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Relationship between volume of services and quality of treatment outcome for complex oesophageal interventions[1]

Extract

[1] Translation of Chapters 1 to 7 of the rapid report V19-04 *Zusammenhang zwischen Leistungsmenge und Qualität des Behandlungsergebnisses bei komplexen Eingriffen am Organsystem Ösophagus* (Version 1.0; Status: 24 April 2020 [German original], 8 July 2020 [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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Key statement

Research question

The aims of this investigation are to

- present and assess the relationship between volume of services (VoS) and quality of treatment outcome in complex oesophageal interventions (research question 1),
- present studies which investigate the extent to which the quality of treatment outcome is impacted by minimum numbers of cases introduced in the healthcare system for complex oesophageal interventions (research question 2).

As supplementary information, the surgical procedures included in and excluded from the studies considered relevant are described in detail.

Conclusion

For the investigation of the relationship between VoS and quality of treatment outcome in complex oesophageal interventions (research question 1), a total of 37 observational studies were included, of which 30 contained usable data. Only 1 study had a high informative value of results.

For hospital VoS, a correlation between VoS and quality of treatment outcome was found for several operationalizations regarding the outcome of mortality. For the outcome of treatment-related complications (anastomotic insufficiency), likewise, a correlation was found between VoS and quality of treatment outcome on the basis of a study with high informative value of results. A correlation was also found with regard to the outcome of failure to rescue. For the additionally defined outcome of rehospitalization, a study with low informative value of results revealed a correlation between VoS and quality of treatment outcome to the disadvantage of high-VoS hospitals.

Regarding physician VoS, for the outcome of mortality, a correlation between VoS and quality of treatment outcome was found only for the operationalization of inpatient mortality. For the outcome of treatment-related complications (anastomotic insufficiency), a study of high informative value of results likewise showed a correlation between VoS and quality of treatment outcome.

No studies of meaningful interpretive value were found to investigate the extent to which the quality of treatment outcome is impacted by specific minimum numbers of cases introduced in the healthcare system for complex oesophageal interventions (research question 2).

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List of abbreviations

Abbreviation	Meaning
AHA	American Heart Association
CIHI	Canadian Institute for Health Information
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
NHS	National Health Service
RCT	Randomized controlled trial
SEER	Surveillance, Epidemiology and End Results Program
SGB	Sozialgesetzbuch (Social Code Book)
VoS	Volume of services

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 (VoS) 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 hospital VoS 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 VoS 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 concrete 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 the treatment outcomes is dependent on the VoS 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 minimum volumes which are binding in Germany in accordance with §137a (3), Sentence 1, No. 2 Social Code Book V.

These minimum volume rules are binding for hospitals registered in accordance with §108 SGB V and specify in which cases a hospital may render the services for which minimum volumes have been set forth [7]. Hospitals may render the services in question only if the hospital owner annually declares vis-a-vis the state associations of the statutory health insurers that the specified minimum volume will be met in the next year as well [7]. However, some exceptions apply. For instance, minimum volumes generally do not apply in case of emergency. In addition, state authorities responsible for hospital planning can define exceptions for services where the implementation of minimum volume rules may jeopardize state-wide service provision to the population.

The current annual minimum volume for complex oesophageal interventions is 10 treatments per hospital site [7].

Complex interventions on the oesophageal system

Surgical procedures on the oesophagus are considered complex interventions or high-risk surgery; in the absence of an acute emergency, they are typically performed as plannable procedures [8-10]. According to the G-BA's minimum volume rules, the complex interventions comprise partial, subtotal, and total oesophagectomy as well as complex oesophageal reconstruction. Other surgical interventions on the oesophagus, such as the implantation or exchange of a magnetic reflux management system, are also included in the complex interventions defined in the minimum volume rules [7].

No general definition of the term "complex intervention" is available in the literature or in medical textbooks [11]. Some publications refer to examples of complex interventions in various specialities [12-16]. However, the scores used to determine an intervention’s degree of complexity differ between individual specialities [17-20].

The oesophagus is a muscular hollow organ about 25 centimetres in length. The upper part of the oesophagus is situated directly posterior to the trachea and anterior to the spine. The inferior part of the oesophagus passes through the diaphragm and meets the stomach. At the entrance to the stomach, a muscular sphincter prevents the reflux of acid and food into the oesophagus [21].

Oesophageal interventions are commonly performed to treat malignant neoplasms [9,22]. In 2015, about 83% of patients treated with complex oesophageal interventions had been diagnosed with malignant neoplasms of the oesophagus [9]. However, other diseases, e.g. benign neoplasms of the upper gastrointestinal tract, diverticula, or achalasia (impaired relaxation of muscles in the lower oesophagus) may also require surgical procedures on the oesophagus [9]. Oesophagectomy is the key curative treatment step in non-metastatic adenocarcinoma and squamous cell carcinoma of the oesophagus [23,24]. Complex oesophageal interventions are generally performed on seriously ill patients (e.g. patients with oesophageal cancer) and substantially impact their further survival [8]. Between 2010 and 2015, various inpatient mortality rates were calculated, ranging from 8.7% in 2014 to 10.3% in 2013 [9].

Oesophagectomy is the complete or partial surgical removal of the oesophagus. Oesophagectomy is followed by oesophageal reconstruction. Different transabdominal and transthoracic variants of oesophagectomy and oesophageal reconstruction exist [23]. The oesophageal intervention consequently consists of 2 parts: resection and reconstruction. Oesophagectomy is also referred to as a two-cavity operation since it involves both the thorax and the abdomen. Both in centres with a high volume of services (VoS) and in centres with a low VoS, the two-cavity operation is increasingly performed minimally invasively in both abdomen and thorax and in any hybrid constellation (minimally invasively or in combination with open surgery) [25]. The introduction of new medical technology and techniques, e.g. minimally invasive and robot-assisted minimally invasive surgery, has reportedly created a new learning curve impacting the quality of treatment outcome in complex oesophageal interventions, even in high-VoS hospitals. This influences particularly the relationship between the physician VoS and the quality of treatment outcome in these complex interventions [26].

2 Research question

The aims of this investigation are to

- present and assess the relationship between VoS and quality of treatment outcome in complex oesophageal interventions (research question 1),
- present studies which investigate the extent to which the quality of treatment outcome is impacted by minimum numbers of cases introduced in the healthcare system for complex oesophageal interventions (research question 2).

As supplementary information, the surgical procedures included in and excluded from the studies considered relevant are described in detail.

3 Course of the project

3.1 Project timeline

On 18/04/2019, 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 relationship between VoS and quality of treatment outcome in complex oesophageal interventions.

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 adult patients who underwent complex oesophageal interventions.

4.1.2 Volume of services

The VoS was defined as the number of performed complex oesophageal interventions 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
  - intraoperative or perioperative mortality
  - inpatient mortality
- Morbidity, such as
  - disease-free survival
  - adverse effects of therapy, such as
    - anastomotic insufficiency
    - anastomotic stenosis
    - perioperative and postoperative bleeding
    - pulmonary complications
    - 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
- Length of hospital stay

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

4.1.4 Study types

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

For 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 complex oesophageal interventions, the quality of the treatment outcome is materially influenced by individual risk factors such as the underlying disease, type of procedure, comorbidities, and complication management. 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 VoS.

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 which had to be met by studies included in the assessment.

Table 1: Overview of inclusion and exclusion criteria for controlled interventional studies

Inclusion criteria	
I1.1	Patients who had a complex oesophageal intervention (also see Section 4.1.1)
I1.2	Study intervention: use of a minimum number of cases (also see Section 4.1.4)
I1.3	Comparator intervention: use of a different or no minimum number of cases (also see Section 4.1.4)
I1.4	Outcomes as formulated in Section 4.1.3
I1.5	Controlled interventional studies as formulated in Section 4.1.4
I1.6	Adjustment as formulated in Section 4.1.5
I1.7	Publication date of January 2000 or later
I1.8	Full publication available[a]
I1.9	Studies which are transferable to the German healthcare system (also see Section 4.1.8)
Exclusion criterion	
E1	Multiple publications without relevant additional information

a: In this context, a study report in accordance with ICH E3 [27] or a report about the study which met the criteria of the TREND statement [28] and allowed an assessment of the study was considered a full publication, so long as the information on 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

Table 2: Overview of inclusion and exclusion criteria for observational studies

Inclusion criteria	
I2.1	Patients who had a complex oesophageal intervention (also see Section 4.1.1)
I2.2	Investigation of the relationship between the VoS and the quality of the treatment outcome (also see Section 4.1.2)
I2.3	Outcomes as formulated in Section 4.1.3
I2.4	Observational studies as formulated in Section 4.1.4
I2.5	Adjustment as formulated in Section 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	
E1	Multiple publications without relevant additional information

a: In this context, a study report in accordance with ICH E3 [27] or a report about the study which met the criteria of the STROBE statement [29] 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

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 [30], for inclusion criteria I1.1/I2.1 (population), I1.2 (use of a minimum number of cases), and I1.3 (comparator intervention with respect to the study's comparator group), and/or I2.2 (VoS), and I1.9/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 inclusion criteria I1.1/I2.1, I1.2/I2.2, and I1.3 as well as I1.9/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 Information retrieval

4.2.1 Focused information retrieval to search for systematic reviews

In preparation of the comprehensive information retrieval, a search for systematic reviews was conducted in the databases of MEDLINE and Cochrane Database of Systematic Reviews as well as on the websites of the National Institute for Health and Care Excellence (NICE) and the Agency for Healthcare Research and Quality (AHRQ). The search was restricted to publication dates of January 2000 or later.

The search strategies for the search in bibliographic databases are found in Appendix A. The search was conducted on 28/08/2019.

The final decision as to which systematic review(s) met the report's inclusion criteria was taken after completing the project outline.

4.3 Comprehensive information retrieval for primary studies

4.3.1 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 [30]. The following primary and further information sources as well as search techniques were considered:

Primary information sources

- Bibliographic databases
  - MEDLINE
  - Embase
  - Cochrane Central Register of Controlled Trials

Further information sources and search techniques

- Use of further search techniques
  - screening of reference lists of systematic reviews found (see Section 4.2.1)
- Requests to authors

4.3.2 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 the additionally considered information sources were screened for studies by 1 reviewer. The studies found were then checked for relevance. The entire process was then checked by a 2nd reviewer. Any discrepancies in any of the listed selection steps were resolved by discussion between the 2 reviewers.

4.4 Information synthesis and analysis

4.4.1 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 so long as 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.

4.4.2 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 relationships [31-33]. 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 relationship between VoS 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 [34]. 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 impacting the informative value of results. Based on the entirety of these quality criteria, the observational studies were categorized by quality into those with high versus low informative value of results.

4.4.3 Assessment of the risk of bias

The risk of bias of the results of the included controlled interventional studies was assessed in accordance with General Methods Version 5.0, Chapter 9 [30].

4.4.4 Summary assessment of information

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

Since categorical analysis is associated with a loss of information (e.g. the linearity assumption may be violated within the individual categories) and might deliver less reliable results than continuous analysis [33], results of continuous modelling were preferred over results from categorical modelling and included in the report, provided that potential non-linear relationships were adequately taken into account in continuous modelling. However, if the studies presented results exclusively from 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 metaanalytical methods were used [30]. A final summary assessment of the information was performed in any case. Where possible, results reported on subgroups (e.g. intervention-specific analyses) were presented separately and summarized.

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 are found in Appendix A. The most recent search was conducted on 13 November 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.

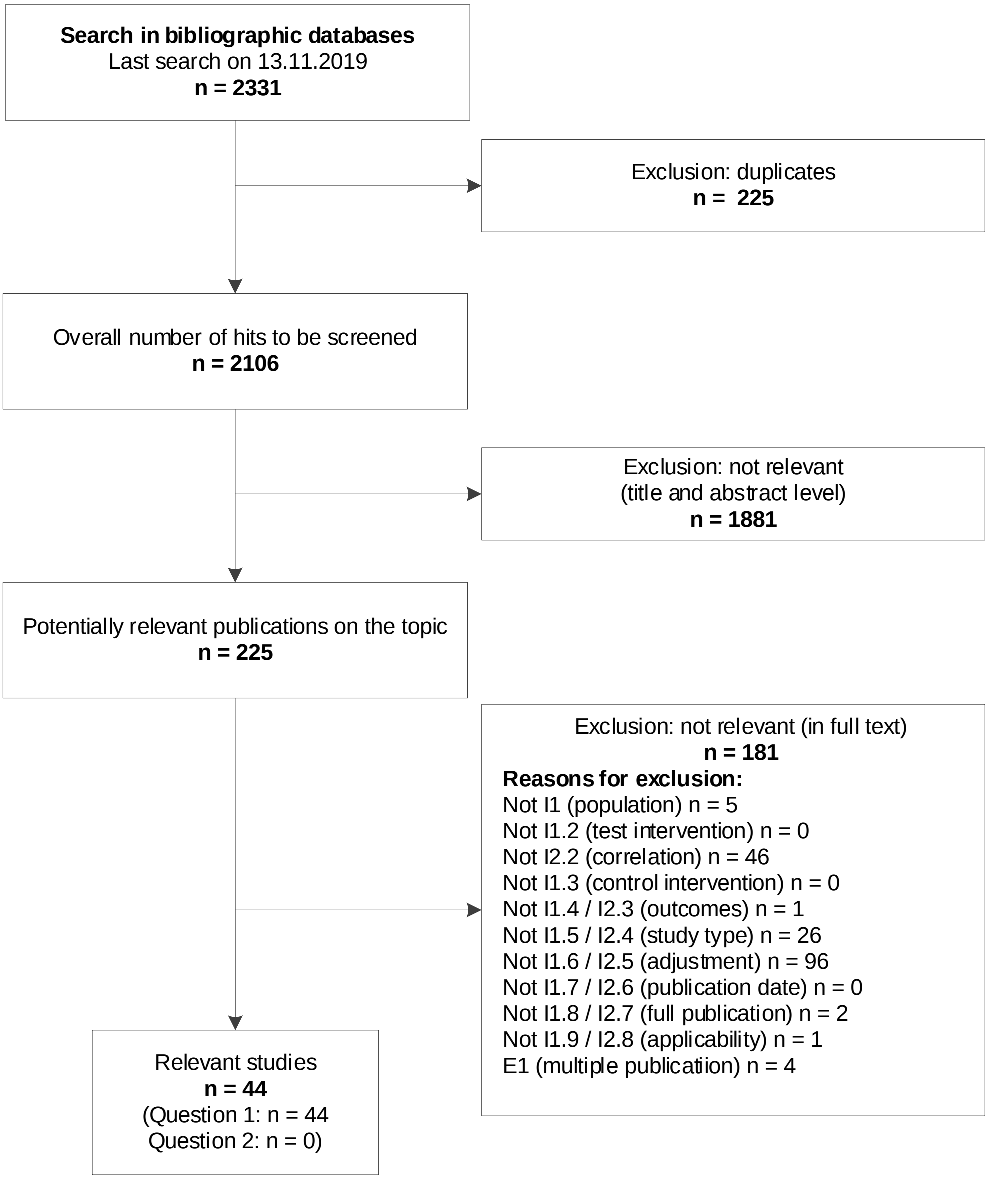

Figure 1: Result of the bibliographic search and study selection

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 focused information retrieval, 12 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.

5.1.2.3 Further relevant studies

The following relevant study, which was not already identified via other search steps, was found on research question 1 (Table 3):

Table 3: Additionally identified relevant studies

Study	Full publication (in professional journals)
Hentschker 2018	Yes [35]

5.2 Resulting study pool

Through the various search steps, a total of 45 relevant studies (45 documents) were found for research question 1 (see also Table 4). The corresponding references are found in Section 9.1 of the full report. Eight studies [36-43] analysed exclusively data from the 1980s and 1990s. Given their outdated evidence, these studies were excluded from the further investigation since the majority of the studies with more current data are likely to provide results of more informative value to answer research question 1. For the further investigation, this left 37 studies to answer research question 1.

No pertinent studies were found to answer research question 2.

Table 4: Study pool for research question 1

Study	**Full publication (in professional journals)**
Allareddy 2010	Yes [44]
Austin 2013	Yes [45]
Avritscher 2014	Yes [46]
Birkmeyer 2006	Yes [47]
Birkmeyer 2007	Yes [48]
Christian 2003	Yes [49]
Clark 2019	Yes [50]
Derogar 2013	Yes [51]
Dikken 2012	Yes [52]
El Amrani 2019	Yes [53]
Ely 2019	Yes [54]
Fedeli 2012	Yes [55]
Finks 2011	Yes [56]
Finley 2011	Yes [57]
Fischer 2017	Yes [58]
Funk 2011	Yes [59]
Gasper 2009	Yes [60]
Ghaferi 2011	Yes [61]
Harrison 2018	Yes [62]
Henneman 2014	Yes [63]
Hentschker 2018	Yes [35]
Ho 2006	Yes [64]
Hollenbeck 2007b	Yes [65]
In 2016	Yes [66]
Kim 2016	Yes [67]
Kothari 2016	Yes [68]
Kozower 2012	Yes [69]
Learn 2010	Yes [70]
Mamidanna 2016	Yes [71]
Modrall 2018	Yes [72]
Nimptsch 2018	Yes [9]
Reames 2014	Yes [73]
Sahni 2016	Yes [74]
Sheetz 2016	Yes [75]
Simunovic 2006	Yes [76]
Varghese 2011	Yes [77]
Wasif 2019	Yes [78]

(continued)

Table 4: Study pool for research question 1 (continued)

Study	**Full publication (in professional journals)**
Studies which analysed data exclusively from the 1980s and 1990s (excluded from further assessment)	
Bilimoria 2008	Yes [36]
Birkmeyer 2002	Yes [37]
Birkmeyer 2003	Yes [38]
Finlayson 2003	Yes [39]
Hollenbeck 2007a	Yes [40]
Kuo 2001	Yes [41]
Urbach 2004	Yes [42]
Wenner 2005	Yes [43]

5.3 Characteristics of the studies included in the assessment

The characteristics of the studies included for research question 1 are presented in Table 5 and summarized below.

Table 5: Characteristics of the studies included for research question 1

Study / study design[a] (data source)	**Recruitment country / follow-up period[b] / study objective**	**Inclusion and exclusion criteria**	**Surgical intervention**	**Total number of units**	**Definition of VoS**
Allareddy 2010 / retrospective observational study (NIS data)	USA / 2000–2003 / investigation of the relationship between hospital VoS and inpatient complications	▪ Age: ≥ 18 years ▪ Performance of oesophagectomy (ICD-9 codes: 42.4, 42.4x, 42.5, 42.5x, 42.6 or 42.6x), coronary artery bypass grafting, percutaneous coronary intervention, elective surgical repair of abdominal aortic aneurysm, or pancreatectomy	Oesophagectomy	2473[c]	Thresholds as per Leapfrog for the oesophagectomy volume per hospital and year: ▪ Low VoS: < 13 ▪ High VoS: ≥ 13
Austin 2013 / retrospective observational study (CIHI and RPDB data)	Canada / 01/04/2002–31/03/2011 / investigation of the relationship between hospital VoS and 30-day mortality	▪ Age: > 18 years ▪ Performance of oesophagectomy, colon or rectal resection (due to colorectal carcinoma) or pancreaticoduodenectomy with unambiguous reference to an ICD-10 code or CCI code for the surgical indication	Oesophagectomy	1305[c, d]	Ranges for the oesophagectomy volume per hospital and year: ▪ Quartile 1: 1–4 ▪ Quartile 2: 5–13 ▪ Quartile 3: 14–21 ▪ Quartile 4: 22–42
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 relationship between hospital VoS and serious postoperative infections	▪ Residents of Texas, USA ▪ Age: ≥ 18 years ▪ Resection of 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	Oesophagectomy	265[c]	For all indications, hospitals were classified into terciles specifically on the basis of case counts within the 5-year observation period.

