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Hospital volume and mortality for 25 types of inpatient treatment in German hospitals – Observational study using complete national data from 2009 to 2014

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Competing interests

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Abstract

Objectives To explore the existence and strength of a relationship between hospital volume and mortality, to estimate minimum-volume thresholds and to assess the potential benefit of centralisation of services.

Design Observational population-based study using complete German hospital discharge data (Diagnosis-Related Group Statistics [DRG Statistics]).

Setting All acute care hospitals in Germany.

Participants All adult patients hospitalised for one out of 25 common or medically important types of inpatient treatment from 2009 to 2014.

Main outcome measure Risk-adjusted in-hospital mortality.

Results Lower in-hospital mortality in association with higher hospital volume was observed in 20 out of the 25 studied types of treatment when volume was categorized in quintiles, and persisted in 17 types of treatment when volume was analysed as a continuous variable. Such a relationship was found in some of the studied emergency conditions and low-risk procedures. It was more consistently present regarding complex surgical procedures. For example, about 22,000 patients receiving open repair of abdominal aortic aneurysm were analysed. In very high volume hospitals risk-adjusted mortality was 4.7% (95% CI 4.1 to 5.4) compared to 7.8% (7.1 to 8.7) in very low volume hospitals. The minimum volume above which risk of death would fall below the average mortality was estimated as 18 cases per year. If all hospitals providing this service would perform at least 18 cases per year one death among 104 (76 to 166) patients could potentially be prevented.

Conclusions Based on complete national hospital discharge data the results confirmed volume-outcome relationships for many complex surgical procedures, as well as for some emergency conditions and low-risk procedures. Following these findings, the study identified areas where centralisation would provide a benefit for patients undergoing the specific type of treatment in German hospitals and quantified the possible impact of centralisation efforts.

Keywords

Volume-outcome relationship, hospital discharge data, in-hospital mortality, Germany

Strengths and limitations of the study

- The strength of this study is the use of current and complete national hospital discharge data, covering virtually every patient who underwent one out of the studied types of treatment during the study period.
- As hospital volumes vary widely among German acute care hospitals this is a proper setting to study volume-outcome relationships.
- In contrast to most other volume-outcome studies, the present approach includes the calculation of minimum volume thresholds along with an assessment of the possible impact of centralization efforts on the population.
- Within this observational retrospective study the statistical association between volume and outcome was tested upon administrative data.
- As information available from administrative data is limited, it is possible that unmeasured differences in disease severity, comorbidity, or appropriateness of patient selection may partly explain the association between volume and outcome.

Introduction

The relationship between hospital volume and patient outcomes has been widely studied. For many inpatient treatments a higher volume was found to be associated with better outcomes, such as for high-risk surgical procedures, medical conditions or elective low-risk surgery.[1-10] Systematic reviews and meta analyses were conducted to aggregate results into a broader frame of knowledge.[11-14] However, the heterogeneity of methods used impairs conclusions from meta analyses. In particular, the categorisation of high volume hospitals varies according to the geographical context.[15-16] Moreover, many studies include only samples of patients or are restricted to patients with a specific type of insurance or within a delimited geographic area. Therefore, it is often uncertain if the association of volume and outcome found in one study may be generalizable to the whole population affected, or even to populations in other countries with different health care systems. Finally, studies reporting better outcome in relation to higher volume often lack an assessment of the clinical and policy significance of their findings.[16]

To date, the volume-outcome relationship in Germany has been studied only for few inpatient services, such as pancreatic resection, abdominal aortic aneurysm repair, hip fracture, or treatment of very low birthweight infants.[17-19] The German acute care hospital market is characterized by a relative overcapacity of hospital beds and high hospitalization rates.[20] Volumes of inpatient treatments vary widely among the about 1,600 German acute care hospitals.[21] In 2004, minimum volume thresholds for specific types of inpatient treatment were established. However, it has been found that many hospitals did not adhere to this regulation, and the debate about the underlying evidence remains controversial.[22-24]

Efforts to improve quality of care by centralisation of services need to rely on evidence that higher volume is associated with better outcome. Therefore, this study aimed to explore the relation of hospital volume and outcome in the German hospital market by using complete national hospital discharge data. For a broad range of common or medically important inpatient services the existence and strength of a relationship between volume and mortality was analysed. Where lower mortality in relation to higher volume was observed minimum volume thresholds, above which mortality would be reduced, were estimated. Impact measures were calculated to assess the potential benefit of centralisation efforts.

