information on palliative surgical cases.

For most outcomes of the outcome category “mortality”, a (predominantly) positive correlation between the volume of services per hospital or physician and the quality of treatment outcome was shown, with a low informative value of results. However, the results did not allow conclusions to be drawn on a specific minimum volume, since the results from comparisons of individual volumes of services with 1 reference category are heterogeneous. With regard to the outcome category “mortality”, the operationalizations of the studies that contained data on the respective outcomes overlapped. For example, the studies Birkmeyer 2002, Birkmeyer 2003, Birkmeyer 2006, Hollenbeck 2007a and Hollenbeck 2007b defined operative mortality as death before discharge from hospital or within 30 days after surgery or during surgery. Therefore, the outcome “in-hospital death” would also be covered here. The definitions of the 30-day and 90-day mortality and treatment-related mortality also overlapped to some extent. Nevertheless, a corresponding allocation to the individual outcomes was made. A more transparent definition of outcomes by the authors of the studies would have enabled a clearer allocation to the respective outcomes.

The studies did not contain any data on the outcomes “disease-free survival” and “health-related quality of life” (including activities of daily living and dependence on the help of others). This could result from the fact that the authors of the studies primarily used administrative data sources, which offer only a limited data basis and thus limited analysis options.

All 23 studies were observational studies; 21 studies could be used for the assessment of the volume of services solely at the hospital level. One study examined the volume of services at both the hospital and physician level. The volume of services solely at the physician level was also examined by 1 study. Thus, it is unclear for the majority of the studies to what extent the individual expertise of the medical personnel affected the results. The effects of the different

characteristics of the study population on the results could also not be conclusively assessed on the basis of the available data. In the studies, risk factors were mainly adjusted at the patient level. Eleven studies also adjusted for risk factors at the physician and/or hospital level. In this context, Nimptsch already pointed out in 2017 that, due to the use of administrative data, insufficient information on the characteristics of the physician or hospital was available to adequately consider risk factors at all 3 levels [57]. In almost all studies, the factors age, sex and comorbidity were adjusted at the patient level, but factors such as severity of the disease, tumour stage, tumour size or histological findings were not. Only 1 to 6 studies adjusted for these factors.

In the included studies, primarily administrative data / discharge data were used as the data basis. Administrative data entail a certain information deficit, as clinical information, such as diagnostic data and/or severity classifications of the disease, are often missing [53,57]. However, if, for example, administrative data are additionally linked to clinical data, as was done in some of the included studies [46,47,50,61] (linking of SEER-Medicare data), it may be assumed that more information was available for analysis at the patient level. In principle, however, the extent to which a comprehensive information base can be drawn upon also depends on the respective structure of the databases used and the respective health care system. In the inpatient setting in Germany, for example, a flat-rate remuneration system (diagnosis-related-group [DRG]-system) is used primarily to depict the services provided and, to a lesser extent, the diagnosis-related constellations. However, the use of flat rates per case does not allow a detailed depiction of the services provided, but only the recording of service batches. In addition, administrative data are collected by many groups of people or institutions, such as physicians or hospitals, etc. This can lead to missing data or inconsistencies as well as errors at the beginning and in the course of the documentation chain and at later points in time during data collection [66,67]. Since the studies did not provide sufficient information on the structure and content of the databases / registries used, limitations exist with regard to the data basis.

The above comments show that the result of a lung resection in patients with lung carcinoma is influenced by a large number of factors, which in turn influence each other. None of the studies included fully considered these factors. Stukenborg 2004 questioned whether there was actually sufficient adjustment for the different factors at the patient level in their study [62].

7 Conclusion

In total, 23 observational studies could be included to investigate the correlation between the volume of services provided and the quality of treatment outcome in the surgical treatment of lung carcinoma; 19 of these studies contained usable data. The informative value of results was low in all studies.

For overall survival, treatment-related mortality, and in-hospital death, a positive correlation between the volume of services provided and the quality of treatment outcome could mostly be shown. Thus, a higher mortality rate is to be assumed with a lower volume of services. Across studies, the available data only showed an inconsistent correlation between the volume of services and the quality of treatment outcome for 30- and 90-day mortality, since different conclusions on this outcome were drawn in the studies.

For outcomes additionally identified (length of hospital stay and re-admission), for which only few usable results were available, it was not possible to derive a correlation between the volume of services per hospital and the quality of treatment outcome.

No (usable) data were reported for the outcome category “morbidity” (comprising disease-free survival, serious, life-threatening or fatal infections, and other serious treatment-related complications) and health-related quality of life, so that no conclusion can be drawn here on the correlation between the volume of services and the quality of treatment outcome.

No relevant studies could be identified to investigate the correlation between the volume of services and the quality of treatment outcome with regard to surgical treatment of other malignant tumours in the lung. No meaningful studies could be identified for the investigation of the effects of minimum case numbers specifically introduced into health care on the quality of treatment outcome with regard to the surgical treatment of lung carcinoma or other malignant tumours in the lung.

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The full report (German version) is published under

https://www.iqwig.de/en/projects-results/projects/health-care/v18-03-relationship-between-volume-of-services-and-quality-of-treatment-outcome-for-lung-cancer-rapid-report.10698.html.