(continued)

Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Birkmeyer 2006 / retrospective observational study (national Medicare claims data and data from the SEER database)	USA / 2000–2002 / investigation of the relationship 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	Oesophagectomy	71 558[d]	Hospitals categorized into quintiles based on VoS in the 3-year observation period: No thresholds were indicated for the oesophagectomy volume per hospital and year: ▪ 1st quintile (low VoS) ▪ 2nd quintile ▪ 3rd quintile ▪ 4th quintile ▪ 5th quintile (high 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 relationship between hospital VoS and 5-year survival rate	▪ Age: 65–99 years ▪ Resection of primary lung, bladder, colon, oesophageal, pancreatic, or gastric carcinoma	Oesophagectomy	822[d]	Hospitals categorized into terciles based on the average weighted VoS from multiple years. Range of oesophagectomy volumes per hospital and year: ▪ Low VoS: 0.3–3.8 ▪ Moderate VoS: 3.8–13.7 ▪ High VoS: 14.4–107.0

(continued)

Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	**Recruitment country / follow-up period[b] / study objective**	**Inclusion and exclusion criteria**	**Surgical intervention**	**Total number of units**	**Definition of VoS**
Christian 2003 / retrospective observational study (UHC data)	USA / 1999–2000 / investigation of the relationship between hospital VoS and operative mortality (before hospital discharge)	▪ Performance of oesophagectomy (ICD-9 codes: 42.4, 42.4x, 42.5, 42.5x, 42.6 or 42.6x), surgical treatment of abdominal aortic aneurysm, coronary artery bypass grafting, or carotid endarterectomy	Oesophagectomy	1634	Hospital VoS was analysed on the basis of 3 different methodologies: (1) Analysis of VoS as a continuous variable (2) On the basis of thresholds as per Leapfrog for the volume of oesophagectomies per hospital and year: ▪ Low VoS: < 7 ▪ High VoS: ≥ 7 (3) By means of hospital categorization into quantiles on the basis of the variation in VoS per hospital and year used in (2): ▪ Quartile 1: < 3 (< 50% of threshold) ▪ Quartile 2: 3–6 (> 50% to < 100% of threshold) ▪ Quartile 3: 7–9 (> 100% to < 150% of threshold) ▪ Quartile 4: ≥ 10 (> 150% of threshold)

(continued)

Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Clark 2019 / retrospective observational study (SID and HCUP data)	USA / 2007–2013 / investigation of the relationship between hospital VoS and operative mortality (before hospital discharge), perioperative complications, and extended length of hospital stay (> 14 days after surgery)	▪ Age: ≥ 18 years ▪ Elective resection of oesophageal cancer in a hospital in the states of New York or Florida	(Partial or total) Oesophagectomy	4330	(1) Thresholds as per Leapfrog for the volume of oesophagectomies per **hospital** and year: ▪ Low VoS: < 20 ▪ High VoS: ≥ 20 (2) Thresholds as per Leapfrog for the volume of oesophagectomies per **physician** and year: ▪ Low VoS: < 7 ▪ High VoS: ≥ 7
Derogar 2013 / retrospective observational study (data from the Swedish cancer, patient, and cause of death register)	Sweden / 1987–2005 / investigation of the relationship between hospital or physician VoS and all-cause mortality	▪ Resection of oesophageal cancer	Oesophagectomy	1335[c]	Ranges for the volume of oesophagectomies per **hospital** and year: ▪ Quartile 1–2: 1–8 ▪ Quartile 3: 9–16 ▪ Quartile 4: ≥ 17 Ranges for the volume of oesophagectomies per **physician** and year: ▪ Quartile 1–2: 1–4 ▪ Quartile 3: 5–9 ▪ Quartile 4: ≥ 10

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Dikken 2012 / retrospective observational study (NCR data)	Netherlands / 1989–2009 / investigation of the relationship between hospital VoS and all-cause survival (survival at 3 months and 3 years postoperatively)	▪ Resection of carcinoma of the oesophagus or cardia of stomach	Oesophagectomy	10 025	Thresholds for the volume of oesophagectomies per hospital and year: ▪ Very low VoS: 1–5 ▪ Low VoS: 6–10 ▪ Moderate VoS: 11–20 High VoS: ≥ 21
El Amrani 2019 / retrospective observational study (PMSI discharge data)	France / 2012–2017 / investigation of the relationship between hospital VoS and postoperative mortality (within 90 days postoperatively or until hospital discharge)	▪ Age: ≥ 18 years ▪ Residents of France ▪ Resection of oesophageal, colon, gastric, liver, pancreatic, or rectal carcinoma	Oesophagectomy	4608[c]	Thresholds for the volume of oesophagectomies per hospital and year: ▪ Low VoS: < 41 ▪ High VoS: ≥ 41
Ely 2019 / retrospective observational study (internal data from KPNC)	USA / 2009–2016 / investigation of the relationship between hospital or physician VoS and length of hospital stay as well as postoperative complications within 30 days (incl. mortality and rehospitalizations)	▪ Age: ≥ 18 years ▪ Resection of oesophageal cancer	Oesophagectomy	461	Thresholds for the volume of oesophagectomies **per hospital or physician** and year: ▪ Low VoS: < 5 ▪ High VoS: ≥ 5

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Fedeli 2012 / retrospective observational study (discharge data of the hospitals in the Veneto region)	Italy / 2000–2009 / investigation of the relationship between hospital VoS and perioperative mortality (up to hospital discharge or within 30 days) as well as 90-day mortality	▪ Resection of oesophageal or gastric carcinoma	▪ (Partial or total) Oesophagectomy ▪ Oesophagogastrectomy	1189[c, d]	Hospital VoS was analysed on the basis of continuous data.
Finks 2011 / retrospective observational study (U.S. Medicare data [incl. MedPAR])	USA / 1999–2008 / investigation of the relationship between hospital VoS and operative mortality (up to hospital discharge or within 30 days)	▪ Age: 65–99 years ▪ Performance of oesophagectomy, pancreas resection, lung resection, cystectomy, surgical treatment of abdominal aortic aneurysm, coronary artery bypass grafting, carotid endarterectomy, or aortic valve replacement surgery with unambiguous reference to an ICD-9 code for the surgical indication ▪ Excluded were patients with ruptured aortic aneurysm, presence of thoracic aneurysm or both and patients with coronary artery bypass grafting and concurrent valve replacement	Oesophagectomy	43 756[c, d]	N/A

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Finley 2011 / retrospective observational study (CIHIDAD discharge data)	Canada / 1998–2007 / investigation of the relationship between hospital VoS and inpatient mortality as well as length of hospital stay	▪ Age: ≥ 18 years ▪ Performance of oesophagectomy	Oesophagectomy	6985	Mean volume of oesophagectomies per hospital and year: ▪ Low VoS: ≤ 6 ▪ Moderate VoS: 7–19 ▪ High VoS: ≥ 20 Hospital VoS was additionally analysed on the basis of continuous data.
Fischer 2017 / retrospective observational study (NOGCA data)	UK / 2011–2013 / investigation of the relationship between hospital or physician VoS and all-cause 30-day or 90-day mortality as well as anastomotic leaks	▪ Curative resection of oesophageal or gastric carcinoma ▪ No hospitals performing < 10 interventions per year	Oesophagectomy or resection of gastric carcinoma at the oesophagogastric junction	4868[c]	Volume ranges of oesophagectomies performed **per hospital** and year: ▪ Quartile 1: ≤ 49 ▪ Quartile 2: 50–65 ▪ Quartile 3: 66–91 ▪ Quartile 4: 92–148 Volume range of oesophagectomies performed **per physician** and year: ▪ Quartile 1: ≤ 5 ▪ Quartile 2: 6–9 ▪ Quartile 3: 10–13 ▪ Quartile 4: 14–28 Hospital VoS was additionally analysed on the basis of continuous data.

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Funk 2011 / retrospective observational study (national MedPAR and AHA survey data)	USA / 2004–2007 / investigation of the relationship between hospital VoS and mortality (within 30 days postoperatively or up to hospital discharge)	▪ Age: ≥ 65 years ▪ Resection of a (benign or malignant) oesophageal tumour	(Partial or total) Oesophagectomy	4498	VoS thresholds for oesophagectomies per hospital within the 4-year observation period: ▪ Low VoS: 1–6 ▪ Moderate VoS: 7–32 ▪ High VoS: ≥ 33
Gasper 2009 / retrospective observational study (OSHPD discharge data)	USA / 1995–2004 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Age: ≥ 18 years ▪ Diagnosis of oesophageal carcinoma with performance of oesophagectomy (ICD-9 codes: 42.4–42.6 or 43.99) or diagnosis of carcinoma of the exocrine pancreas or islets of Langerhans, duodenum, bile duct, or ampulla of Vater with pancreatectomy or diagnosis of a hepatocellular carcinoma with partial hepatectomy and unambiguous reference to an ICD-9 code	Oesophagectomy/oesophagus resection	2404[c]	VoS thresholds for oesophagectomies / oesophagus resections per hospital within the 5-year observation period: ▪ Quintile 1: < 6 ▪ Quintile 2: 6–10 ▪ Quintile 3: 11–20 ▪ Quintile 4: 21–30 ▪ Quintile 5: > 30
Ghaferi 2011 / retrospective observational study (data from the Centers for Medicare and Medicaid Services)	USA / 2005-2007 / investigation of the relationship between hospital VoS and inpatient mortality or 30-day mortality as well as 8 serious postoperative complications	▪ Age: 65–99 years ▪ Performance of oesophagectomy, gastrectomy, or pancreatectomy due to cancer	Oesophagectomy	3443[c, d, f]	Mean number (range) of oesophagectomies per hospital and year: ▪ Quintile 1: < 1.3 (1–4) ▪ Quintile 2: N/A ▪ Quintile 3: N/A ▪ Quintile 4: N/A ▪ Quintile 5: > 15 (15–102)

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Harrison 2018 / retrospective observational study (SID and HCUP data)	USA / 2009–2011 / investigation of the relationship between hospital VoS and inpatient mortality, length of hospital stay, and postoperative complications	▪ Age: ≥ 18 years ▪ Performance of oesophagectomy or lobectomy/pneumonectomy for confirmed diagnosis of oesophageal or lung cancer	Oesophagectomy	1324[c]	Thresholds for the number of oesophagectomies per hospital and year: ▪ Low VoS: < 20 ▪ High VoS: ≥ 20
Henneman 2014 / retrospective observational study (data from the Netherlands Cancer Registry)	Netherlands / 1989–2009 / investigation of the relationship between hospital VoS and all-cause mortality after 6 and 24 months.	▪ Resection of invasive, non-metastatic oesophageal carcinoma	Oesophagectomy	10 025	Ranges for the volume of oesophagectomies per hospital and year: ▪ Quartile 1: 1–20 ▪ Quartile 2: 21–40 ▪ Quartile 3: 41–60 ▪ Quartile 4: > 60
Hentschker 2018 / retrospective observational study (billing data of the umbrella organization of company health insurance funds in Germany)	Germany / 2005–2007 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Performance of a complex surgical intervention at the oesophagus or pancreas; liver, kidney, or stem cell transplantation; implantation of total knee endoprosthesis or coronary artery bypass grafting	Complex oesophageal interventions (not further specified)	9673[c, d]	Annual hospital VoS was analysed using 2 different procedures: (1) by means of continuous data (2) by means of the MV defined by law: ▪ MV not reached: < 5 (2005) or < 10 (2006 and 2007) ▪ MV reached: ≥ 5 (2005) or ≥ 10 (2006 and 2007) (3) by means of hospital categorization into terciles

(continued)

Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	**Recruitment country / follow-up period[b] / study objective**	**Inclusion and exclusion criteria**	**Surgical intervention**	**Total number of units**	**Definition of VoS**
Ho 2006 / retrospective observational study (discharge data from statewide hospital discharge abstract files)	USA / 1988–2000 / investigation of the relationship between physician VoS and operative mortality until hospital discharge	▪ Data from hospitals in the US states of Florida, New Jersey, and New York ▪ Resection of oesophageal carcinoma (ICD-9 codes: 42.40, 42.41, 42.42 or 43.99) or bronchial, colon, or rectal carcinoma or performance of Whipple procedure (duodenopancreatectomy)	(Partial or total) Oesophagectomy	10 023[c]	VoS is reported as the average volume **per hospital or per physician** for the individual time periods (1988–1991, 1992–1996, 1997–2000). Hospital or physician VoS was analysed on the basis of continuous data.
Hollenbeck 2007b / retrospective observational study (HCUP NIS data)	USA / 1993–2003 / investigation of the relationship between hospital VoS and operative mortality up to hospital discharge and/or length of hospital stay	▪ Resection of oesophageal, lung, prostate, bladder, pancreatic, or liver carcinoma with unambiguous ICD-9 code for the surgical indication	Oesophagectomy	4020[c]	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 number of cases within the observation period.
In 2016 / retrospective observational study (NCDB data)	USA / 2007–2011 / investigation of the relationship between hospital VoS and all-cause mortality 30 and/or 90 days postoperatively	▪ Age: ≥ 18 years ▪ Resection of nonmetastatic gastro-oesophageal carcinoma	Oesophagectomy	15 796	Ranges for the average volume of oesophagectomies per hospital and year: ▪ Quartile 1: 1–3 ▪ Quartile 2: 4-9 ▪ Quartile 3: 10–20 ▪ Quartile 4: > 20

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Kim 2016 / retrospective observational study (discharge data of participating hospitals and AHA surveys)	USA / 2000–2011 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Age: ≥ 21 years ▪ No referral to another hospital ▪ Resection of oesophageal, lung, colon, pancreatic, or rectal carcinoma	Oesophagectomy	4827[c]	No differentiation between hospitals with low vs. high VoS. Reported were the mean and maximum volumes in the years 2000 and 2011 as well as the mean and SD for the entire observation period. In addition, quartiles were reported: ▪ Quartile 1: 2 ▪ Quartile 2: 4 ▪ Quartile 3: 12 ▪ Quartile 4: 20
Kothari 2016 / retrospective observational study (data from SID, HCUP, and AHA surveys)	USA / 2007–2011 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Age: ≥ 18 years ▪ Resection of an oesophageal, pancreatic, or rectal carcinoma in a hospital in Florida or California	▪ (Partial or total) Oesophagectomy	1540[c]	Thresholds for the volume of oesophagectomies per hospital and year: ▪ Low VoS: < 20 ▪ High VoS: ≥ 20
Kozower 2012 / retrospective observational study (NIS discharge data)	USA / 2007 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Performance of oesophagectomy (ICD-9 codes: 42.4, 42.40, 42.41, 42.42, and 43.99) or resection of oesophageal carcinoma	▪ Oesophagectomy	1210	Range of oesophagectomy figures per hospital and year: ▪ Quintile 1: 1 ▪ Quintile 2: 2 ▪ Quintile 3: 3 ▪ Quintile 4: 4–7 ▪ Quintile 5: 8–120 Hospital VoS was additionally analysed on the basis of continuous data.

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Learn 2010 / retrospective observational study (HCUP NIS discharge data)	USA / 1997–2006 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Age: ≥ 18 years ▪ Resection of oesophageal, lung, pancreatic, or gastric carcinoma with unambiguous ICD-9 code (42.40, 42.41, 42.42) for the surgical indication	▪ Partial or total oesophagectomy (not further specified)	3440[c, d]	Thresholds for the number of oesophagectomies per hospital and year (classification 1997–1999): ▪ Low VoS: 1–2 ▪ Moderate VoS: 3–6 ▪ High VoS: > 6
Mamidanna 2016 / retrospective observational study (HES data from NHS)	USA / 2000–2010 / investigation of the relationship between physician VoS and operative mortality within 30 days postoperatively (before hospital discharge)	▪ Age: ≥ 18 years ▪ First elective resection of oesophageal, gastric, or pancreatic carcinoma ▪ No emergency surgeries	▪ Oesophagectomy	16 572[c]	Physicians were categorized on the basis of mean annual case numbers: ▪ Low VoS: 2–8 ▪ Moderate VoS: 9–12 ▪ High VoS: 13–29
Modrall 2018 / retrospective observational study (NIS data)	USA / 2003–2009 / investigation of the relationship between physician VoS and operative mortality up to hospital discharge	▪ Open oesophagectomy (ICD-9 codes: 42.40–42.42, 42.51–42.59)	▪ Open oesophagectomy	2883[c]	Thresholds for mean volume of open oesophagectomies **per physician** and year: ▪ Low VoS (< 90[th] percentile) < 5[g] ▪ High VoS (≥ 90[th] percentile): ≥ 5[g]

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Nimptsch 2018 / retrospective observational study (DRG statistics)	Germany / 2010–2015 / investigation of the relationship between hospital VoS and inpatient mortality, frequency of complications, and complication-associated mortality	Adult patients (< 20 years of age) with a complex oesophageal intervention	▪ Total oesophagus resection ▪ Gastrectomy with subtotal oesophagus resection ▪ Partial oesophagus resection ▪ Reconstruction of oesophageal passage: ▫ as a separate procedure ▫ with splenectomy ▫ cholecystectomy ▫ with resection of other abdominal organs[g]	22 681[d]	The classification of hospitals by VoS was done on the basis of the case volume for the observation period of 2010 through 2015 (median [IQR]): ▪ Very low VoS: 2 (1–4) ▪ Low VoS: 10 (9–11) ▪ Moderate VoS: 15 (14–17) ▪ High VoS: 26 (23–32) ▪ Very high VoS: 62 (49–76) ▪ **Post hoc analysis:** Hospitals were classified into terciles by VoS on the basis of case volume for the observation period of 2010 through 2015 (median [IQR]): ▪ Lower tercile: 1 (1–2) ▪ Middle tercile: 5 (3–7) ▪ Upper tercile: 14 (11–22)

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	**Recruitment country / follow-up period[b] / study objective**	**Inclusion and exclusion criteria**	**Surgical intervention**	**Total number of units**	**Definition of VoS**
Reames 2014 / retrospective observational study (national Medicare data [incl. MedPAR])	USA / 2000–2009 / investigation of the relationship between hospital VoS and surgical mortality (up to hospital discharge or 30 days after surgery)	▪ Age: 65–99 years ▪ Performance of oesophagectomy, colectomy, or pancreatectomy, or one of 3 other cardiac and 2 vascular procedures, with unambiguous reference to an ICD-9 code for the surgical indication	Oesophagectomy (open, laparoscopic, and minimally invasive)	29 630[c, d]	Hospital VoS was analysed for 2-year periods using 2 different methodologies: (1) by means of continuous data (2) by means of thresholds for the volume of oesophagectomies per hospital and year: ▪ Very low VoS: < 2[h] or < 3[h] ▪ Low VoS: N/A ▪ Moderate VoS: N/A ▪ High VoS: N/A ▪ Very high VoS: > 12[h] or > 17[h] or > 18[h]