Methods

Data

German acute care hospitals are obliged to submit their inpatient discharge data annually to a nationwide database, which is available for research purposes. This database (Diagnosis-Related Group Statistics [DRG Statistics] provided by the Research Data Centres of the Federal Statistical Office and the statistical offices of the 'Länder') contains discharge information on every inpatient episode, covering patients of all types of insurance. Principal and secondary diagnoses are coded according to the German adaptation of the International Classification of Diseases (ICD-10-GM). Procedures are coded according to the German procedure coding system (OPS, Operationen- und Prozedurenschlüssel). Information on sex, age, source of admission, discharge disposition, and length of stay are also included. Based on an anonymized hospital identifier every inpatient episode can be assigned to the treating hospital.[25] The analyses included data of the years 2009 to 2014. Data were accessed via controlled remote data analysis.

Patient population

To study a broad range of hospital services five groups of inpatient treatments comprising 25 single conditions or procedures were analysed:

- Common emergency conditions (6)
- Elective heart and thoracic surgery (4)
- Elective major visceral surgery (6)
- Elective vascular surgery (4)
- Elective low-risk surgery (5)

Each type of treatment was defined by specific inclusion and exclusion criteria in order to minimize confounding by differences in case-mix. Treatments for emergency conditions (e.g. acute myocardial infarction) were restricted to direct admissions by excluding patients who had been transferred-in from another acute care hospital. Elective surgical treatments were defined by restriction to certain medical indications (e.g. colorectal resection for carcinoma) or exclusion of complicated constellations (e.g. aortic valve replacement excluding combined other heart surgery). All definitions refer to adult patients aged 20 years and older. Inclusion and exclusion criteria are listed in Appendix Table 1.

Hospital volume

Volume of patients treated by a hospital was calculated for each year of observation corresponding to the respective definition of a studied type of treatment. Aiming to compare results in the context of the current literature, hospitals were ranked into quintiles of approximately equal case numbers according to their annual volume. Additionally, hospital volume was analysed as a continuous variable.

Within a sensitivity analysis hospital volume was additionally determined on the basis of wider case definitions in order to fully consider all treatments which might enhance a hospital's experience regarding a specific condition or procedure (e.g., all colorectal resections regardless from medical indication). This approach led to a higher estimation of annual volume per hospital in most cases and resulted in a slightly different ranking of hospitals. Within this analysis restrictions in case definition, as described above, were subsequently applied for outcome measurement.

Outcome measure, risk adjustment and statistical analysis

In-hospital mortality, defined as death before discharge, was studied as outcome measure. Observed and risk-adjusted mortality were stratified by volume quintiles.

Risk-adjusted mortality for each volume quintile was calculated by using generalized estimating equations (GEE) with a logit link function, accounting for clustering of patients within hospitals. Using the pooled data of the entire observation period one GEE model was fitted for each studied treatment. Depending on the type of treatment, models included comorbidities, which most likely have been present on admission (e.g. diabetes, chronic liver disease), specific indicators of disease severity (e.g. ST-elevation myocardial infarction), or extension of surgery (e.g. concomitant resection of other visceral organs in patients with pancreatic resection). 5-year age groups, sex, and calendar year of treatment were considered within each model. The definitions and treatment-specific applications of covariates for risk adjustment are displayed in Appendix tables 2 and 3.

In order to estimate the independent impact of hospital volume on in-hospital mortality, hospital volume was subsequently entered into each model, taken as a categorically variable. Odds ratios for in-hospital death by hospital volume quintile were calculated.

To further explore the relationship between volume and outcome GEE models with volume as a continuous variable were fitted for each treatment. In a first step, hospital volume was taken as the only predictor (simple model). In a second step the treatment-specific covariates, as described above, were entered into the model (full model) and odds ratios for in-hospital death according to an increment of one case, as well as of 50 cases per year were calculated.

Where the regression coefficient of a one-case increment of hospital volume remained statistically significant after consideration of covariates, minimum volume thresholds were estimated from the simple model using Benders Value of Acceptable Risk Limit.[26] This value is calculated from the function of the logistic regression coefficient of hospital volume. It denotes the threshold where mortality is expected to fall below a predefined acceptable risk. The acceptable risk was set to the average mortality of the respective treatment during the observation period.

The clinical relevance of thresholds was assessed by the population impact number (PIN). The PIN was calculated as reciprocal of the difference between the average mortality risk in the entire patient population and the adjusted risk among patients treated by hospitals with volumes above the threshold (population-based risk difference PRD).[27] In the context of this study, the PIN can be interpreted as average number of patients within a treatment group among whom one death is attributable to treatment by a below-threshold volume hospital, due to excess risk of mortality in these hospitals. In other words, among this number of patients one death could hypothetically be prevented if all hospitals providing the respective inpatient service had annual volumes equal or higher than the threshold.