Appendix A – Search strategies

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) 1946 to January Week 5 2019
- Ovid MEDLINE(R) Daily Update February 07, 2019
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations 1946 to February 07, 2019
- Ovid MEDLINE(R) Epub Ahead of Print February 07, 2019

#	**Searches**
1	exp Lung Neoplasms/
2	((lung* or bronchus*) and (cancer* or carcinoma* or metastas*)).ti,ab.
3	mesothelioma*.ti,ab.
4	or/1-3
5	surgery.fs.
6	(resection* or lobectom* or surger*).ti,ab.
7	(surgical* adj1 (procedure* or treatment*)).ti,ab.
8	or/5-7
9	and/4,8
10	Pneumonectomy/
11	pneumonectomy*.ti,ab.
12	(pulmonary* adj1 (lobectomy* or metastasectomy*)).ti,ab.
13	or/10-12
14	or/9,13
15	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
16	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.
17	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
18	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) adj2 (volume* or caseload* or experience* or characteristic* or performance*)).ab,ti.
19	((improve* adj2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
20	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
21	(referral* adj3 (selective* or volume* or rate*)).ti,ab.

#	**Searches**
22	or/15-21
23	and/14,22
24	23 not (exp animals/ not humans.sh.)
25	24 not (comment or editorial).pt.
26	..l/ 25 yr=2000-Current

2. Embase

Search interface: Ovid

- Embase 1974 to 2019 February 07

#	**Searches**
1	exp lung tumor/
2	lung non small cell cancer/
3	lung small cell cancer/
4	pleura mesothelioma/
5	((lung* or bronchus*) and (cancer* or carcinoma* or metastas*)).ti,ab.
6	mesothelioma*.ti,ab.
7	or/1-6
8	exp cancer surgery/
9	lobectomy/
10	lymphadenectomy/
11	metastasis resection/
12	(resection* or lobectom* or surger*).ti,ab.
13	(surgical* adj1 (procedure* or treatment*)).ti,ab.
14	or/8-13
15	and/7,14
16	lung resection/
17	lung lobectomy/
18	pneumonectomy*.ti,ab.
19	(pulmonary* adj1 (lobectomy* or metastasectomy*)).ti,ab.
20	or/16-19
21	or/15,20
22	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
23	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.

#	Searches
24	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
25	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) adj2 (volume* or caseload* or experience* or characteristic* or performance*)).ab,ti.
26	((improve* adj2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
27	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
28	(referral* adj3 (selective* or volume* or rate*)).ti,ab.
29	or/22-28
30	and/21,29
31	30 not medline.cr.
32	31 not (exp animal/ not exp human/)
33	32 not (Conference Abstract or Conference Review or Editorial).pt.
34	..l/ 33 yr=2000-Current

3. The Cochrane Library

Search interface: Wiley

- Cochrane Database of Systematic Reviews: Issue 2 of 12, February 2019
- Cochrane Central Register of Controlled Trials: Issue 2 of 12, February 2019

ID	Search
#1	[mh "Lung Neoplasms"]
#2	((lung* or bronchus*) and (cancer* or carcinoma* or metastas*)):ti,ab
#3	mesothelioma*:ti,ab
#4	#1 or #2 or #3
#5	[mh /SU]
#6	(resection* or lobectom* or surger*):ti,ab
#7	(surgical* NEAR/1 (procedure* or treatment*)):ti,ab
#8	#5 or #6 or #7
#9	#4 and #8
#10	[mh ^"Pneumonectomy"]
#11	pneumonectomy*:ti,ab
#12	(pulmonary* NEAR/1 (lobectomy* or metastasectomy*)):ti,ab
#13	#10 or #11 or #12

ID	Search
#14	#9 or #13
#15	((minim* or high* or low or patient or outcome* or importance*) NEAR/3 (volume* or caseload)):ti,ab
#16	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) NEAR/2 (factor* or effect*)):ti,ab
#17	((hospital* or center* or centre* or unit*) NEAR/5 (type or level or small* or size)):ti,ab
#18	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) NEAR/2 (volume* or caseload* or experience* or characteristic* or performance*)):ti,ab
#19	((improve* NEAR/2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)):ti,ab
#20	((surgeon* or surgical* or physician* or provider* or specialist*) NEAR/3 outcome*):ti,ab
#21	(referral* NEAR/3 (selective* or volume* or rate*)):ti,ab
#22	#15 or #16 or #17 or #18 or #19 or #20 or #21
#23	#14 and #22 with Cochrane Library publication date Between Jan 2000 and Dec 2019, in Cochrane Reviews
#24	#14 and #22 with Cochrane Library publication date Between Jan 2000 and Dec 2019, in Trials

4. Health Technology Assessment Database

Search interface: Centre for Reviews and Dissemination

Line	Search
1	MeSH DESCRIPTOR Lung Neoplasms EXPLODE ALL TREES
2	((lung* or bronchus*) and (cancer* or carcinoma* or metastas*))
3	(mesothelioma*)
4	#1 OR #2 OR #3
5	(resection* or lobectom* or surger*)
6	(surgical* NEAR1 (procedure* or treatment*))
7	#5 OR #6
8	#4 AND #7
9	MeSH DESCRIPTOR Pneumonectomy
10	(pneumonectomy*)
11	(pulmonary* NEAR1 (lobectomy* or metastasectomy*))
12	#9 OR #10 OR #11

Line	Search
13	((minim* or high* or low or patient or outcome* or importance*) NEAR3 (volume* or caseload))
14	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) NEAR2 (factor* or effect*))
15	((hospital* or center* or centre* or unit*) NEAR5 (type or level or small* or size))
16	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) NEAR2 (volume* or caseload* or experience* or characteristic* or performance*))
17	((improv* NEAR2 outcome*) AND (hospital* or center* or centre* or unit* or surgeon*))
18	((surgeon* or surgical* or physician* or provider* or specialist*) NEAR3 outcome*)
19	(referral* NEAR3 (selective* or volume* or rate*))
20	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
21	#8 OR #12
22	#20 AND #21
23	(#22) FROM 2000 TO 2019
24	(#23) IN HTA