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	**Recruitment country / follow-up period[b] / study objective**	**Inclusion and exclusion criteria**	**Surgical intervention**	**Total number of units**	**Definition of VoS**
Sahni 2016 / retrospective observational study (U.S. Medicare data [incl. MedPAR])	USA / 2008–2013 / investigation of the relationship between physician VoS and mortality 30 days after hospital admission	▪ Age: ≥ 66 years ▪ Physicians with appropriate expertise ▪ Resection of lung, bladder, pancreatic, or oesophageal carcinoma (or performance of cardiovascular surgery) with unambiguous ICD-9 code for the surgical indication	▪ Other total gastrectomy ▪ Oesophagectomy (not further specified) ▪ Intrathoracic oesophagostomy ▪ Intrathoracic oesophagogastrostomy ▪ Intrathoracic oesophageal anastomosis with interposition of small bowel ▪ Other intrathoracic oesophagoenterostomy ▪ Intrathoracic oesophageal anastomosis with interposition of large bowel ▪ Other intrathoracic oesophagocolostomy	3314[c]	Physicians were categorized by VoS on the basis of annual volume of surgeries: ▪ Quartile 1: 0.4 ▪ Quartile 2: 0.9 ▪ Quartile 3: 1.9 ▪ Quartile 4: 6.0

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Sahni 2016 (continued)			▪ Intrathoracic oesophageal anastomosis with other interposition ▪ Other intrathoracic anastomosis of the oesophagus ▪ Antesternal oesophagostomy ▪ Antesternal oesophagogastros-tomy ▪ Antesternal oesophageal anastomosis with interposition of small bowel ▪ Other antesternal oesophagoenteros-tomy ▪ Antesternal oesophageal anastomosis with interposition of large bowel ▪ Other antesternal oesophagocolos-tomy		

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Sahni 2016 (continued)			▪ Other antesternal oesophageal anastomosis with interposition ▪ Other antesternal anastomosis of the oesophagus ▪ Partial oesophagectomy ▪ Total oesophagectomy		
Sheetz 2016 / retrospective observational study (U.S. Medicare data [incl. MedPAR])	USA / 2007–2010 / investigation of the relationship of hospital VoS and 30-day mortality, major complications, and failure to rescue	▪ Patients who underwent colectomy, pancreas resection, oesophagectomy, surgical treatment of abdominal aorta aneurysm, revascularization of the lower limbs, amputation of the lower limbs, with unambiguous ICD-9 code for the surgical indication ▪ Excluded were patients < 65 years of age	▪ Oesophagectomy	13 361[c, d]	Hospitals categorized into quintiles by VoS: ▪ Very low ▪ Low ▪ Moderate ▪ High ▪ Very high

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Table 5: Characteristics of the studies included for research question 1 (continued)

Study / study design[a] (data source)	Recruitment country / follow-up period[b] / study objective	Inclusion and exclusion criteria	Surgical intervention	Total number of units	Definition of VoS
Simunovic 2006 / retrospective observational study (data from the Ontario Cancer Registry, CIHI, and RPDB)	Canada / 1990–2000 / investigation of the relationship between hospital VoS and inpatient mortality	▪ Patients with an initial diagnosis of cancer of the oesophagus, lung, breast, colon, or liver ▪ Resection of oesophageal, lung, breast, colon, or liver carcinoma	Oesophagus resection with anastomosis	629[c]	Hospitals were categorized by increasing VoS on the basis of a 3-year surgery volume: ▪ Low VoS: ≤ 7 ▪ Low to moderate VoS: 8–19 ▪ Moderate to high VoS: 20–43 ▪ High VoS: ≥ 44
Varghese 2011 / retrospective observational study (Washington State CHARS discharge data)	USA / 2000–2007 / investigation of the relationship between hospital VoS and length of hospital stay, rehospitalization within 30 days after hospital, discharge into an inpatient care facility, need for revision surgery, or 90-day mortality	▪ Age: ≥ 18 years ▪ Performance of elective oesophagectomy (ICD-9 codes: 42.40-42.42, 42.52, 42.62, 43.5, and 43.99) without complex reconstructions ▪ Residence in the State of Washington, USA ▪ Excluded were patients who died within 14 days after surgery	▪ Oesophagectomy ▪ Oesophagogastrec-tomy ▪ Intrathoracic oesophagogastros-tomy ▪ Antesternal oesophagogastros-tomy ▪ Partial gastrectomy with anastomosis to the oesophagus	1352[c]	Thresholds for oesophagectomy volume per hospital and year: ▪ Low VoS: < 13 ▪ High VoS: ≥ 13
Wasif 2019 / retrospective observational study (NCDB data)	USA / 2003–2011 / investigation of the relationship between hospital VoS and 30-day and/or 90-day mortality	▪ Surgery of the oesophagus, colon, liver, or pancreas without metastatic disease or with a palliative treatment goal	Oesophagectomy	17 617[c]	Range of cancer-related oesophagectomies per hospital and year[i]: ▪ Low VoS (< 33rd percentile): 1–3[h] ▪ Moderate VoS (34th to 67th percentiles): 3–9[h] ▪ High VoS (≥ 68th percentiles): 7–63[h]

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Table 5: Characteristics of the studies included for research question 1 (continued)

a: If a study, e.g. secondary data analysis / registry study, specified a data source, it is entered here.
b: In secondary data analyses / registry studies, for instance, the follow-up duration is the data collection period.
c: Number of performed procedures on the oesophagus.
d: IQWiG calculations.
e: Only a general reference is made to surgical interventions in cancer patients (“cancer-directed surgery”).
f: Patient volume in hospitals in VoS quintile 1 (n = 1883) and VoS quintile 5 (n = 1560).
g: Throughout most of the observation period.
h: Thresholds varied between the 2-year analysis periods (Reames 2014) and in the individual years of the observation period (Wasif 2019).
i: The VoS definition differs between the publication’s text and abstract.

AHA: American Hospital Association; CCi: Canadian Classification of Interventions; CHARS: Comprehensive Hospital Abstract Reporting Systems; CIHI(DAD): Canadian Institute for Health Information (Discharge Abstract Database); DRG: diagnosis-related group; HCUP(NIS): Healthcare Cost and Utilization Project (Nationwide Inpatient Sample); HES: Hospital Episode Statistic; HIV: human immunodeficiency virus; ICD: International Classification of Diseases; ICU: intensive care unit; KPNC: Kaiser Permanente Northern California; MedPAR: Medicare Provider Analysis and Review files; MV: minimum volume; NCDB: National Cancer Data Base; NCI: National Cancer Institutes; NCR: Netherlands Cancer Registry; NHS: National Health Service; NIS: National Inpatient Sample; NOGCA: National Oesophago-Gastric Cancer Audit; OSHPD: California Office of Statewide Health Planning and Development; PMSI: national database of the Programme de Médicalisation des Systèmes d’Information; RPDB: Ontario Registered Persons Database; SD: standard deviation; SEER: Surveillance Epidemiology and End Results Program; SID: State Inpatient Databases; UHC: University HealthSystem Consortium Clinical Database; VATS: video-assisted thoracoscopic surgery; VoS: volume of services; vs.: versus

5.3.1 Study design and data source

The 37 included studies were retrospective observational studies.

Five studies [56,61,73-75] used administrative data from the U.S. Centers for Medicare and Medicaid Services. 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 and 19.3% by Medicaid [79]. Another 2 studies used Medicare data linked with the registry of the U.S. Surveillance Epidemiology and End Results Program (SEER) [47,48]. Eight studies used databases of the Healthcare Cost and Utilization Project (U.S. National (Nationwide) Inpatient Sample, State Inpatient Database). These databases include comprehensive information on inpatient care [44,50,62,65,68-70,72].

Austin 2013, Finley 2011, and Simunovic 2006 used data from the National Cancer Registry in Ontario and/or the database of the Canadian Institute for Health Information (CIHI) as well as the Ontario Registered Persons Database (RPDB). Derogar 2013, Dikken 2012, Henneman 2014, In 2016, and Wasif 2019 likewise used data from national cancer registries.

The German studies Hentschker 2018 and Nimptsch 2018 used billing data from the umbrella organization of company health insurance funds in Germany as well as the DRG statistics.

Avritscher 2014 employed data from the Texas Discharge Research Dataset. Christian 2003 used administrative data from the database of the University HealthSystem Consortium.

El Amrani 2019, Fedeli 2012, Gasper 2009, Ho 2006, Kim 2016, and Varghese 2011 conducted analyses of past hospitalizations' billing data from national/regional databases. Kim 2016 additionally analysed surveys from the American Heart Association (AHA). These AHA surveys were also analysed by Funk 2011, using them alongside data on hospital inpatient services (MedPAR).

Ely 2019 used internal data of Kaiser Permanente Northern California. Fischer 2017 used data from the U.K. National Oesophago-Gastric Cancer Audit. Mamidanna 2016 analysed hospital statistics from the National Health Service (NHS).

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

Twenty-five of the 37 studies were conducted in the USA [44,46-50,54,56,59-62,64-70,72-75,77,78], 3 studies in Canada [45,57,76], 2 studies in the UK [58,71], 2 studies in Germany [9,35], 2 studies in the Netherlands [52,63], and 1 study each in France [53], Italy [55], and Sweden [51].

The studies' follow-up periods ranged from 1 year [69] to 21 years [63].

The objectives of 35 studies comprised, at minimum, the investigation of the relationship between VoS and mortality or survival rates. One study investigated the relationship between VoS and complications during the inpatient stay [44]. Avritscher 2014 analysed the correlation between VoS and serious postoperative infections. In addition to the outcome of mortality, several studies additionally investigated effects on further outcomes such as postoperative complications, length of hospital stay, or need for revision surgery due to complications [9,50,54,58,61,62,75,77].

5.3.3 Key inclusion and exclusion criteria of the studies

Specific information regarding age restrictions specified for the study population was provided by 25 of the 37 studies. The data varied from ≥ 18 years [44-48,50,54,57,58,60,62,68,70,71,77], ≥ 20 years [80], ≥ 21 years [67], ≥ 65 years [75], to 65 through 99 years [47, 48, 56, 61, 73] and ≥ 66 years [74].

Six studies focused exclusively on the surgical treatment of oesophageal cancer [50,51,54,59,63,69]. Only the intervention, but not the corresponding indication, was reported by 12 studies [35,44,45,49,56,57,72,73,75,77,80]. The remaining 19 studies included not only the resection of oesophageal carcinoma, but also carcinoma resection or interventions in other organ systems such as the stomach, pancreas, colon, liver, and/or lung.

5.3.4 Surgical interventions

Twenty-two studies reported oesophagectomy/oesophagus resection as the surgical intervention, without providing any further detail [44-49,51-54,56,57,60-63,65,66,69,71,75,78]. Clark 2019, Fedeli 2012, Funk 2011, Ho 2006, Kim 2016, Kothari 2016, and Learn 2010 distinguished between partial and total oesophagectomy. Fedeli 2012 additionally included oesophago-gastrectomies. Alongside oesophagectomy, Fischer 2017 looked at resections of gastric cancer at the oesophagogastric junction. Simunovic 2006 included oesophagectomies with anastomosis.

Reames 2014 distinguished between open laparoscopic and minimally invasive oesophagectomy. Modrall 2018, in contrast, considered only open oesophagectomy.

Hentschker 2018 focused on complex oesophageal interventions as per the wording of the G-BA’s minimum volume rules.

Nimptsch 2018, Sahni 2016, and Varghese 2011 listed the surgical interventions at the oesophagus in great detail (see Table 5). Annex C of the full report lists the employed intervention/procedure codes in detail.

5.3.5 Definition of VoS

In 28 of the 37 included studies, VoS was defined as the number of procedures performed per hospital and year. Out of these 28 studies, 3 studies additionally defined the VoS as the number of procedures performed annually per physician [50,51,58]. Four studies defined VoS exclusively per physician and year [54,64,72,74].

Specific thresholds to distinguish hospitals and/or physicians with high versus low VoS were reported by 8 studies [35,44,53,54,62,68,72,77]. Christian 2003 and Clark 2019 used the thresholds of the Leapfrog Group, amongst others. The Leapfrog Group is a U.S. nonprofit organization aiming to improve the quality and safety of healthcare [81]. In addition, Christian 2003 analysed hospital VoS as a continuous variable as well as VoS quintiles. Avritscher 2014, Birkmeyer 2007, Finley 2011, Funk 2011, Learn 2010, Mamidanna 2016, and Wasif 2019 reported thresholds or ranges for distinguishing hospitals with high, moderate, and low VoS. Funk 2011 analysed VoS for the observation period of 4 years.

Based on the number of procedures performed in the 3-year observation period, Simunovic 2006 categorized hospitals by VoS into low versus low to moderate versus moderate to high versus high and reported specific thresholds. Fedeli 2012 analysed hospital VoS using continuous data. These data were provided as supplementary information by Henneman 2014 as well. Ho 2006 reported VoS as a mean per hospital and physician for the individual periods (e.g. 1997 through 2000) and also analysed VoS using continuous data. Hentschker 2018 analysed hospital VoS using continuous data and additionally using the minimum volumes legally required in Germany for complex oesophageal interventions.

Twelve studies categorized the VoS per hospital and/or physician into quartiles or quintiles and reported the corresponding ranges or specific thresholds [45,47,49,51,58,60,61,63,66,67,69,74]. In Gasper 2009, thresholds were defined on the basis of VoS in the 5-year observation period. While Avritscher 2014 stated that the VoS per hospital or physician was classified as low, moderate, or high based on the case numbers in the observation period, no specific thresholds were reported. Avritscher 2014 analysed VoS for the observation period of 5 years. Similarly, Sheetz 2016 categorized hospital VoS into very low, low, moderate, high, and very high but did not report specific thresholds.

Nimptsch 2018 and Reames 2014 classified hospital VoS as very low, low, moderate, high, and very high. Nimptsch 2018 defined these categories using the case volume in the observation period (6 years). In addition, the authors performed a post hoc analysis, for which hospital VoS was categorized into terciles for the specified 6-year observation period. Reames 2014 analysed VoS for 2-year periods, as described above, as well as on the basis of continuous data.

Only Finks 2011 provided no information about the definition of VoS.

5.3.6 Data on the study population

The key characteristics of the study populations for research question 1 are presented in Appendix B, Table 20 of the full report and summarized below.

The 37 studies analysed different volumes of patients and/or cases of oesophageal interventions. These volumes ranged from 265 [46] to 43 756 [56]. Specific information on age was provided by 36 of the 37 studies. Only 1 study did not report any information on age [47]. In 30 studies, the composition of the study population was additionally broken down by sex. The remaining 7 studies did not report any data on this topic.

Data on underlying diseases were provided by 24 of the 37 studies [9,46-48,50-55,58-60,62,63, 65,66,69-72,74,76,78]. Four studies investigated oesophageal as well as gastric cardia carcinoma and/or gastric carcinoma or Barett's oesophagus [52,55,58,59,63]. Nimptsch 2018 listed the considered underlying diseases in great detail. They included malignant neoplasms of the oesophagus, malignant neoplasms of neighbouring organs or secondary malignant neoplasms, oesophageal perforation, benign neoplasms of the upper gastrointestinal tract, diverticulosis, achalasia, and obstruction of oesophagus.

Data on patient comorbidities were reported in 25 studies [44,48-51,53,54,56-62,64,66,68-71, 73-75,77,78].

5.4 Assessment of the informative value of results

Table 6 presents the informative values of results. For 1 study (Fischer 2017), the informative value of results was rated as high. This rating was due to high-quality data, adequate patient flow, adequate consideration of cluster effects as well as risk adjustment, adequate handling of missing data, and adequate reporting of relevant aspects.

For each of the other 36 studies, the informative value of results was rated as low. This was particularly due to data being of low quality or incomplete, lack of information on patient flow, non-consideration of relevant risk factors, and unclear information on the handling of missing data.

All but 2 studies [65,77] described in detail the methods used to adequately account for cluster effects. Hollenbeck 2007b referred to the SUDAAN software (statistical software for the analysis of correlated data) without describing the exact procedure. While Varghese 2011 stated merely generally that cluster effects on the hospital level were taken into account, the statistical method was not described. For both studies, this aspect was therefore rated as "unclear" in the assessment of the informative value of results.

Only Fischer 2017 adjusted for risk factors on all 3 levels (patient, hospital, and physician). In 18 studies, the authors adjusted for factors on the patient level only, and in 15 studies, for factors on the patient and hospital level. The remaining studies adjusted for factors on the patient level and on the physician level. On the patient level, the adjustment typically included factors such as age, sex, ancestry, comorbidities, and year of surgery. Few studies adjusted for the underlying disease or the type of surgical procedure. Some of the studies adjusting for factors on the physician level accounted for speciality in addition to physician VoS. As essential factors on the hospital level, most studies considered VoS as well as academic status.

Table 7 and Table 8 show an overview of the relevant risk factors accounted for in the studies on the level of patients, physicians, and hospitals.

In 7 studies, the authors exclusively conducted a continuous analysis of VoS [50,55,57,58,64, 67,70]. Both continuous and categorical VoS analyses were performed in 7 other studies [9,35,49,69,71,73,74]. Two studies conducted neither continuous nor categorical VoS analysis: Finks 2011 reported no information on VoS analysis, while Sheetz 2016 presented the relative explanatory value of the VoS alongside other patient and hospital characteristics. The remaining 21 studies each conducted a categorical analysis of the VoS.

Information on a check of model quality was reported in only 6 studies, and data on the validation of the statistical models used, in only 4 studies.