The level of statistical significance was set to .05. The analyses were conducted using SAS Version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Common emergency conditions

Lower in-hospital mortality in association with higher hospital volume was observed in four out of the six studied types of common emergency treatment when volume was categorized in quintiles and persisted in two types of treatment when volume was analysed as a continuous variable.

From 2009 to 2014 nearly 1.1 million patients were treated for acute myocardial infarction (table 1). Risk-adjusted mortality was 8.9% (95% CI 8.8 to 9.0) in the very high volume quintile versus 11.4% (11.3 to 11.6) in the very low volume quintile (figure 1). Adjusted odds ratios of in-hospital death were significantly reduced in the low to very high volume quintiles when compared to the very low volume quintile (table 2). A statistically significant effect of volume on mortality was also observed when volume was analysed as a continuous variable. An increment of 50 cases per year was associated with reduced odds of death (figure 2). The minimum hospital volume where risk of mortality would fall below the average mortality of 9.8% was calculated as 309 cases per year. Stratification by this threshold resulted in a population-based risk difference (PRD) of 0.7% (0.7 to 0.8) and a population impact number (PIN) of 137 (127 to 149, table 3). This means that out of 137 patients hospitalized for acute myocardial infarction one death would be prevented if annual volumes in treating hospitals were at least 309.

In total, 2.3 million patients treated for heart failure were studied. Risk-adjusted mortality was 8.5% (95% CI 8.4 to 8.6) in the very high volume quintile versus 9.2% (9.1 to 9.3) in the very low volume quintile (figure 1). For volume as a continuous variable no association was found after consideration of covariates (table 3).

During the observation period 1.2 million patients were hospitalized for ischemic stroke (table 1). Adjusted mortality in the very high volume quintile was 6.9% (95% CI 6.8 to 7.0) versus 7.3% (7.2 to 7.4) in the very low volume quintile (figure 1). After consideration of covariates no measurable effect of hospital volume as a continuous variable was observed (table 3).

Among the 1.3 million patients treated for pneumonia (table 1) higher hospital volume was associated with higher in-hospital mortality. Adjusted mortality was 11.5% (95% CI 11.3 to 11.6) in the very high volume quintile, 12.3% (12.2 to 12.5) in the medium volume quintile and 10.8% (10.7 to 10.9) in the very low volume quintile (figure 1), and the odds ratios were higher in the low to very high volume quintiles when compared to the very low volume quintile (table 2). When considered as a continuous variable hospital volume was not associated with mortality (table 3).

For the more than 1.15 million patients with chronic obstructive pulmonary disease (COPD, table 1) adjusted mortality was 3.1% (95% CI 3.0 to 3.2) in the very high volume quintile and 4.3% (4.2 to 4.4) in the very low volume quintile (figure 1). Hospital volume as a continuous variable had an independent effect on mortality (figure 2) and the minimum volume to achieve a lower-than-average risk of death was calculated as 271 patients per year. This threshold was estimated to prevent one death among 170 (158 to 185) COPD patients (table 3).

The analysis of 711,000 patients hospitalized for hip fracture (table 1) revealed slightly higher mortality in low to high volume quintiles when compared to the very low volume quintile (figure 1). Hospital volume as a continuous variable had no effect on mortality (table 3).

Elective heart and thoracic surgery

For each out of the four studied types of heart and thoracic surgery lower in-hospital mortality in association with higher hospital volume was observed.

From 2009 to 2014 about 52,600 patients were treated with isolated surgical aortic valve replacement (table 1). Adjusted mortality was 2.4% (95% CI 2.1 to 2.7) in the very high volume quintile versus 3.1% (2.8 to 3.4%) in the very low volume quintile (figure 1). Reduced odds of death were found in the medium to very high volume quintiles when compared to the very low volume quintile (table 2). As a continuous variable hospital volume demonstrated an independent effect on mortality (figure 2). The minimum volume to achieve a lower-than-average risk of death was calculated as 147 annual treatments. This threshold resulted in a non-significant PRD of 0.2% (-0.02 to 0.3) and a PIN of 516 (288 to 2589, table 3).