Table 6: Informative value of results

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
Allareddy 2010	No	Unclear	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	In part	Yes	None	Low
Austin 2013	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Unclear	In part	Yes	None	Low
Avritscher 2014	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	Yes	Yes	None	Low
Birkmeyer 2006	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	In part	No	None	Low
Birkmeyer 2007	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Unclear	In part	Yes	None	Low
Christian 2003	Unclear	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	Yes	Yes	None	Low
Clark 2019	Unclear	Unclear	Continuous	Unclear	Yes	Yes	No[b,c]	Unclear	No	Unclear	No	Yes	Voluntary nature of hospital participation unclear	Low
Derogar 2013	Yes	Yes	Categorical	Yes	Yes	Yes	No[b]	Yes	No	Unclear	Yes	Yes	None	Low
Dikken 2012	Yes	Yes	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	In part	Yes	None	Low

(continued)

Table 6: Informative value of results (continued)

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
El Amrani 2019	Yes	Unclear	Categorical	Unclear	Yes	Yes	No[b,c]	Unclear	No	Unclear	Yes	Yes	▪ Voluntary nature of hospital participation unclear ▪ VoS threshold defined depending on outcome.	Low
Ely 2019	Unclear	Unclear	Categorical	Yes	Yes	Yes	Unclear	Unclear	No	Unclear	In part	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low
Fedeli 2012	Yes	Unclear	Continuous	Unclear	Yes	Yes	No[b,c]	Unclear	No	Unclear	Yes	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low

(continued)

Table 6: Informative value of results (continued)

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
Finks 2011	No	Unclear	Other[d]	Unclear	Yes	Yes	No[b,c]	Unclear	No	Unclear	No	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low
Finley 2011	Unclear	Unclear	Continuous	Yes	Yes	Yes	No[b,c]	Unclear	No	No	Yes	Yes	Voluntary nature of hospital participation unclear	Low
Fischer 2017	Yes	Yes	Continuous	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Voluntary nature of hospital participation unclear	High
Funk 2011	No	Unclear	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	No	In part	Yes	Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective.	Low
Gasper 2009	Yes	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Unclear	In part	Unclear	None	Low
Ghaferi 2011	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	No	In part	No	Voluntary nature of hospital participation unclear	Low
Harrison 2018	No	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Unclear	Yes	No[e]	Voluntary nature of hospital participation unclear	Low

(continued)

Table 6: Informative value of results (continued)

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
Henneman 2014	Unclear	Yes	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Yes	In part	Yes	Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective.	Low
Hentschker 2018	Yes	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[c]	Yes	No	Unclear	Yes	Yes	None	Low
Ho 2006	Unclear	Unclear	Continuous	Unclear	Yes	Yes	No[c]	Unclear	No	Unclear	In part	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low
Hollenbeck 2007b	Unclear	Unclear	Categorical	Yes	Yes	Unclear	No[b,c]	Unclear	Yes	Unclear	In part	Yes	None	Low
In 2016	Unclear	Yes	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	Yes	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low

(continued)

Table 6: Informative value of results (continued)

Study	**High quality of individual data**[a]	**Adequate patient flow**	**Volume analysis**	**Plausible procedure for determining the volume thresholds**	**Suitable model class**	**Adequate procedure for considering cluster effects**	**Adequate risk adjustment**	**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**
Kim 2016	Unclear	Unclear	Continuous	Unclear	Yes	Yes	No[c]	Unclear	Yes	Unclear	In part	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low
Kothari 2016	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Yes	No	Yes	Voluntary nature of hospital participation unclear	Low
Kozower 2012	No	No	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[b,c]	Unclear	Yes	Yes	In part	Yes	None	Low
Learn 2010	Yes	Unclear	Continuous	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	Yes	Yes	None	Low
Mamidanna 2016	Yes	Yes	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[b]	Unclear	No	Unclear	Yes	Yes	Voluntary nature of hospital participation unclear	Low
Modrall 2018	Unclear	No	Categorical	No	Yes	Yes	No[c]	Yes	No	Unclear	Yes	No	Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective.	Low

(continued)

Table 6: Informative value of results (continued)

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for determining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
Nimptsch 2018	Yes	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[b,c]	Unclear	Yes	Unclear	In part	No	None	Low
Reames 2014	No	Yes	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[b,c]	Unclear	Yes	Yes	Yes	No	None	Low
Sahni 2016	No	Unclear	▪ Continuous ▪ Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	In part	Yes	None	Low
Sheetz 2016	Unclear	Unclear	▪ Other[f]	Unclear	Yes	Yes	No[c]	Unclear	Yes	Unclear	No	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low
Simunovic 2006	Yes	Unclear	Categorical	Yes	Yes	Yes	No[c]	Unclear	No	Unclear	Yes	Yes	None	Low
Varghese 2011	Unclear	Yes	Categorical	Yes	Yes	Unclear	No[b,c]	Yes	No	No	Yes	No	Voluntary nature of hospital participation unclear	Low

(continued)

Table 6: Informative value of results (continued)

Study	High quality of individual data[a]	Adequate patient flow	Volume analysis	Plausible procedure for deter-mining the volume thresholds	Suitable model class	Adequate procedure for considering cluster effects	Adequate risk adjustment	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
Wasif 2019	Unclear	Unclear	Categorical	Yes	Yes	Yes	No[b,c]	Unclear	No	Unclear	Yes	Yes	▪ Investigation of the relationship between VoS and quality of the treatment outcome was not the primary study objective. ▪ Voluntary nature of hospital participation unclear	Low

a: "Yes" or "no" was stated only if unambiguous information was available for the specific study.
b: No risk adjustment on the hospital level.
c: No risk adjustment on the physician level.
d: No information on this topic found in the study.
e: Representation of results without taking into account cluster effects.
f: Relative explanatory value of the VoS together with other patient and hospital characteristics.
VoS: volume of services

Table 7: Patient-level risk factors considered in the adjustment

Study	Risk adjustment level																								
	Patient																								
	Age	**Sex**	**Ancestry**	**Underlying disease**	**Comorbidities**	**Severity of disease**	**Lymph node involvement**	**Presence of metastases**	**Tumour stage**	**Tumour localization**	**Histological findings / grading**	**Year of diagnosis**	**Type of surgical procedure**	**Day of the week of surgery**	**Year of surgery**	**Accompanying treatment**	**Inpatient complications**	**Time span between inpatient admission and surgery**	**Length of hospital stay**	**Urgency of inpatient admission**	**Transfer to another acute-care hospital**	**Place of residence**	**Socioeconomic status[a]**	**Social deprivation**	**Type of health insurance**
Allareddy 2010	x	x	-	x	x	-	-	-	-	-	-	-	x	-	x	-	-	-	-	x	-	-	-	-	-
Austin 2013	x	x	-	-	x	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Avritscher 2014	x	x	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	-	-
Christian 2003	x	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	x	x	-	-	-	x
Clark 2019	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x
Derogar 2013	x	x	-	-	x	-	-	-	x	-	x	-	-	-	x	x	-	-	-	-	-	-	-	-	-
Dikken 2012	x	x	-	-	-	-	-	-	x	-	x	x	-	-	-	x	-	-	-	-	-	-	x	-	-
El Amrani 2019	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ely 2019[a]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fedeli 2012	x	x	-	-	x	-	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-
Finks 2011	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-	x	-	-
Finley 2011	x	x	-	-	x	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Fischer 2017	x	x	-	-	x	x	x	-	x	x	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-

(continued)

Table 7: Patient-level risk factors considered in the adjustment (continued)

Study	**Risk adjustment level**																								
	Patient																								
	Age	**Sex**	**Ancestry**	**Underlying disease**	**Comorbidities**	**Severity of disease**	**Lymph node involvement**	**Presence of metastases**	**Tumour stage**	**Tumour localization**	**Histological findings / grading**	**Year of diagnosis**	**Type of surgical procedure**	**Day of the week of surgery**	**Year of surgery**	**Accompanying treatment**	**Inpatient complications**	**Time span between inpatient admission and surgery**	**Length of hospital stay**	**Urgency of inpatient admission**	**Transfer to another acute-care hospital**	**Place of residence**	**Socioeconomic status[a]**	**Social deprivation**	**Type of health insurance**
Funk 2011	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-
Gasper 2009	x	x	x	-	x	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x
Ghaferi 2011	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-
Harrison 2018	x	x	x	-	x	-	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	x	x	-	x
Henneman 2014	x	x	-	-	-	-	-	-	x	-	x	x	-	-	-	x	-	-	-	-	-	-	x	-	-
Hentschker 2018	x	x	-	x	x	-	-	-	-	-	-	-	-	x	-	-	-	-	-	x	-	-	-	-	-
Ho 2006	x	x	x	-	x	-	-	-	x	x	-	-	x	-	-	-	-	-	x	x	-	x	-	-	x
Hollenbeck 2007b	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-	-	-	x
In 2016	x	x	x	-	x	-	-	-	x	x	x	x	-	-	-	x	-	-	-	-	-	-	x	-	x
Kim 2016	x	x	x	-		-	-	-	x	-	-	-	-	-	-	-	-	-	-	x	-	x	-	-	-
Kothari 2016	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-
Kozower 2012	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Learn 2010	x	x	-	-	x	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Mamidanna 2016	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-
Modrall 2018	x	x	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x

(continued)

Table 7: Patient-level risk factors considered in the adjustment (continued)

Study	**Risk adjustment level**																								
	Patient																								
	Age	**Sex**	**Ancestry**	**Underlying disease**	**Comorbidities**	**Severity of disease**	**Lymph node involvement**	**Presence of metastases**	**Tumour stage**	**Tumour localization**	**Histological findings / grading**	**Year of diagnosis**	**Type of surgical procedure**	**Day of the week of surgery**	**Year of surgery**	**Accompanying treatment**	**Inpatient complications**	**Time span between inpatient admission and surgery**	**Length of hospital stay**	**Urgency of inpatient admission**	**Transfer to another acute-care hospital**	**Place of residence**	**Socioeconomic status[a]**	**Social deprivation**	**Type of health insurance**
Nimptsch 2018	x	x	-	x	x	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Reames 2014	x	x	x	-	x	-	-	-	-	-	-	-	x	-	x	-	-	-	-	x	-	-	x	-	-
Sahni 2016	x	x	x	-	x	-	-	-	-	-	-	-	x	x	x	-	-	x	-	-	-	-	-	-	-
Sheetz 2016	x	-	x	-	x	-	-	-	-	-	-	-	x	-	-	-	-	-	-	x	-	-	-	-	-
Simunovic 2006	x	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-
Varghese 2011	x	x	-	x	x	-	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	x
Wasif 2019	x	x	x	-	x	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	x	-	x

a: It is unclear which factors were adjusted for.
-: The studies do not report any data on this factor.

Table 8: Physician-level and hospital-level risk factors considered in the adjustment

Study	Risk adjustment level																	
	Physician	Hospital																
	Physician's specialization	Academic status	Number of hospital beds	Number of examined nurses per bed	Availability of a wound care service	Infection control (isolation rooms)	Hospital legal form (for-profit vs. not-for-profit)	Rural vs. urban hospital	VoS for minimally invasive procedures	Market concentration	Quality assurance processes	Operating costs	Full-time physicians	Lung transplantation centre	Thoracic surgery department	Bariatric surgery centre	Haematooncology centre	Availability of positron emission tomography
Allareddy 2010	-	x	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Austin 2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Avritscher 2014	-	x	-	x	x	x	x	x	-	-	-	-	-	-	-	-	-	-
Birkmeyer 2006	-	x	-	-	-	-	x	-	-	-	x	-	-	-	-	-	-	-
Birkmeyer 2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Christian 2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clark 2019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Derogar 2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dikken 2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
El Amrani 2019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ely 2019[a]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fedeli 2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Finks 2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Finley 2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

(continued)

Table 8: Physician-level and hospital-level risk factors considered in the adjustment (continued)

Study	**Risk adjustment level**																	
	Physician	**Hospital**																
	Physician's specialization	**Academic status**	**Number of hospital beds**	**Number of examined nurses per bed**	**Availability of a wound care service**	**Infection control (isolation rooms)**	**Hospital legal form (for-profit vs. not-for-profit)**	**Rural vs. urban hospital**	**VoS for minimally invasive procedures**	**Market concentration**	**Quality assurance processes**	**Operating costs**	**Full-time physicians**	**Lung transplantation centre**	**Thoracic surgery department**	**Bariatric surgery centre**	**Haematooncology centre**	**Availability of positron emission tomography**
Fischer 2017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Funk 2011	-	-	x	x	-	-	-	-	-	-	-	-	-	x	-	x	x	x
Gasper 2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ghaferi 2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harrison 2018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Henneman 2014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hentschker 2018	-	x	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-
Ho 2006	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hollenbeck 2007b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
In 2016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kim 2016	-	x	-	-	-	-	x	x	-	-	-	x	x	-	-	-	-	-
Kothari 2016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kozower 2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Learn 2010	-	x	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-

(continued)

Table 8: Physician-level and hospital-level risk factors considered in the adjustment (continued)

Study	**Risk adjustment level**																	
	Physician	**Hospital**																
	Physician's specialization	**Academic status**	**Number of hospital beds**	**Number of examined nurses per bed**	**Availability of a wound care service**	**Infection control (isolation rooms)**	**Hospital legal form (for-profit vs. not-for-profit)**	**Rural vs. urban hospital**	**VoS for minimally invasive procedures**	**Market concentration**	**Quality assurance processes**	**Operating costs**	**Full-time physicians**	**Lung transplantation centre**	**Thoracic surgery department**	**Bariatric surgery centre**	**Haematooncology centre**	**Availability of positron emission tomography**
Mamidanna 2016	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Modrall 2018	-	x	x	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Nimptsch 2018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Reames 2014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sahni 2016	x	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sheetz 2016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Simunovic 2006	-	x	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-
Varghese 2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Wasif 2019	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-

a: It is unclear which factors were adjusted for.
-: The studies do not report any data on this factor.
VoS: volume of services

5.5 Overview of outcomes relevant for the assessment

Avritscher 2014, Clark 2019, Ely 2019, Harrison 2018, Kothari 2016, Sheetz 2016, and Wasif 2019 provided no usable results. Detailed reasoning on this topic is found in Section 5.6.

Data on relevant outcomes were extracted from the 30 remaining studies. Table 9 presents an overview of the available data on relevant outcomes from the included studies.

Results on the correlation between VoS and quality of the treatment outcome were reported by 30 of the 37 included studies. Fifteen of the 30 studies [45,47,48,51-53,56,58,59,63,66,73,74, 76,77] reported results on the outcome of all-cause mortality. One of the 30 studies [65] provided results on the outcome of intraoperative or perioperative mortality. Data on the outcome of inpatient mortality were reported by 15 of the 30 studies [9,35,44,49,55,57,60,61, 64,67,69-72,76].

Results on the outcome category of morbidity or the outcome of adverse effects of therapy were available from 5 of the 30 studies [44,58,61,77,80]. In this context, adverse effects of therapy include therapy-related complications such as anastomotic insufficiency and/or pneumonia, wound infections, and cardiac complications. Complication-related mortality (failure to rescue) is also included in the outcome of adverse effects of therapy.

The outcome of length of hospital stay was covered by 3 of the 30 studies [57,65,77].

One study [77] reported results on the additionally defined outcome of rehospitalization.

The included studies provided no data on the outcomes of disease-free survival and health-related quality of life, including activities of daily living and dependence on help from others.

Table 9: Matrix of relevant outcomes

Study	**Outcomes**							
	Mortality			**Morbidity**		**Health-related quality of life**	**Length of hospital stay**	**Other outcomes**
	All-cause mortality	**Intra- or perioperative mortality**	**Inpatient mortality**	**Disease-free survival**	**Adverse effects of therapy[a]**			**Rehospitalization**
Allareddy 2010	-	-	●	-	●	-	-	-
Austin 2013	●	-	-	-	-	-	-	-
Avritscher 2014	-	-	-	-	○	-	-	-
Birkmeyer 2006	●	-	-	-	-	-	-	-
Birkmeyer 2007	●	-	-	-	-	-	-	-
Christian 2003	-	-	●			-	-	-
Clark 2019	-	-	○	-	○	-	○	-
Derogar 2013	●	-	-	-	-	-	-	-
Dikken 2012	●		-	-	-	-	-	-
El Amrani 2019	●	-	-	-	-	-	-	-
Ely 2019	-	-	-	-	○	-	○	-
Fedeli 2012	-	-	●	-	-	-	-	-
Finks 2011	●	-	-	-	-	-	-	-
Finley 2011	-	-	●	-	-	-	●	-
Fischer 2017	●	-	-	-	●	-	-	-
Funk 2011	●	-	-	-	-	-	-	-
Gasper 2009	-	-	●	-	-	-	-	-
Ghaferi 2011	-	-	●	-	●	-	-	-
Harrison 2018	-	-	○	-	○	-	○	-
Henneman 2014	●	-	-	-	-	-	-	-
Hentschker 2018	-	-	●	-	-	-	-	-

(continued)

Table 9: Matrix of relevant outcomes (continued)

Study	**Outcomes**							
	Mortality			**Morbidity**		**Health-related quality of life**	**Length of hospital stay**	**Other outcomes**
	All-cause mortality	**Intra- or perioperative mortality**	**Inpatient mortality**	**Disease-free survival**	**Adverse effects of therapy**			**Rehospitalization**
Ho 2006	-	-	●	-	-	-	-	-
Hollenbeck 2007b	-	●	-	-	-	-	●	-
In 2016	●	-				-	-	-
Kim 2016	-	-	●	-	-	-	-	-
Kothari 2016	-	-	○	-	-	-		-
Kozower 2012	-	-	●	-	-	-	-	-
Learn 2010	-	-	●	-	-	-	-	-
Mamidanna 2016	-	-	●	-	-	-	-	-
Modrall 2018	-	-	●	-	-	-	-	-
Nimptsch 2018	-	-	●	-	○	-	○	-
Reames 2014	●	-	-	-	-	-	-	-
Sahni 2016	●	-	-	-	-	-	-	-
Sheetz 2016	○	-	-	-	○	-	-	-
Simunovic 2006	●	-	●	-	-	-	-	-
Varghese 2011	●	-	-	-	●	-	●	●
Wasif 2019	○	-	-	-	-	-	-	-

●: Data were reported and were usable.
○: Data were reported but were not usable for the benefit assessment.
-: - No data were reported (no further information), or the outcome was not surveyed.

5.6 Results on relevant outcomes

The results on the outcomes relevant for the report are presented below. Avritscher 2014, Clark 2019, Ely 2019, Harrison 2018, Kothari 2016, Sheetz 2016, and Wasif 2019 were deemed relevant, but did not provide any usable results for the presentation and assessment of the relationship between VoS and quality of treatment outcome:

- While Avritscher 2014 investigated the outcome of serious postoperative infections, the study did not provide any usable results, since it did not report them separately for oesophageal interventions.
- Clark 2019 adapted a bivariate mixed logistic model. No odds ratios or other correlation estimates were found, nor were any estimated model coefficients or statements regarding their significance. The results were described primarily by interpreting graphic representations.
- Ely 2019 investigated the impact of introduced "regionalization" on length of hospital stay and postoperative complications. In this context, regionalization refers to the 2014 establishment of 4 centres of excellence, where surgeons were asked to perform their procedures. The employed statistical model shows regionalization to be the explanatory variable alongside hospital VoS and physician VoS. Although results for hospital VoS and/or physician VoS from a model without regionalization could have been used to answer research question 1, the study did not provide such results. Therefore, the reported data are not usable for assessing the relationship between hospital and physician VoS and the outcome of length of hospital stay.
- Harrison 2018 presented results on relevant outcomes only in the form of analyses disregarding cluster effects. The authors neither provided any reasoning for this approach nor discussed to what extent the results would change if cluster effects were taken into account.
- Kothari 2016 reported no point or interval estimators for the comparison of hospitals with low versus high VoS.
- Sheetz 2016 did not present separate results for VoS; within a statistical model, the study reported only the relative effect of patient and hospital characteristics on between-hospital variance with regard to the outcome of failure to rescue.
- Wasif 2019 described a correlation which decreases over time between VoS and quality of treatment outcome. However, this study does not provide sufficient data for generally testing the statistical significance of this conclusion.

Insofar as the study data were analysed at different times, only analyses containing data from 2000 or later were used (see Section 5.2).

5.6.1 Mortality

5.6.1.1 Results on the outcome of all-cause mortality

Results on the outcome of all-cause mortality were reported by 17 of the 37 included studies. Two studies reported no usable results. One study had a high informative value of results (see Table 10 and Table 11).

Early mortality (within 6 months)

Studies of high informative value of results

Results on the hospital level

Fischer 2017 reported point and interval estimators for VoS increases by 5 patients per hospital and year. For 90-day postoperative mortality, the result was just short of statistical significance (OR: 0.98; 95% CI: [0.96; 1.01]).

Results on the physician level

For physician VoS, likewise, Fischer 2017 did not find any statistically significant difference in 90-day postoperative mortality in favour of high-VoS physicians on the basis of a continuous analysis of VoS (OR for a VoS increase by 5 patients: 0.97; 95% CI: [0.85; 1.11]).

Studies of low informative value of results

Results on the hospital level

For the outcome of all-cause mortality (early mortality), Birkmeyer 2006, El Amrani 2019, Funk 2011, Henneman 2014, In 2016, Reames 2014, and Varghese 2011 each reported statistically significant differences in favour of high-VoS hospitals. In this context, Birkmeyer 2006 reported point and interval estimators for the comparison of hospitals with low versus high VoS for 30-day postoperative mortality (OR: 2.34; 95% CI: [1.58; 3.46]). El Amrani 2019 compared hospitals with low VoS (< 41 oesophagectomies) versus high VoS (≥ 41 oesophagectomies) with regard to 90-day mortality. The study used high-VoS hospitals as the reference category (OR: 1.61; 95% CI: [1.00; 2.57]; 0.047). In Funk 2011, hospitals with a low or moderate VoS were compared with high-VoS hospitals (≥ 33 oesophagectomies). For the comparison of the low VoS category (1 to 6 oesophagectomies) with the reference category (≥ 33 oesophagectomies), a statistically significant difference in favour of high-VoS hospitals was shown for 30-day postoperative mortality (OR: 2.2; 95% CI: [1.3; 3.7]). For the comparison of the moderate VoS category (7 to 32 oesophagectomies) versus the reference category, the lower confidence limit was 1.0, with no p-value being reported. Hence, it was impossible to draw any conclusions about statistical significance. Nevertheless, an overall trend in favour of high-VoS hospitals can be discerned across all category comparisons.

For all considered VoS categories, Henneman 2014 showed statistically significant differences in favour of hospitals with the higher respective VoS concerning 6-month mortality. The authors of the In 2016 study categorized hospital VoS into quartiles and conducted a categorical analysis using the 1st quartile (1 through 3 oesophagectomies) as the reference category for 90-

day mortality. For all comparisons of VoS categories with the reference category, statistically significant differences as well as a clear trend in favour of high-VoS hospitals were found. For 30-day postoperative mortality, Reames 2014 formed VoS categories on the basis of hospital VoS within 2-year periods. For all periods, statistically significant differences in favour of high-VoS hospitals were found (2000 through 2001: OR: 2.25; 95% CI: [1.57; 3.23]; 2002 through 2003: OR: 1.92; 95% CI: [1.36; 2.70]; 2004 through 2005: OR: 3.18; 95% CI: [2.41; 4.18]; 2006 through 2007: OR: 2.41; 95% CI: [1.66; 3.52]; 2008 through 2009: OR: 3.68; 95% CI: [2.66; 5.11]). For 90-day mortality, Varghese 2011 reported point and interval estimators for the comparison of hospitals with a low annual VoS versus high annual VoS. The study showed a statistically significant difference in favour of high-VoS hospitals (OR: 0.50; 95% CI: [0.27; 0.91]). The authors used the thresholds defined by the Leapfrog Group (low: < 13 oesophageal interventions; high: ≥ 13 oesophageal interventions).

In a categorical analysis of VoS with regard to all-cause mortality within 3 months after diagnosis, Dikken 2012 reported a linear trend with decreasing point estimators for the individual comparisons. A statistically significant difference, however, was shown exclusively for the comparison of hospitals with very low VoS (1 to 5 oesophagectomies; reference category) versus high-VoS hospitals (≥ 21 oesophagectomies) (HR: 0.44; 95% CI: [0.25; 0.76]).

For 3-month postoperative mortality, Derogar 2013 showed statistically significant differences for hospital VoS only in some categories. The statistically significant difference referred to the comparison of the reference category (quartiles 1 and 2: 1 to 8 oesophagectomies) versus a hospital VoS of 9 to 16 oesophagectomies. No statistically significant difference in favour of high-VoS hospitals was found for the comparison of the reference category with high VoS in quartile 4 (≥ 17 oesophagectomies).

Austin 2013 categorized annual hospital VoS into quartiles. For 30-day postoperative mortality, the comparison of the reference category (quartile 4: 22 to 42 oesophagectomies) with quartile 1 (1 to 4 oesophagectomies) showed a difference in favour of high-VoS hospitals, but with unclear statistical significance (OR: 2.02; 95% CI: [1.00; 4.09]). For the remaining comparisons, no statistically significant differences were found in favour of high-VoS hospitals.

Finks 2011 did not report any point and/or interval estimators for 30-day postoperative mortality, but analysed the outcome of operative mortality using the Blinder Oaxaca method to determine what percentage of the difference between 1999/2000 and 2007/2008 can be explained by a change in hospital VoS. While the case volume remained approximately unchanged, the number of hospitals declined over time. Simultaneously, the percentage of patients who received surgery in hospitals in the top decile of hospital VoS increased. The authors reported that 32% of the decline in risk-adjusted mortality between 1999/2000 (10.0%) and 2007/2008 (8.9%) is explained by this shift.

Results on the physician level

For annual physician VoS, Derogar 2013 reported no statistically significant differences with regard to the outcome of all-cause mortality.

Likewise, Sahni 2016 reported no statistically significant difference between an increase in physicians' annual VoS and mortality within 30 days of inpatient admission.

Late mortality ≥ 2 years

Studies of low informative value of results

Results on the hospital level

Birkmeyer 2007 showed a statistically significant difference in favour of high-VoS hospitals when all patients were included in analysis (HR: 0.71; 95% CI: [0.54; 0.92]). In an analysis including only patients who survived the surgery, the result was just below statistical significance with regard to 5-year survival (HR: 0.76; 95% CI: [0.58; 1.01]). However, the analysis rested on only 822 patients.

Henneman 2014 initially defined 4 VoS categories but then based the categorical analysis of VoS on different VoS categories. For conditional 2-year mortality, this analysis showed statistically significant differences in 4 out of 6 comparisons as well. For instance, up to a VoS of 60 oesophagectomies, statistically significant differences were found in favour of high-VoS hospitals.

For conditional 3-year survival, Dikken 2012 showed a linear trend in favour of high-VoS hospitals, but the results were not statistically significant.

For annual hospital VoS, Derogar 2013 and Simunovic 2006 reported no statistically significant differences for the outcome of all-cause mortality.

Results on the physician level

Derogar 2013 showed some statistically significant differences for physician VoS. These statistically significant differences were found for the comparison of the reference category (quartiles 1 and 2: 1 to 4 oesophagectomies) versus a physician VoS of 5 to 9 oesophagectomies. No statistically significant difference in favour of high-VoS physicians was found for the comparison of the reference category versus high VoS in quartile 4 (≥ 10 oesophagectomies).

Summary for the outcome of all-cause mortality

All things considered, for early mortality (within 6 months), a correlation between hospital VoS and quality of treatment outcome was found, with the informative value of results generally being low. For physician VoS, data of largely low informative value of results showed no correlation between VoS and the quality of treatment outcome.

For late survival (≥ 2 years), inconsistent results made it impossible to derive any correlation between hospital VoS and quality of treatment outcome. Likewise, for the same outcome, no correlation was found between physician VoS and quality of treatment outcome, at an exclusively low informative value of results.

Table 10: Results part 1 – all-cause mortality (survival data)

Study	Outcome definition	N	VoS specification	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Birkmeyer 2007	**5-Year survival:** Vital status 5 years after surgery or at the end of follow-up (31/12/2002)	Total: 822[a, b]	Annual **hospital** VoS:	N/A	**Categorical analysis**
		275	Low: 0.3–3.8	47.9[a, b] (17.4)	**High-VoS vs. low-VoS hospitals:**
		287	Moderate: 3.8–13.7	N/A	**All patients:** 0.71 [0.54; 0.92]; N/A
		260	High: 14.4–107.0	87.6[a, b] (33.7)	Patients who survived surgery: 0.76 [0.58; 1.01]; N/A
Derogar 2013	**Overall survival:** all postoperative deaths due to any cause	Total: 1335	Annual **hospital** VoS	N/A	**Categorical analysis:** p-value for the trend: 0.92
		N/A	Quartiles 1 and 2: 1–8		Reference category
		N/A	Quartile 3: 9–16		1.03 [0.87; 1.23]; > 0.05
		N/A	Quartile 4: ≥ 17		0.96 [0.78; 1.18]; > 0.05
		Total: 1335	Annual **physician** VoS:	N/A	**Categorical analysis:** p-value for the trend: 0.13
		N/A	Quartiles 1 and 2: 1–4		Reference category
		N/A	Quartile 3: 5–9		0.83 [0.70; 0.98]; < 0.05
		N/A	Quartile 4: ≥ 10		0.89 [0.70; 1.14]; > 0.05
	Early mortality: Death within 3 months after surgery	Total: 1335	Annual **hospital** VoS	N/A	**Categorical analysis:** p-value for the trend: 0.05
		N/A	Quartiles 1 and 2: 1–8		Reference category
		N/A	Quartile 3: 9–16		0.59 [0.36; 0.95]; < 0.05
		N/A	Quartile 4: ≥ 17		0.64 [0.35; 1.18]; > 0.05
		Total: 1335	Annual **physician** VoS:	N/A	**Categorical analysis:** p-value for the trend: 0.99
		N/A	Quartiles 1 and 2: 1–4		Reference category
		N/A	Quartile 3: 5–9		1.11 [0.73; 1.67]; > 0.05
		N/A	Quartile 4: ≥ 10		1.00 [0.49; 2.04]; > 0.05

(continued)

Table 10: Results part 1 – all-cause mortality (survival data) (continued)

Study	Outcome definition	N	VoS specification	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Dikken 2012	**Overall survival:** 3 months from diagnosis until death	Total: 10 025	Categories formed on the basis of annual **hospital** VoS:	N/A	**Categorical analysis:**
		N/A	Very low: 1–5		Reference category
		N/A	Low: 6–10		0.88 [0.74; 1.05]; N/A
		N/A	Moderate: 11–20		0.83 [0.63; 1.09]; N/A
		N/A	High: ≥ 21		0.44 [0.25; 0.76]; N/A
	Conditional 3-year survival: 3 years from diagnosis until death for patients who survived the first 3 months after diagnosis	Total: 10 025	Categories formed on the basis of the VoS **per hospital** and year:	N/A	**Categorical analysis:**
		N/A	Very low: 1–5		Reference category
		N/A	Low: 6–10		1.02 [0.94; 1.10]; N/A
		N/A	Moderate: 11–20		0.94 [0.84; 1.05]; N/A
		N/A	High: ≥ 21		0.86 [0.73; 1.01]; N/A

(continued)

Table 10: Results part 1 – all-cause mortality (survival data) (continued)

Study	Outcome definition	N	VoS specification	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Henneman 2014	**6-Month mortality**: 6 months from diagnosis until death	10 025	Categories formed on the basis of annual **hospital** VoS:	N/A	N/A
		7103	1–20		
		865	21–40		
		890	41–60		
		1167	> 60		
		N/A		N/A	**Categorical analysis:**
			20		Reference category
			30		0.83 [0.76; 0.91]; N/A
			40		0.73 [0.65; 0.83]; N/A
			50		0.68 [0.6; 0.78]; N/A
			60		0.67 [0.58; 0.77]; N/A
			70		0.67 [0.54; 0.83]; N/A
			80		0.68 [0.49; 0.94]; N/A
	Conditional 2-year mortality: 2 years from diagnosis until death for patients who survived the first 6 months after diagnosis	10 025		N/A	**Categorical analysis:**
		N/A	20		Reference category
		N/A	30		0.92 [0.89; 0.96]; N/A
		N/A	40		0.88 [0.83; 0.93]; N/A
		N/A	50		0.86 [0.79; 0.93]; N/A
		N/A	60		0.85 [0.75; 0.97]; N/A
		N/A	70		0.86 [0.71; 1.05]; N/A
		N/A	80		0.88 [0.66; 1.16]; N/A

(continued)

Table 10: Results part 1 – all-cause mortality (survival data) (continued)

Study	Outcome definition	N	VoS specification	OS raw n (%)	Adjusted hazard ratio [95% CI]; p-value
Simunovic 2006	**Late survival:** From inpatient admission until death or end of follow-up (31/12/2000), excluding patients with inpatient death event	Total: 629	**Hospital** VoS for a 6-year period:	N/A	**High-VoS vs. low-VoS hospitals[c]:**
		147	Low: ≤ 7		1.2 [0.8; 1.6]; 0.37
		174	Low to moderate VoS: 8–19		1.3 [1.0; 1.8]; 0.06
		155	Moderate to high VoS: 20–43		1.0 [0.8; 1.4]; 0.76
		153	High ≥ 44		Reference category

a: IQWiG calculations.
b: It is unclear whether this figure indicates the total number of patients or the number of survivors.
c: Values > 1 indicate an advantage for high-VoS hospitals.
CI: confidence interval; N: number of analysed patients; n: number of patients with an event; N/A: not available; OS: overall survival; VoS: volume of services; vs.: versus

Table 11: Results part 2 – all-cause mortality (binary data)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Austin 2013	**30-Day mortality:** Death within 30 days after surgery	Total: 1305[a]	Annual **hospital** VoS (range):	N/A	**Categorical analysis:** **High-VoS vs. low-VoS hospitals[b]:**
		N/A	Quartile 1: 1–4	N/A (7.0)	2.02 [1.00; 4.09]; N/A
		N/A	Quartile 2: 5–13	N/A (4.2)	1.30 [0.67; 2.53]; N/A
		N/A	Quartile 3: 14–21	N/A (2.5)	0.69 [0.31; 1.53]; N/A
		N/A	Quartile 4: 22–42	N/A (3.7)	Reference category
Birkmeyer 2006	**Operative mortality:** Death before hospital discharge or within 30 days after surgery	Total: 6438	Annual **hospital** VoS:		**Categorical analysis:** **High-VoS vs. low-VoS hospitals (1st quintile vs. 5th quintile)[b]:** 2.34 [1.58; 3.46]; N/A Reference category: High-VoS hospitals
		715[a]	1st quintile (low VoS)	N/A	
		1045[a]	2nd quintile	N/A	
		1162[a]	3rd quintile	N/A	
		1418[a]	4th quintile	N/A	
		2098[a]	5th quintile (high VoS)	N/A	
El Amrani 2019	**Postoperative mortality:** Death within 90 days or death as an inpatient	Total: 4608	Categories formed on the basis of the annual oesophagectomy volume **per hospital**:	382 (8.3)	**Categorical analysis:** **Low-VoS vs. high-VoS hospitals[b]:**
		N/A	Low VoS: < 41	339 (8.8)	1.61 [1.00; 2.57]; 0.047
		N/A	High VoS: ≥ 41	43 (5.7)	Reference category

(continued)

Table 11: Results part 2 – all-cause mortality (binary data) (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Finks 2011	Operative mortality: Death before hospital discharge or 30 days postoperatively	Total: 43 756[a]	N/A	N/A	N/A[c]
Fischer 2017	Death within 90 days postoperatively	Total: 4859	Annual **hospital** VoS:	215 (4.4)	**Continuous analysis:** With an increase in the treating hospital's annual VoS by 5 patients: 0.98 [0.96; 1.01]; N/A
		1253	Quartile 1: 0–49	57[a] (5.0)	
		1148	Quartile 2: 50–65	57[a] (5.0)	
		1360	Quartile 3: 66–91	52[a] (3.8)	
		1107	Quartile 4: 92–148	43[a] (3.9)	
		Total: 4859	Annual **physician** VoS:	N/A	**Continuous analysis:** With an increase in the treating physician's annual VoS by 5 patients: 0.97 [0.85; 1.11]; N/A
		1144	Quartile 1: 0–5	51[a] (4.5)	
		1156	Quartile 2: 6–9	62[a] (5.4)	
		1292	Quartile 3: 10–13	52[a] (4.0)	
		1169	Quartile 4: 14–28	15[a] (1.3)	
Funk 2011	**Mortality:** Death within 30 days postoperatively or as an inpatient	Total: 4498	Categories formed on the basis of the oesophagectomy figures **per hospital** for the period of 4 years:	319[a] (7.1)	**Categorical analysis:** **Low-VoS vs. high-VoS hospitals[b]:**
		1435	Low: 1–6	N/A	2.2 [1.3; 3.7]; N/A
		1531	Moderate: 7–32	N/A	1.6 [1.0; 2.5]; N/A
		1532	High: ≥ 33	N/A	Reference category

(continued)

Table 11: Results part 2 – all-cause mortality (binary data) (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
In 2016	**90-Day mortality:** Death during surgery up to 90 days postoperatively (including 30-day mortality)	Total: 14 802	Annual **hospital** VoS:	1317[a] (8.9)	**Categorical analysis:**
		3700	1st quartile: 1–3	477[a] (12.9)	Reference category
		3712	2nd quartile: 4–9	345[a] (9.3)	0.69 [0.58; 0.82]; N/A
		3722	3rd quartile: 10–20	279[a] (7.5)	0.57 [0.48; 0.71]; N/A
		3668	4th quartile: > 20	216[a] (5.9)	0.43 [0.33; 0.56]; N/A
Reames 2014	**Operative mortality:** Death before discharge or death within 30 days after surgery	29 630[a]	Categories formed on the basis of the **hospital** VoS per 2-year period:	N/A	**Categorical analysis:**
		6315	**2000–2001 period:**		
		N/A	Very low: < 2	N/A	2.25 [1.57; 3.23]; N/A
		N/A	Very high: > 12	N/A	Reference category
		6046	**2002–2003 period:**		
		N/A	Very low: < 2	N/A	1.92[b] [1.36; 2.70]; N/A
		N/A	Very high: > 12	N/A	Reference category
		5464	**2004–2005 period:**		
		N/A	Very low: < 2	N/A	3.18[b] [2.41; 4.18]; N/A
		N/A	Very high: > 17	N/A	Reference category
		5204	**2006–2007 period:**		
		N/A	Very low: < 2	N/A	2.41[b] [1.66; 3.52]; N/A
		N/A	Very high: > 17	N/A	Reference category
		6601	**2008–2009 period:**		
		N/A	Very low: < 3	N/A	3.68[b] [2.66; 5.11]; N/A
		N/A	Very high: > 18	N/A	Reference category

(continued)

Table 11: Results part 2 – all-cause mortality (binary data) (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Sahni 2016	Mortality within 30 days after hospital admission	Total: 3314	Annual **physician** VoS: ▪ Quartile 1: 0.4 ▪ Quartile 2: 0.9 ▪ Quartile 3: 1.9 ▪ Quartile 4: 6.0	N/A	Increase in the treating physician's annual VoS: N/A Relative risk: 1.01 [N/A]; 0.15
Sheetz 2016	**30-Day mortality**	Total: 13 361[a]	No usable results[d]		
Varghese 2011	**90-Day mortality:** Death 90 days after surgery	Total: 1352	Threshold as per Leapfrog for annual **hospital** VoS:	N/A	**Categorical analysis:**
		514	Low: < 13	56[a] (10.9)	Reference category
		838	High: ≥ 13	59[a] (7.0[a])	0.50 [0.27; 0.91]; < 0.05
Wasif 2019	**90-Day mortality:** Death 90 days after surgery	Total: 17 617[e]	Annual **hospital** VoS:	1533 (8.9)	No usable results[f]
		5898	Low: < 33rd percentile	N/A	
		5873	Moderate: 34–67th percentile	N/A	
		5846	High: > 68th percentile	N/A	

a: IQWiG calculations.
b: Values > 1 indicate an advantage for high-VoS hospitals.
c: Finks 2011 reports that 32% of the drop in mortality between 1999/2000 and 2007/2008 is explained by the redistribution of patients to fewer hospitals with a higher VoS (relative explanatory value as per Blinder-Oaxaca).
d: Sheetz 2016 did not present separate results for VoS; instead, the authors reported only the relative explanatory value of VoS in conjunction with other patient and hospital characteristics.
e: Number of included patients.
f: Wasif 2019 described a correlation which decreases over time between VoS and quality of treatment outcome. However, this study does not provide sufficient data for generally testing the statistical significance of this conclusion.
CI: confidence interval; N: number of analysed patients; n: number of patients with an event; N/A: not available; n.s.: not statistically significant; SD: standard deviation; VoS: volume of services; vs.: versus

5.6.1.2 Results on the outcome of intraoperative or perioperative mortality

Results on the outcome of intraoperative or perioperative mortality were reported in 1 of the 37 studies. The study had a low informative value of results. Physician VoS was not considered (Table 12).

For the outcome of intraoperative or perioperative mortality, Hollenbeck 2007b reported a statistically significant difference in favour of high-VoS hospitals in comparison with low-VoS hospitals. Hollenbeck 2007b categorized VoS into deciles, and the lowest decile (mean: 1.0 oesophagectomy; SD: 0) was compared to the highest decile (mean: 19.5 oesophagectomies; SD: 5.9) (OR: 2.2; 95% CI: [1.3; 3.5]).

Summary on the outcome of intraoperative or perioperative mortality

In summary, on the basis of one study of low informative value of results, a correlation between VoS and quality of treatment outcome was shown in favour of high-VoS hospitals for the outcome of intraoperative or perioperative mortality.

Table 12: Results – intraoperative or perioperative mortality

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Hollenbeck 2007b	**Operative mortality:** Intraoperative or postoperative mortality before hospital discharge	Total: 4020	Mean number of performed oesophagectomies **per hospital** across the 11-year study duration	N/A	**Categorical analysis: Low-VoS vs. high-VoS hospitals (lowest vs. highest decile)[a]:**
		N/A	Low-VoS hospitals (bottom decile): Mean (SD): 1.0 (0)	N/A (14.9)	2.2 [1.3; 3.5]; N/A
		N/A	High-VoS hospitals (top decile): Mean (SD): 19.5 (5.9)	N/A (4.8)	Reference category

a: Values > 1 indicate an advantage for high-VoS hospitals.
CI: confidence interval; N: number of analysed patients; n: number of patients with an event; N/A: not available; SD: standard deviation; VoS: volume of services; vs.: versus

5.6.1.3 Results on the outcome of inpatient mortality

Results on the outcome of inpatient mortality were reported by 18 of the 37 included studies. Three studies provided no usable results. None of the studies had a high informative value of results (see Table 13).

Results on the hospital level

In Allareddy 2010, Fedeli 2012, Finley 2011, Ghaferi 2011, Hentschker 2018, Learn 2010, and Nimptsch 2018, statistically significant differences in favour of high-VoS hospitals were shown for the outcome of inpatient mortality. Allareddy 2010 compared high-VoS hospitals to low-VoS hospitals (OR: 0.53; 95% CI: [0.35; 0.82]). The study used the threshold defined by the Leapfrog group (high VoS: ≥ 13; low VoS: < 13). Fedeli 2012 did not specify the VoS, but showed a statistically significant reduction of inpatient death for a rise in the treating hospital's annual VoS by 10 cases (OR: 0.96; 95% CI: [0.94; 0.98]). Ghaferi 2011 compared hospitals with very low mean annual VoS (< 1.3 oesophagectomies) with hospitals with very high mean VoS (> 15 oesophagectomies) (OR: 3.70; 95% CI: [2.74; 4.98]). Finley 2011 conducted continuous analysis of the VoS. For an increase in the treating hospital's annual VoS by 10 cases, it showed a statistically significant reduction in inpatient mortality (OR: 0.85; 95% CI: [0.77; 0.94]). Hentschker 2018 conducted a continuous analysis of hospital VoS for the years of 2005, 2006, and 2007. It showed a statistically significant reduction in inpatient mortality at a VoS increase by 1% per year for all 3 years (coefficient [standard error] for mortality in 2005: -0.029 [0.008]; in 2006: -0.031 [0.007]; in 2007: -0.027 [0.008]). Point and interval estimators in Learn 2010 are likely provided for a VoS increase by 1 case (OR: 0.95; 95% CI: [0.93; 0.97]). Nimptsch 2018 categorized VoS into quintiles. In addition, a continuous analysis of VoS was conducted. Both point and interval estimators were reported for an increase in annual VoS by 1 case (OR: 0.99; 95% CI: [0.99; 0.99]), by 10 cases (OR: 0.92; 95% CI: [0.99; 0.94]), and by 50 cases (OR: 0.65; 95% CI: [0.59; 0.72]). With increasing VoS per year, the results trended in favour of hospitals with higher VoS.

Gasper 2009 conducted a categorical analysis for the period of 2000 through 2004. The analysis showed no statistically significant differences in favour of high-VoS hospitals.

Christian 2003, Ho 2006, Kim 2016, Kozower 2012, and Simunovic 2006 showed no statistically significant differences in favour of high-VoS hospitals. Christian 2003 conducted a continuous analysis of the VoS (OR: 1.01; 95% CI: [1.00; 1.03]) and used the threshold defined by the Leapfrog Group (high VoS: ≥ 13; low VoS: < 13). Ho 2006 conducted continuous analysis for 3-year periods (1997 through 2000) and for a VoS increase by 1 unit on the logarithmic scale (OR: 0.93; 95% CI: [0.84; 1.04]). Kim 2016 conducted a continuous analysis of the VoS as well and looked at an increase by 1 case per year (OR: 0.99; 95% CI: [0.98; 1.01]). Kozower 2012 likewise presented the results of a continuous analysis of the VoS and calculated the following point and interval estimators: OR: 0.97; 95% CI: [0.88; 1.08]). Simunovic 2006 investigated hospital VoS for a period of 6 years and conducted a categorical analysis yielding results which were not statistically relevant for any comparison.

Results on the physician level

Ho 2006 and Mamidanna 2016 reported statistically significant differences in favour of high-VoS physicians. Ho 2006 reported point and interval estimators for physician VoS for 3-year periods (1997 through 2000) and for 1-unit increases on the logarithmic scale (OR: 0.80; 95% CI: [0.71; 0.90]). Mamidanna conducted a continuous analysis of physician VoS (OR: 0.966; 95% CI: [0.945; 0.988]).

Modrall 2018 compared physicians with high (≥ 5) vs. low VoS (< 5). Categorical analysis showed a result just below statistical significance (OR: 0.64; 95% CI: [0.41; 1.00]; p-value: 0.051).

Summary on the outcome of inpatient mortality

All things considered, on the basis of studies of low informative value of results, correlations between hospital VoS as well as physician VoS and quality of treatment outcomes were derived for the outcome of inpatient mortality.

Table 13: Results – inpatient mortality

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Allareddy 2010	Inpatient mortality	Total: 2473	**Hospital** VoS categories, formed on the basis of MV as per Leapfrog (≥ 13):	N/A	**Categorical analysis:**
		1591[a]	Hospital with VoS < 13	154 (9.68)	Reference category
		882[a]	Hospital with VoS ≥ 13	39 (4.42)	0.53 [0.35; 0.82]; < 0.01
Christian 2003	Inpatient mortality	Total: 1634	VoS categories **per hospital**, formed on the basis of MV as per Leapfrog (≥ 13):	92 (5.6%)	**Continuous analysis:** Rise in annual hospital VoS by 1 case: 1.01 [1.00; 1.03]; 0.10
		1292	Hospital with VoS ≥ 13	N/A	
		342[a]	Hospital with VoS < 13	N/A	
Clark 2019	Inpatient mortality	Total: 4330	**Hospital** VoS categories, formed on the basis of MV as per Leapfrog (≥ 20):	173 (4.0)	No usable results[b]
		N/A	Low: < 20	N/A	
		N/A	High: ≥ 20	N/A	
		Total: 4330	Thresholds as per Leapfrog for the annual number of oesophagectomies **per physician**:	N/A	No usable results[b]
		N/A	Low: < 7		
		N/A	High: ≥ 7		
Fedeli 2012	Inpatient mortality	Total: 1187[a] ▪ Total oesophagectomies: 231[a] ▪ Partial oesophagectomies: 553[a] ▪ Oesophagogastrectomies: 403[a]	N/A	▪ Total oesophagectomies: 22[a] (9.5) ▪ Partial oesophagectomies: 20[a] (3.6) ▪ Oesophagogastrectomies: 15[a] (3.7)	**Continuous analysis:** Rise in the treating hospital's annual VoS by 10 cases: 0.96 [0.94; 0.98]; < 0.001

(continued)

Table 13: Results – inpatient mortality (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Finley 2011	Inpatient mortality	Total: 6985	Categories formed on the basis of the annual number of oesophagectomies **per hospital**:	N/A	**Continuous analysis:** At a rise in the treating hospital's annual VoS by 10 cases: ▪ **Comparison between hospitals:** 0.85 [0.77; 0.94]; 0.001 ▪ Within the same hospital: 0.96 [0.82; 1.12]; 0.58
		N/A	Low: ≤ 6	N/A (9.8)	
		N/A	Moderate: 7–9	N/A (7.1)	
		N/A	High: ≥ 20	N/A (4.8)	
Gasper 2009	Inpatient mortality	Total: 2404	Hospital VoS based on the number of oesophagectomies for the period of 5 years	N/A	N/A
	2000–2004 (period C)				
		Total: 1210		N/A	**Categorical analysis**
		N/A	< 6	N/A (14.9)	1.65 [0.78; 2.68]; N/A
		N/A	6–10	N/A (12.4)	1.45 [0.78; 2.68]; N/A
		N/A	11–20	N/A (9.9)	1.19 [0.57; 2.47]; N/A
		N/A	21–30	N/A (8.8)	0.94 [0.45; 1.98]; N/A
		N/A	> 30	N/A (7.1)	Reference category
Ghaferi 2011	**Inpatient mortality:** 30-Day mortality or inpatient mortality	Total: N/A	Categories on the basis of the mean annual **hospital** VoS:	N/A	**Categorical analysis:**
		1883	Very low: < 1.3		3.70[c] [2.74; 4.98]; N/A
		N/A	Low: N/A		N/A
		N/A	Moderate: N/A		N/A
		N/A	High: N/A		N/A
		1560	Very high: > 15		Reference category[d]

(continued)

Table 13: Results – inpatient mortality (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Harrison 2018	Inpatient mortality	Total: 1324	Categories formed on the basis of annual **hospital** VoS:	N/A	No usable results[e]
		N/A	Low: < 20	N/A	
		N/A	High: ≥ 20	N/A	
Hentschker 2018	Inpatient mortality	Total: 9673[c]	▪ Annual **hospital** VoS	N/A	**Continuous analysis:** Per increase in VoS by 0.01 per year[f]:
		2898	▪ 2005	N/A	-0.029 (0.008)[g]; p < 0.01
		3107	▪ 2006	N/A	-0.031 (0.007)[g]; p < 0.01
		3190	▪ 2007	376[c] (11.8%)	-0.027 (0.008)[g]; p < 0.01
Ho 2006	Inpatient mortality	Total: 10 023	▪ **Hospital** VoS for 3-year periods (mean) ▪ **Physician** VoS for 3-year periods (mean)	N/A	**Continuous analysis:** Per increase in VoS by 1 unit (on a logarithmic scale) ▪ Hospital VoS: 0.93 [0.84; 1.04]; N/A ▪ Physician VoS: 0.80 [0.71; 0.90]; N/A
		1997–2000			
		N/A	**Hospital** VoS: 3.8	N/A (10.5)	
		N/A	**Physician** VoS: 2.1		
Kim 2016	Inpatient mortality	Total: 4827	Annual **hospital** VoS ▪ 50% quantile: 2 ▪ 75% quantile: 4 ▪ 90% quantile: 12 ▪ 95% quantile: 20	N/A	**Continuous analysis:** Increase in the treating hospital's annual VoS by 1 case: 0.99 [0.98; 1.01][h]; > 0.05
Kothari 2016	Risk-adjusted inpatient mortality	Total: 1540	Annual **hospital** VoS:	No usable results[i]	
		N/A	Low: < 20		
		391	High: ≥ 20		

(continued)

Table 13: Results – inpatient mortality (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Kozower 2012	Inpatient mortality	Total: 1210	Annual **hospital** VoS ▪ Quintile 1: 1 ▪ Quintile 2: 2 ▪ Quintile 3: 3 ▪ Quintile 4: 4–7 ▪ Quintile 5: 8–120	10 (12.8) 11 (13.4) 4 (6.4) 12 (5.5) 17 (2.2)	**Continuous analysis:** Increase in the treating hospital's annual VoS[j] 0.97 [0.88; 1.08]; N/A
Learn 2010	**Inpatient mortality:** Death during hospital stay	Total: 3476	**Hospital** VoS based on oesophagectomy volume in 1997–1999: ▪ Low: 1–2 ▪ Moderate: 3–6 ▪ High: > 6	N/A	**Continuous analysis:** Increase in the treating hospital's annual VoS[j] 0.95 [0.93; 0.97]; < 0.001
Mamidanna 2016	**Inpatient mortality:** 30-Day postoperative mortality	Total: 16 572 5030 6859 4683	Annual **physician** VoS: Low: 1–8 Moderate: 9–12 High: 13–29	N/A 271[a] (5.4) 300[a] (4.4) 140[a] (3.0)	**Continuous analysis:** 0.966 [0.945; 0.988]; < 0.05
Modrall 2018	Inpatient mortality	Total: 2883A,[a, k] N/A N/A	Annual **physician** VoS: Low (< 90th percentile): < 5 High (≥ 90th percentile): ≥ 5	N/A	**Categorical analysis:** Reference category 0.64 [0.41; 1.00]; 0.051
Nimptsch 2018	Risk-adjusted inpatient mortality	Total: 22 681[a] 4517 4540 4494 4402 4728	Median annual **hospital** VoS (IQR): Very low: 2 (1–4) Low: 10 (9–11) Moderate: 15 (14–17) High: 26 (23–32) Very high: 62 (49–76)	N/A 553 (12.2) 453 (10.0) 449 (10.0) 384 (8.7) 323 (6.8)	**Continuous analysis:** ▪ Increase in annual VoS by 1 case: 0.99 [0.99; 0.99]; N/A ▪ Increase in annual VoS by 10 cases: 0.92 [0.90; 0.94]; N/A ▪ Increase in annual VoS by 50 cases: 0.65 [0.59; 0.72][i]; N/A

(continued)

Table 13: Results – inpatient mortality (continued)

Study	Outcome definition	N	VoS specification	Mortality, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Simunovic 2006	Inpatient mortality From inpatient admission for surgery	Total: 629	**Hospital** VoS for a 6-year period:	N/A	**Categorical analysis:**
		147	Low: ≤ 7	19[a] (12.9)	0.9[c] [0.3; 2.5]; 0.83
		174	Low to moderate: 8–19	20[a] (11.5)	0.8[c] [0.3; 1.9]; 0.59
		155	Moderate: 20–43	9[a] (5.8)	0.5[c] [0.2; 1.2]; 0.10
		153	High: ≥ 44	18[a] (11.8)	Reference category

a: IQWiG calculations.
b: In Clark 2019, a bivariate mixed logistic model was adapted. No odds ratios or other correlation estimates were found, nor were any estimated model coefficients or statements regarding their significance. The results are, for the most part, described by way of graphics.
c: Values > 1 indicate an advantage for high-VoS hospitals.
d: Presumably, very-high-VoS hospitals were used as the reference category.
e: Harrison 2018 presented results on relevant outcomes only in the form of analyses disregarding cluster effects. The authors neither provided any reasoning for this approach nor discussed to what extent results would change if cluster effects were taken into account.
f: The years 2005, 2006, and 2007 were based on different minimum volumes: 2005: ≥ 5; 2006 and 2007: ≥ 10.
g: Coefficient (standard error) from a linear model (ordinary least squares); negative values indicate a reduction of mortality by the stated coefficient at a VoS increase of 1% per year.
h: Was read off diagram.
i: No point or interval estimators reported for the comparison of low-VoS versus high-VoS hospitals.
j: Increase in annual VoS presumably by 1 case.
k: Demographic data presented for only 2814 patients.
IQR: interquartile range; MV: minimum volume; N/A: not available; N: number of included patients n: number of patients with an event; VoS: volume of services

5.6.2 Morbidity

5.6.2.1 Results on the outcome of disease-free survival

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

5.6.2.2 Results on the outcome of adverse effects of therapy

5.6.2.2.1 Treatment-related complications

Results on the outcome of treatment-related complications were reported by 8 of the 37 studies (see Table 14). Five studies provided no usable results. One study (Fischer 2017) with usable results on the outcome of treatment-related complications had a high informative value of results.

Study of high informative value of results

Results on the hospital level

At an increase of the treating hospital's annual VoS by 5 patients, Fischer 2017 showed a statistically significant difference (OR: 0.96; 95% CI: [0.93; 0.98]) in favour of higher-VoS hospitals. The result pertains to the occurrence of anastomotic insufficiency following oesophagectomy.

Results on the physician level

For physician VoS, Fischer 2017 likewise reported a statistically significant reduction in the occurrence of anastomotic insufficiency with an increase in annual VoS by 5 patients in favour of high-VoS physicians (OR: 0.81; 95% CI: [0.72; 0.92]).

Studies of low informative value of results

Results on the hospital level

Ghaferi 2011 compared hospitals in the categories of very high VoS (> 15 oesophagectomies) versus very low VoS (< 1.3 oesophagectomies) and showed a statistically significant difference in favour of very-high-VoS hospitals (OR: 1.35; 95% CI: [1.11; 1.65]). For the remaining comparisons, no point and/or interval estimators were presented. The point and interval estimators for several postoperative complications were presented collectively.

Allareddy 2010 compared high-VoS hospitals with low-VoS hospitals. For this purpose, the threshold specified by the Leapfrog Group (high VoS: ≥ 13 oesophagectomies; low VoS: < 13 oesophagectomies) was used. The point and interval estimators for the individual complications were presented separately. However, the categorical analysis of VoS did not show any statistically significant difference for the individual complications in favour of hospitals with a high VoS (≥ 13 oesophagectomies as per the Leapfrog Group).

Summary on the outcome of treatment-related complications

In summary, 1 study of high informative value of results showed a correlation between VoS and quality of the treatment outcome for the occurrence of anastomotic insufficiency, which was subsumed under the outcome of treatment-related complications. This correlation was found in favour of both high-VoS hospitals and high-VoS physicians.

On the basis of the two studies with low informative value of results, no consistent correlation between hospital VoS and quality of treatment outcomes was found for the outcome of treatment-related complications.

Table 14: Results – treatment-related complications

Study	Outcome definition	N	VoS specification	Complication rates, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Allareddy 2010	**Complications:**	Total: 2473 Hospitals with low annual VoS < 13: 1591[a] Hospitals with high annual VoS ≥ 13: 882[a]	Definition of categories on the basis of MV as per Leapfrog (≥ 13): Low: < 13 High: ≥ 13	N in high-VoS hospitals / N in low-VoS hospitals	**Categorical analysis:** Reference category: Low-VoS hospitals
	Cardiac			101 (11.45) / 143 (8.99)	1.25 [0.88; 1.76]; N/A
	Neurological			N/A[b]	N/A[c]
	Respiratory			94 (10.66) / 218 (13.70)	0.77 [0.50; 1.18]; N/A
	Gastrointestinal			83 (9.41) / 134 (8.42)	1.06 [0.73; 1.53]; N/A
	Urinary			15 (1.70) / 29 (1.82)	1.05 [0.51; 2.16]; N/A
	Vascular			N/A[b] / 19 (1.19)	N/A[c]
	Iatrogenic			90 (10.20) / 186 (11.69)	0.91 [0.64; 1.29]; N/A
	Infections			50 (5.67) / 97 (6.10)	0.97 [0.62; 1.52]; N/A
	Haemorrhagic			36 (4.08) / 60 (3.77)	0.93 [0.60; 1.45]; N/A
	Impaired wound healing, wound dehiscence			22 (2.49) / 36 (2.26)	N/A[c]
	Sepsis			45 (5.10) / 119 (7.48)	0.75 [0.49; 1.15]; N/A
	Other complications[d]			67 (7.60) / 99 (6.22)	1.35 [0.91; 1.99]; N/A
Avritscher 2014	**At least 1 severe postoperative infection:** ▪ Pneumonia ▪ Wound infection ▪ Bacteraemia/sepsis	265	N/A	65 (25)	No usable results[e]

(continued)

Table 14: Results – treatment-related complications (continued)

Study	Outcome definition	N	VoS specification	Complication rates, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Clark 2019	Postoperative complications:	Total: 4330	Thresholds as per Leapfrog for the annual oesophagectomy volume **per hospital**: ▪ Low: < 20 ▪ High: ≥ 20	N/A	No usable results[f]
		Total: 4330	Thresholds as per Leapfrog for the annual oesophagectomy volume **per physician**: ▪ Low: < 7 ▪ High: ≥ 7	N/A	
	Pulmonary	N/A	N/A	1660 (38.3)	
	Cardiac			919 (21.2)	
	Gastrointestinal			336 (7.8)	
	Digestive system complications (GI DSC)			325 (7.5)	
	Haematological			1017 (23.5)	
	Infectious			677 (15.6)	
	Neurological			311 (7.2)	
Ely 2019	Complications within 30 days after surgery	Total: 461	Categories formed on the basis of annual **hospital** VoS:	N/A	No usable results[g]
		81	Low: < 5		
		380	High: ≥ 5		
		N/A	Categories defined on the basis of annual **physician** VoS:	N/A	No usable results[g]
		152	Low < 5		
		309	High: ≥ 5		

(continued)

Table 14: Results – treatment-related complications (continued)

Study	Outcome definition	N	VoS specification	Complication rates, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Fischer 2017	Anastomotic insufficiency	Total: 4859	Annual **hospital** VoS:	306[a] (6.3)	At an increase of the treating hospital's annual VoS by 5 patients: 0.96 [0.93; 0.98]; N/A
		1253	Quartile 1: 0–49	89[a] (7.1)	
		1148	Quartile 2: 50–65	102[a] (8.9)	
		1360	Quartile 3: 66–91	86[a] (6.3)	
		1107	Quartile 4: 92–148	28[a] (2.5)	
		Total: 4859	Annual **physician** VoS:	N/A	At an increase of the treating physician's annual VoS by 5 patients: 0.81 [0.72; 0.92]; N/A
		1144	Quartile 1: 0–5	90[a] (7.9)	
		1156	Quartile 2: 6–9	82[a] (7.1)	
		1292	Quartile 3: 10–13	59[a] (4.6)	
		1169	Quartile 4: 14–28	15[a] (1.3)	
Ghaferi 2011	Postoperative complications[h]	Total: N/A	Mean annual hospital VoS:	N/A	**Categorical analysis**
		1883	Very low: < 1.3		1.35[i] [1.11; 1.65]; N/A
		N/A	Low: N/A		N/A
		N/A	Moderate: N/A		N/A
		N/A	High: N/A		N/A
		1560	Very high: > 15		Reference category[j]
Harrison 2018	Postoperative complications[k]	Total: 1324	Categories defined on the basis of the annual hospital VoS:	N/A	No usable results[l]
		N/A	Low: < 20	N/A	
		N/A	High: ≥ 20	N/A	
Sheetz 2016	Major complications[m]	Total: 13 361[a]	N/A	N/A	No usable results[n]

(continued)

Table 14: Results – treatment-related complications (continued)

a: IQWiG calculations.
b: If N ≤ 10, no information is provided.
c: No estimate possible since the multivariable model did not converge.
d: See corresponding ICD-9 CM codes in Table 1 of the publication.
e: The effect estimator for the comparison of high vs. low VoS does not specifically pertain to oesophagectomy.
f: In Clark 2019, a bivariate mixed logistic model was adapted. No odds ratios or other correlation estimates were found, nor were any estimated model coefficients or statements regarding their significance. The results are, for the most part, described by way of graphics.
g: Alongside hospital and physician VoS, the employed model also includes the variable "regionalization", for which interdependency can be expected. Consequently, the data on the relationship between hospital and physician VoS and the outcome of length of hospital stay are not usable.
h: Postoperative complications comprise respiratory failure, pneumonia, myocardial infarction, deep venous thrombosis / pulmonary embolism, acute kidney failure, bleeding, and wound infection.
i: Values > 1 indicate an advantage for high-VoS hospitals.
j: Presumably, very-high-VoS hospitals were used as the reference category.
k: Postoperative complications pertained to lung, wound, infections, urinary tract, gastrointestinal tract, cardiovascular system, and systemic complications.
l: Harrison 2018 presented results on relevant outcomes only in the form of analyses disregarding cluster effects. The authors did not supply any reasoning for this approach or nor discussed to what extent results would change if cluster effects were taken into account.
m: The study considered respiratory failure, pneumonia, myocardial infarction, deep venous thrombosis / pulmonary embolism, kidney failure, wound infection, and (gastrointestinal) bleeding as relevant complications.
n: Sheetz 2016 did not present separate results for VoS; instead, the authors reported only the relative explanatory value of VoS in conjunction with other patient and hospital characteristics.

CI: confidence interval; MV: minimum volume; N: number of analysed patients; n: number of patients with (at least 1) event; N/A: not available; VoS: volume of services; vs.: versus

5.6.2.2.2 Failure to rescue

Results on the outcome of failure to rescue were provided by 3 of the 37 included studies. Nimptsch 2018 and Sheetz 2016 reported no usable results. All 3 studies had a low informative value of results. The study with usable results did not account for physician VoS regarding the outcome of failure to rescue.

Ghaferi 2011 compared hospitals in the categories of very high VoS (> 15 oesophagectomies) and very low VoS (< 1.3 oesophagectomies) and showed a statistically significant difference in favour of hospitals in the very-high-VoS category (OR: 3.18; 95% CI: [2.39; 4.22]). For the remaining comparisons, no point and/or interval estimators were presented.

Summary on the outcome of failure to rescue

In summary, for the outcome of failure to rescue, a correlation between hospital VoS and quality of treatment outcome can be derived on the basis of 1 study of low informative value of results.

Table 15: Results – failure to rescue

Study	Outcome definition	N	VoS specification	Cases with complications, raw, n (%) / deaths with at least 1 complication n (%)	Adjusted odds ratio [95% CI]; p-value
Ghaferi 2011	**Failure to rescue:** Death due to one of the following complications ▪ Respiratory failure ▪ Pneumonia ▪ Myocardial infarction ▪ Deep venous thrombosis / pulmonary embolism ▪ Acute renal failure ▪ Bleeding ▪ Wound infection	Total: N/A 1883 N/A N/A N/A 1560	Mean annual **hospital** VoS: Very low: < 1.3 Low: N/A Moderate: N/A High: N/A Very high: > 15	N/A	**Categorical analysis:** 3.18[a] [2.39; 4.22]; N/A N/A N/A N/A Reference category[b]
Nimptsch 2018	**Failure to rescue:** Inpatient mortality in patients with documented complication ▪ Surgical complications[c] ▪ Septic complications[d] ▪ Cardiovascular complications[e]	Total: 22 681[f] 4517 4540 4494 4402 4728	Median annual VoS (IQR): Very low: 2 (1–4) Low: 10 (9–11) Moderate: 15 (14–17) High: 26 (23–32) Very high 62 (49–76)	N/A 2540 (56.2) / 509 (20.0) 2377 (52.4) / 424 (17.8) 2448 (54.5) / 421 (17.2) 2533 (57.5) / 367 (14.5) 2519 (53.3) / 311 (12.3)	N/A
Sheetz 2016	**Failure to rescue:** Complication-related mortality	Total: 13 361[f]	N/A	N/A	No usable data[g]

a: Values > 1 indicate an advantage for high-VoS hospitals.
b: Presumably, very-high-VoS hospitals were used as the reference category.
c: Endoscopic intervention in case of suspected anastomotic insufficiency, pleural drainage/puncture, surgical procedure on the pleura, chlyothorax, relaparotomy or rethoracotomy, transfusion of whole blood or erythrocytes (≥ 6 units).
d: Mediastinitis, pleural empyema, peritonitis, pneumonia, and sepsis.
e: Stroke, heart attack, pulmonary embolism.
f: IQWiG calculations.
g: The authors of the study did not present separate results for VoS; instead the authors reported only the relative explanatory value of VoS in conjunction with other patient and hospital characteristics.
CI: confidence interval; IQR: interquartile range; N: number of analysed patients; n: number of patients with (at least 1) event; N/A: not available

5.6.2.2.3 Further serious treatment-related complications

Usable results on the outcome of complication-related reintervention were reported by 1 of the 37 included studies (see Table 16). The study has a low informative value of results. The relationship between physician VoS and quality of treatment outcome was not investigated for the outcome of further serious treatment-related complications.

For the outcome of complication-related reintervention, Varghese 2011 found no statistically significant difference between hospital VoS and quality of treatment outcome in favour of high-VoS hospitals.

Summary for the outcome of further serious treatment-related complications

In summary, on the basis of 1 study of low informative value of results, no correlation between hospital VoS and treatment outcome was found for the outcome of complication-related reintervention.

Table 16: Results – complication-related reintervention

Study	Outcome definition	N	VoS specification	Number of reinterventions, raw n (%)	Adjusted odds ratio [95% CI]; p-value
Varghese 2011	Complication-related reintervention	Total: 1352	Threshold as per Leapfrog for the annual hospital VoS:	N/A	Categorical analysis:
		514	Low-VoS hospitals: < 13	86[a] (16.7)	Reference category
		838	High-VoS hospitals: ≥ 13	109[a] (13.0 [a])	0.69 [0.46; 1.03]; n.s.

a: IQWiG calculations.
CI: confidence interval; N: number of included patients n: number of patients with an event; N/A: not available; n.s.: not statistically significant; VoS: volume of services

5.6.3 Results on the outcome of health-related quality of life, including activities of daily living and dependence on help from others

None of the included studies reported data on the outcome of health-related quality of life.

5.6.4 Results on the outcome of length of hospital stay

Seven of the 37 included studies reported results on the outcome of length of hospital stay (see Table 17). Four studies reported no usable results. All 7 studies had a low informative value of results. The studies with usable data did not consider physician VoS.

In a continuous analysis comparing hospitals, Finley 2011 considered an increase in annual VoS by 10 cases and showed a statistically significant 10% rise in probability of an extended length of stay for patients in higher-VoS hospitals (OR: 1.10; 95% CI: [1.02; 1.19]).

In Hollenbeck 2007b, patients who underwent surgery in low-VoS hospitals had a higher probability of a longer hospital stay than patients in higher-VoS hospitals (OR: 1.7; 95% CI: [1.0; 2.9]). The lowest confidence limit was 1.0, with the p-value not being reported; therefore, it was not possible to draw an unequivocal conclusion about the significance of the observed difference.

Varghese 2011 compared low-VoS hospitals with high-VoS hospitals. The authors used the thresholds defined by the Leapfrog Group (low: < 13 oesophageal interventions; high: ≥ 13 oesophageal interventions). As was also acknowledged by the authors, the categorical analysis showed no statistically significant difference in favour of high-VoS hospitals (OR: 0.55; 95% CI: [0.43; 1.00]).

Summary for the outcome of length of hospital stay

In summary, for the outcome of length of hospital stay, the available studies with low informative value of results do not allow deriving a consistent correlation between hospital VoS and the quality of treatment outcome.

Table 17: Results – length of hospital stay

Study	Outcome definition	N	VoS specification	Length of stay in days (%)	Adjusted odds ratio [95% CI]; p-value
Clark 2019	**Extended length of stay:** ≥ 14 days from admission to discharge	Total: 4330	Thresholds as per Leapfrog for the annual oesophagectomy volume **per hospital**:	1450 (33.5)	No usable results[a]
		N/A	Low: < 20	N/A	
		N/A	High: ≥ 20	N/A	
		Total: 4330	Thresholds as per Leapfrog for the annual oesophagectomy volume **per physician**:	N/A	No usable results[a]
		N/A	Low: < 7		
		N/A	High: ≥ 7		
Ely 2019	Length of hospital stay	Total: 461	Categories defined on the basis of annual **hospital** VoS:	N/A	No usable results[b]
		81	Low: < 5		
		380	High: ≥ 5		
		Total: 461	Categories defined on the basis of annual **physician** VoS:	N/A	No usable results[b]
		152	Low: < 5		
		309	High: ≥ 5		
Finley 2011	Length of hospital stay	Total: 6985	Categories defined on the basis of annual oesophagectomy volume **per hospital**:	N/A	**Continuous analysis:** Increase in annual VoS by 10 cases[c]
			Low: ≤ 6		▪ **Comparison between hospitals:** 1.10 [1.02; 1.19]; N/A
			Moderate: 7–9		▪ Within the same hospital: 1.02 [0.99; 1.05]; N/A
			High: ≥ 20		
Harrison 2018	Length of hospital stay	1324	Categories defined on the basis of annual **hospital** VoS:	N/A	No usable results[d]
		N/A	Low: < 20		
		N/A	High: ≥ 20		

(continued)

Table 17: Results – length of hospital stay (continued)

Study	Outcome definition	N	VoS specification	Length of stay in days (%)	Adjusted odds ratio [95% CI]; p-value
Hollenbeck 2007b	**Extended length of stay:** Patients whose length of stay was beyond the 90th percentile in each study year	Total 4020	**Hospital** VoS over the 11-year observation period	N/A	**Categorical analysis:** **Low-VoS hospitals vs. high-VoS hospitals (bottom decile vs. top decile)[e]:**
		N/A	Low (bottom decile): Mean (SD): 1.0 (0)	11.3	1.7 [1.0; 2.9]; N/A
		N/A	High (top decile): Mean (SD): 19.5 (5.9)	5.2	Reference category
Nimptsch 2018	Length of hospital stay	Total: 22 681	Median annual VoS (IQR):	In days, mean	N/A
		4517	Very low: 2 (1–4)	30.2	
		4540	Low: 10 (9–11)	29.8	
		4494	Moderate: 15 (14–17)	30.8	
		4402	High: 26 (23–32)	31.1	
		4728	Very high 62 (49–76)	27.9	
Varghese 2011	**Extended length of stay:** more than 14 days	Total: 1352	Threshold as per Leapfrog for annual **hospital** VoS:	N/A	**Categorical analysis:**
		514	Low: < 13	166[f] (32.3)	Reference category
		838	High: ≥ 13	262 (27.0)[f]	0.55 [0.43; 1.00]; n.s.

a: In Clark 2019, a bivariate mixed logistic model was adapted. No odds ratios or other correlation estimates were found, as were no estimated model coefficients or statements regarding their significance. The results are, for the most part, described by visuals.
b: Alongside hospital and physician VoS, the employed model also includes the variable “regionalization”, for which interdependency can be expected. Consequently, the data on the relationship between hospital and physician VoS and the outcome of length of hospital stay are not usable.
c: No data provided on the mean VoS of the hospitals analysed.
d: The study’s authors presented results on relevant outcomes only in the form of analyses disregarding cluster effects. The authors neither supplied any reasoning for this approach nor discussed to what extent results would change if cluster effects were taken into account.
e: Values > 1 indicate an advantage for high-VoS hospitals.
f: IQWiG calculations.

CI: confidence interval; IQR: interquartile range; N: number of included patients n: number of patients with an event; N/A: not available; n.s.: not statistically significant; SD: standard deviation; VoS: volume of services; vs.: versus

5.6.5 Results on further outcomes

5.6.5.1 Rehospitalization

Usable results on the outcome of rehospitalization were reported by 1 of the 37 included studies (see Table 18). The study has a low informative value of results. For the outcome of rehospitalization, the relationship between physician VoS and quality of treatment outcomes was not investigated.

For the outcome of rehospitalization within 30 days after hospital discharge, Varghese 2011 found a statistically significant difference between hospital VoS and quality of treatment outcome. However, the results show a disadvantage for high-VoS hospitals (OR: 1.28; 95% CI: [1.01; 1.62]).

Summary for the outcome of rehospitalization

For the outcome of rehospitalization within 30 days after hospital discharge, a correlation between hospital VoS and quality of treatment outcomes was found on the basis of 1 study of a low informative value of results, albeit to the disadvantage of high-VoS hospitals.

Table 18: Results – rehospitalization

Study	Outcome definition	N	VoS specification	Rehospitalization (%)	Adjusted odds ratio [95% CI]; p-value
Varghese 2011	**Rehospitali-zation:** Within 30 days after hospital discharge	Total: 1352	Threshold as per Leapfrog for the annual hospital VoS:	N/A	Categorical analysis:
		514	Low: < 13	102[a] (19.8)	Reference category
		838	High: ≥ 13	190[a] (22.7)[a]	1.28[b] [1.01; 1.62]; p < 0.05

a: IQWiG calculations.
b: Values > 1 indicate a disadvantage for high-VoS hospitals.
CI: confidence interval; N: number of included patients n: number of patients with an event; N/A: not available; VoS: volume of services

5.6.6 Metaanalyses

Due to considerable differences between studies in their definitions of the VoS, no metaanalysis of results was performed for any of the reported outcomes. Further, the studies considered different adjustment factors in their analyses. In addition, the studies used very heterogeneous outcome operationalizations.

5.7 Overall evaluation of results

A total of 37 studies were found which investigated the relationship between VoS and quality of treatment outcome in complex oesophageal interventions (research question 1), but 7 of them reported no usable data.

For the outcome category of mortality, data on 3 outcomes (all-cause mortality, intraoperative or perioperative mortality, and inpatient mortality) were available. Due to the operationalizations used in the included studies, the outcome of all-cause mortality was categorized into early mortality (within 6 months) and late mortality (≥ 2 years). For early mortality, a correlation was found between hospital VoS and quality of treatment outcome on the basis of the majority of the studies of low informative value of results. For the same outcome, however, studies of mostly low informative value of results showed no correlation between physician VoS and quality of treatment outcome. For late survival, due to inconsistent results, it was not possible to derive the relationship between hospital VoS and quality of treatment outcome, with all studies on this topic having a low informative value of results. Likewise, for the same outcome, no correlation was found between physician VoS and quality of treatment outcome, at an exclusively low informative value of results. With regard to the outcome of intraoperative or perioperative mortality, on the basis of 1 study of low informative value of results, a correlation was found between VoS and quality of treatment outcome in favour of high-VoS hospitals. This study did not investigate physician VoS. For the outcome of inpatient mortality, a correlation was found in favour of high-VoS hospitals and physicians, with the informative value of results being rated as low.

Regarding the outcome category of morbidity, data were found for the outcome of adverse effects of therapy. For the treatment-related complication of anastomotic insufficiency, 1 study of high informative value of results showed a correlation between hospital and physician VoS on the one hand and quality of treatment outcome on the other. The remaining studies with a low informative value of results investigated multiple treatment-related complications, in some cases in a combination. It was not possible to derive any consistent correlation between hospital VoS and the quality of treatment outcome. The studies did not consider physician VoS for these outcomes.

For the outcome of failure to rescue, a correlation was found between hospital VoS and quality of treatment outcome on the basis of a study with low informative value of results. The studies on this outcome did not consider physician VoS.

One study of low informative value of results investigated reintervention due to complications as another serious treatment-related complication. However, no correlation was found between hospital VoS and quality of treatment outcome. This study did not consider physician VoS.

Due to the studies' inconsistent results on the outcome of length of hospital stay, it was not possible to derive any correlation between hospital VoS and quality of treatment outcome, with all studies having a low informative value of results. The studies did not provide any data on physician VoS for these outcomes.

One study with low informative value of results identified rehospitalization within 30 days of hospital discharge as an additional outcome. In this regard, a correlation between hospital VoS and quality of treatment outcome was found, albeit to the disadvantage of high-VoS hospitals.

No data were reported for the outcomes of disease-free survival or health-related quality of life, including activities of daily living and dependence on help from others. For these outcomes, it was therefore impossible to derive any conclusions on the relationship between VoS and quality of treatment outcomes.

Since no studies of meaningful interpretive value were found, it was not possible to draw a conclusion on the extent to which the quality of treatment outcomes is impacted by specific minimum numbers of cases introduced for complex oesophageal interventions.

Table 19 below summarizes the results of the included studies on the relevant outcomes.

Table 19: Overview of the observed results for the outcomes and any VoS-outcome correlation

	Outcomes										
	Mortality				**Morbidity**						**Other**
	All-cause mortality		**Intraoperative or perioperative mortality**	**Inpatient mortality**	**Disease-free survival**	**Adverse effects of therapy**			**Health-related QoL**	**Length of hospital stay**	**Rehospitalization**
	Early (up to 6 months)	**Late (≥ 2 years)**				**Treatment-related complications[a]**	**Failure to rescue**	**Complication-related reintervention**			
	Hospital level										
Results of outcomes following oesophageal interventions when comparing high vs. low VoS	(↑)	(↑↔)	(↑)	(↑)	-	↑[a] / (↑↔)[b]	(↑)	(↔)	-	(↓↔)	(↓)
	Physician level:										
Results of outcomes following oesophageal interventions when comparing high versus low VoS	(↔)	(↔)	-	(↑)	-	↑[a] / -[b]	-	-	-	-	-
Relationship between VoS and quality of treatment outcome	Correlation **in favour** of high VoS only on the hospital level.	No correlation found.	Correlation **in favour** of high VoS only on the hospital level	Correlation **in favour** of high VoS on both levels.	No conclusion can be drawn.	Correlation **in favour** of high VoS on both levels for anastomotic insufficiency.	Correlation **in favour** of high VoS on the hospital level.	No correlation found.	No conclusion can be drawn.	No correlation found.	Correlation **to the disadvantage** of high VoS on the hospital level.

(continued)

Table 19: Overview of the observed results for the outcomes and any VoS-outcome correlation (continued)

↑: One study with high informative value of results shows a statistically significant difference in outcome in favour of high-VoS hospitals and/or physicians.
(↑): Largely based on 1 or more studies with low informative value of results showing statistically significant differences in outcome in favour of high-VoS hospitals and/or physicians. Studies with results which are not statistically significant point in the same direction or do not call the association into question.
(↔): Studies with high and/or low informative value of results showed no statistically significant differences in favour of high-VoS hospitals and/or physicians.
(↓): One study with low informative value of results shows a statistically significant difference in outcome to the disadvantage of high-VoS hospitals and/or physicians.
(↑↔) or (↓↔): Several studies with low informative value of results showed inconsistent results for the outcome.
-: The included studies did not report any (usable) data.
a: Limited to anastomotic insufficiency.
b: Pertains to multiple treatment-related complications (see Table 14).
QoL: quality of life; VoS: volume of services

6 Discussion

6.1 Objective and chief findings

The objective of this rapid report was to present and assess a potential relationship between VoS and the quality of treatment outcome in complex oesophageal interventions (research question 1). Another objective was to present the effects of introducing a minimum number of cases into the healthcare system on the quality of treatment outcomes (research question 2). The backdrop to the G-BA commissioning this project was the resumption of discussions on the existing minimum volume for complex oesophageal interventions.

Initially, a total of 45 studies were found which investigated the relationship between VoS and quality of treatment outcome in complex oesophageal interventions (research question 1). For research question 2, no studies of meaningful interpretive value were found which investigated whether minimum volumes specifically introduced in the healthcare system had any effect on the quality of treatment outcomes.

Eight of the 45 included studies were excluded from the analysis due to their outdated data. The 8 studies reported data exclusively from the 1980s and 1990s. These 8 studies were excluded from the further assessment since surgical techniques have changed [8] and techniques which did not yet exist in those decades, such as staplers, are now being used to create anastomoses, in conjunction with sealing and dissection instruments (e.g. LigaSure, Ultracision). Particularly for the treatment of anastomotic insufficiency, which is associated with increased mortality rates, the new EndoVAC method has been in use since the early 2000s, for instance [82-84]. Three of the included studies [51,52,63] analysed data from 1987 through 2009. Since it was unclear which percentage of their data came from procedures done in the 1980s and 1990s, it was not possible to unequivocally exclude these studies from the further investigation.

On the hospital level, a correlation between hospital VoS and quality of treatment outcome following oesophageal interventions was found for the majority of outcomes in the mortality outcome category. Regarding physician VoS, a correlation between VoS and quality of treatment outcome was found for only 1 of 2 outcomes in the mortality outcome category; it showed mortality decreasing at a high VoS.

For the outcome of all-cause mortality, some of the studies' operationalizations overlapped with the outcome of inpatient mortality. For instance, Birkmeyer 2006, El Amrani 2019, Hollenbeck 2007b, and Reames 2014 defined operative mortality as death before hospital discharge or within 30 days after surgery, or within 90 days, or in hospital [47,53,65,73]. These operationalizations would consequently also cover, at least in part, the outcome of inpatient mortality. A transparent distinction between outcomes by the studies' authors would have enabled a less ambiguous allocation to the respective outcome.

At the same time, a disadvantage for high-VoS hospitals was found for the additionally defined outcome of rehospitalization. Accordingly, patients undergoing surgery in high-VoS hospitals had a higher probability of rehospitalization within 30 days after hospital discharge. However, this result was based only on 1 study of low informative value of results, and the study's authors themselves intimated that the exact reason for rehospitalization was unknown [77].

With respect to the outcome of length of hospital stay, while no consistent correlation was found across all studies, 1 study of low informative value of results showed a statistically significant difference, again to the disadvantage of high-VoS hospitals. In this study, patients in high-VoS hospitals had a 10% higher probability of extended hospitalization. The study's authors suspected that any postoperative complications might be treated earlier in high-VoS hospitals, resulting in a longer average length of hospital stay [57]. All things considered, it remains unclear whether an increased length of hospital stay should be interpreted as an advantage or disadvantage for patients.

Overall, however, the results did not allow any conclusions to be drawn regarding any specific minimum volume, since different studies often reported heterogeneous results from comparisons between specific VoS and a reference category. In addition, the studies widely differed in terms of their definition of VoS categories, and no specific criteria were reported for the definition of the individual VoS categories. For instance, the quartiles defined by Derogar 2013 on the basis of annual VoS are combined in the categorical analysis of VoS (this applies to quartiles 1 and 2). Therefore, it remains unclear to what extent the results for the low VoS categories of quartiles 1 and 2 would be significant if they had been considered separately. Any potentially significant result would be obscured by the existing combination of the two quartiles. Derogar 2013 did not provide any reasoning for this approach [51]. For the outcome of intraoperative and perioperative mortality, Hollenbeck 2007b as well found a statistically significant difference in favour of high-VoS hospitals, but this result has to be questioned in view of the VoS categories defined by the authors of the study. VoS was categorized into deciles on the basis of case volume over the 11-year study duration. This process relegated hospitals with a case volume of 1.0 to the bottom decile, while hospitals with a mean case volume of 19.5 were placed in the top decile; these two categories were then compared in categorical analysis. However, it is unclear how many hospitals and patients were allocated to the two VoS categories [65].

6.2 Interventions/procedures considered

In their methods sections, many of the included studies reported the individual intervention/procedure codes of services considered. However, this detailed presentation of considered services was discontinued in the results section, where most studies discussed the services collectively. Consequently, no conclusions can be drawn regarding the results for the individual services which were specifically represented by intervention and procedural codes. The list of interventional/procedural codes included in the studies is found in Annex C of the full report.

6.3 Use of administrative data

The included studies were primarily based on administrative/discharge data. Administrative data are associated with an information deficit since they often lack clinical information such as findings data and/or severities of disease [77,85,86]. Where administrative data are additionally linked with clinical data, however, as was done in 3 of the included studies [47,48,76] (e.g. linking of SEER Medicare data), more information can be assumed to have been available for the patient-level analysis. Generally, however, the extent to which a comprehensive evidence base is available depends on the structure of the databases used and the respective healthcare system. In the German inpatient setting, for instance, a flat-fee diagnosis-related group (DRG) system primarily reflects the service provided and less so the diagnosis-related constellations. DRGs fail to reflect the services provided in any detail, but rather record bundles of services. Further, administrative data are collected by many groups of people or facilities, such as physicians, hospitals, etc. This can be associated with missing data or inconsistencies as well as errors at the start and in the course of the documentation chain as well as at later times during the data collection process [87,88]. The underlying data are subject to limitations since the studies did not provide sufficient information on the structure and contents of the databases and registers used.

6.4 Transferability to the German healthcare system

Twenty-five of the 37 analysed studies are from the USA, and 3 further studies, from Canada. Healthcare structures in the USA differ from those in Germany, for instance in terms of specialist training. Another important difference between the healthcare systems lies in the fact that in the USA, complex oesophageal interventions are performed by thoracic surgeons, while in Europe, they are primarily performed by visceral surgeons.

In the interpretation of study results, differences in the respective countries' healthcare structures must therefore be borne in mind. Therefore, the transferability of these studies to the German healthcare system must be critically questioned.

6.5 Minimum volumes in Europe

Alongside the minimum volume rules in place in Germany (see Section 1), quality assurance efforts exist on a European level. Between 2011 and 2014, for instance, the Dutch quality initiative "Dutch Upper Gastrointestinal Cancer Audit (DUCA)" collected and analysed all surgical therapies of gastric and oesophageal cancer throughout the country using internet-based quality assurance tools. On the basis of 100% participation in the data collection and the subsequent analysis, an annual minimum volume of 20 procedures per hospital has been laid down as a requirement in the Netherlands [89].

Similar investigations have been done in Denmark. These have led to the centralization of care in centres which qualified for oesophagectomy by meeting the corresponding minimum volume [90].

7 Conclusion

For the investigation of the relationship between VoS and quality of treatment outcome in complex oesophageal interventions (research question 1), a total of 37 observational studies were included, of which 30 contained usable data. Only 1 study had a high informative value of results.

For hospital VoS, a correlation between VoS and quality of treatment outcome was found for several operationalizations regarding the outcome of mortality. For the outcome of treatment-related complications (anastomotic insufficiency), likewise, a correlation was found between VoS and quality of treatment outcome on the basis of a study with high informative value of results. A correlation was also found with regard to the outcome of failure to rescue. For the additionally defined outcome of rehospitalization, a study with low informative value of results revealed a correlation between VoS and quality of treatment outcome to the disadvantage of high-VoS hospitals.

Regarding physician VoS, for the outcome of mortality, a correlation between VoS and quality of treatment outcome was found only for the operationalization of inpatient mortality. For the outcome of treatment-related complications (anastomotic insufficiency), a study of high informative value of results likewise showed a correlation between VoS and quality of treatment outcome.

No studies of meaningful interpretive value were found to investigate the extent to which the quality of treatment outcome is impacted by specific minimum numbers of cases introduced in the healthcare system for complex oesophageal interventions (research question 2).

References for English extract

Please see full rapid report for full reference list.

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Appendix A – Search strategies

A.1 – Bibliographic searches

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) 1946 to October Week 5 2019,
- Ovid MEDLINE(R) Daily Update November 12, 2019

The following filter was adopted: [91]

#	**Searches**
1	Esophagectomy/
2	Esophageal Neoplasms/
3	Esophagus/
4	Esophageal Diseases/
5	or/2-4
6	(surgery or therapy).fs.
7	and/5-6
8	(esophagectom* or oesophagectom*).ti,ab.
9	((esophageal* or oesophageal* or esophagus* or oesophagus*) adj5 (surger* or resection*)).ti,ab.
10	or/1,7-9
11	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
12	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.
13	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
14	((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.
15	((improve* adj2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
16	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
17	(referral* adj3 (selective* or volume* or rate*)).ti,ab.
18	or/11-17
19	and/10,18
20	(animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
21	hi.fs. or case report.mp.
22	or/20-21
23	19 not 22
24	23 and 2000:3000.(dt).

Search interface: Ovid

- Ovid MEDLINE(R) Epub Ahead of Print and In-Process & Other Non-Indexed Citations November 12, 2019

#	**Searches**
1	(esophagectom* or oesophagectom*).ti,ab.
2	((esophageal* or oesophageal* or esophagus* or oesophagus*) and (surger* or resection*)).ti,ab.
3	or/1-2
4	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
5	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.
6	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
7	((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.
8	((improve* adj2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
9	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
10	(referral* adj3 (selective* or volume* or rate*)).ti,ab.
11	or/4-10
12	and/3,11
13	(animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
14	hi.fs. or case report.mp.
15	or/13-14
16	12 not 15
17	16 and 2000:3000.(dt).

2. Embase

Search interface: Ovid

- Embase 1974 to 2019 November 12

#	**Searches**
1	exp esophagus surgery/
2	exp esophagus tumor/
3	su.fs.
4	and/2-3
5	(esophagectom* or oesophagectom*).ti,ab.
6	((esophageal* or oesophageal* or esophagus* or oesophagus*) adj5 (surger* or resection*)).ti,ab.
7	or/1,4-6
8	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
9	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.
10	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
11	((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.
12	((improve* adj2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
13	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
14	(referral* adj3 (selective* or volume* or rate*)).ti,ab.
15	or/8-14
16	and/7,15
17	16 not medline.cr.
18	17 not (exp animal/ not exp human/)
19	18 not (Conference Abstract or Conference Review or Editorial).pt.
20	19 and 2000:3000.(dc).

3. The Cochrane Library

Search interface: Wiley

- Cochrane Central Register of Controlled Trials, Issue 11 of 12, November 2019

#	Searches
#1	[mh ^"Esophagectomy"]
#2	[mh ^"Esophageal Neoplasms"]
#3	[mh ^"Esophagus"]
#4	[mh ^"Esophageal Diseases"]
#5	#2 or #3 or #4
#6	([mh "surgery"] or [mh "therapy"])
#7	#5 and #6
#8	(esophagectom* or oesophagectom*):ti,ab
#9	((esophageal* or oesophageal* or esophagus* or oesophagus*) NEAR/5 (surger* or resection*)):ti,ab
#10	#1 or #7 or #8 or #9
#11	((minim* or high* or low or patient or outcome* or importance*) NEAR/3 (volume* or caseload)):ti,ab
#12	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) NEAR/2 (factor* or effect*)):ti,ab
#13	((hospital* or center* or centre* or unit*) NEAR/5 (type or level or small* or size)):ti,ab
#14	((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
#15	((improve* NEAR/2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)):ti,ab
#16	((surgeon* or surgical* or physician* or provider* or specialist*) NEAR/3 outcome*):ti,ab
#17	(referral* NEAR/3 (selective* or volume* or rate*)):ti,ab
#18	#11 or #12 or #13 or #14 or #15 or #16 or #17
#19	#10 and #18
#20	#19 with Publication Year from 2000 to 2019, in Trials

A.2 – Searches for systematic reviews

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to August 27, 2019

The following filter was adopted:

- Wong [92] – High specificity strategy

#	Searches
1	(esophag* or oesophag*).mp.
2	((minim* or high* or low or patient or outcome* or importance*) adj3 (volume* or caseload)).ab,ti.
3	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) adj2 (factor* or effect*)).ab,ti.
4	((hospital* or center* or centre* or unit*) adj5 (type or level or small* or size)).ab,ti.
5	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) adj2 (volume* or caseload* or experience* or characteristic*)).ab,ti.
6	((improved adj1 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)).ti,ab.
7	((surgeon* or surgical* or physician* or provider* or specialist*) adj3 outcome*).ti,ab.
8	(referral* adj3 (selective* or volume* or rate*)).ti,ab.
9	((hospital* or center* or centre* or unit* or surgeon* or surgical* or physician* or provider*) adj5 assessment*).ti,ab.
10	or/2-9
11	cochrane database of systematic reviews.jn.
12	(search or MEDLINE or systematic review).tw.
13	meta analysis.pt.
14	or/11-13
15	14 not (exp animals/ not humans.sh.)
16	and/1,10,15
17	16 and (english or german).lg.
18	..l/ 17 yr=2000-Current

2. The Cochrane Library

Search interface: Wiley

- Cochrane Database of Systematic Reviews: Issue 8 of 12, August 2019

#	Searches
#1	esophag* or oesophag*
#2	((minim* or high* or low or patient or outcome* or importance*) NEAR/3 (volume* or caseload)):ti,ab
#3	((hospital* or center* or centre* or unit* or surgeon* or provider* or physician*) NEAR/2 (factor* or effect*)):ti,ab
#4	((hospital* or center* or centre* or unit*) NEAR/5 (type or level or small* or size)):ti,ab
#5	((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
#6	((improve* NEAR/2 outcome*) and (hospital* or center* or centre* or unit* or surgeon*)):ti,ab
#7	((surgeon* or surgical* or physician* or provider* or specialist*) NEAR/3 outcome*):ti,ab
#8	(referral* NEAR/3 (selective* or volume* or rate*)):ti,ab
#9	#2 or #3 or #4 or #5 or #6 or #7 or #8
#10	#1 and #9 with Cochrane Library publication date Between Jan 2000 and Dec 2019, in Cochrane Reviews