In-hospital mortality of the 50,800 patients treated with transcatheter aortic valve replacement (table 1) was 5.2% (95% CI 4.8 to 5.7) in the very high volume quintile versus 7.6% (7.1 to 8.2) in the very low volume quintile (figure 1). Hospital volume as a continuous variable revealed an independent effect on mortality (figure 2) and the minimum volume to fall below the average mortality of 6.6% was calculated as 157 cases per year. Application of this threshold was estimated to prevent one death among 133 (101 to 193) patients (table 3). This means that among 133 patients with transcatheter aortic valve replacement one death would be prevented if all providing hospitals would perform this treatment at least 157 times per year.

184,000 patients were treated with an isolated coronary artery bypass graft (table 1). According to hospital quintiles no constant association of volume and mortality was found (figure 1, table 2). However, an independent effect of hospital volume on mortality was observed when volume was analysed as a continuous variable (figure 2) and the minimum volume to achieve a risk of death below the average of 2.1% was calculated as 475 cases per year. This threshold led to a PIN of 658 (445 to 1271, table 3).

In total, 74,000 patients with partial lung resection for carcinoma were studied (table 1). In the very high volume quintile adjusted mortality was 2.0% (95% CI 1.8 to 2.3) versus 3.8% (3.6 to 4.1) in the very low volume quintile (figure 1). The observed independent effect of hospital volume when analysed continuously resulted in a minimum volume of 108 cases per year. This threshold was estimated to prevent one death among 168 (137 to 217) patients (table 3).

Elective major visceral surgery

Lower mortality associated with higher hospital volume was found for all six studied types of elective visceral surgery.

During the observation period 331,000 colorectal resections for carcinoma were performed in German hospitals (table 1). Mortality was 5.2% (95% CI 5.0 to 5.4) in the very high volume quintile and 6.6% (6.4 to 6.8) in the very low volume quintile (figure 1). In comparison to the very low volume quintile odds of death were statistically significantly reduced in the medium to very high volume quintiles (table 2). Hospital volume as a continuous variable had an independent effect on mortality (figure 2). The minimum volume to achieve a risk of death below the average of 6.0% was calculated as 82 annual treatments, associated with a PIN of 197 (167 to 241, table 3).

179,000 colorectal resections were performed for diverticulosis (table 1). Adjusted mortality was 3.1% (95% CI 2.9 to 3.3) in the very high volume quintile versus 3.9% (3.8 to 4.1) in the very low volume quintile (figure1). Hospital volume as a continuous variable had an independent effect on mortality and a minimum volume of 44 was calculated to achieve a risk of death below the average of 3.5%. This threshold was associated with a PIN of 364 (269 to 564, table 3).

During the observation period 68,000 patients with total nephrectomy for carcinoma were identified (table 1). In the very high volume quintile adjusted mortality was 1.9% (95% CI 1.7 to 2.2) and in the very low volume quintile 2.3% (2.1 to 2.6). The independent effect of hospital volume as a continuous variable demonstrated borderline statistical significance (figure 2) and the minimum volume to achieve lower-than-average mortality was calculated as 40 cases per year. Application of this threshold would prevent one death among 459 (295 to 1056) nephrectomy patients (table 3).

Adjusted mortality among the 44,000 patients receiving cystectomy for carcinoma (table 1) was 4.0% (95% CI 3.6 to 4.4) in the very high volume quintile versus 5.5% (5.0 to 6.0) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower mortality (figure 2). This relation of volume and outcome resulted in a minimum volume of 31 cases per year to fall below the average mortality of 4.7%. Application of this threshold was associated a PIN of 227 (150 to 480, table 3).

Among the 18,000 patients with complex oesophageal surgery for carcinoma adjusted mortality was 5.8% (95% CI 5.1 to 6.6) in the very high volume quintile versus 10.5% (9.5 to 11.6) in the very low volume quintile. As a continuous variable hospital volume had an independent effect on mortality and the minimum volume to fall below the average mortality of 8.5% was calculated as 22 cases per year. If all hospitals would perform at least 22 complex oesophageal surgeries per year one death among 47 (38 to 62) patients could be prevented (table 3).

A pancreatic resection for carcinoma was performed in 35,000 patients in total (table 1). Adjusted mortality was 6.4% (95% CI 5.8 to 7.0) in the very high volume quintile versus 11.7% (10.9 to 12.5) in the very low volume quintile (figure 1). Continuous increment of hospital volume was associated with lower mortality and the minimum volume where risk of death would fall below the average mortality of 8.8% was calculated as 29 cases per year. This threshold resulted in a PIN of 46 (39 to 58, table 3).

Elective vascular surgery

In three out of the four studied types of elective vascular surgery higher hospital volume was associated with lower in-hospital mortality.

During the observation period 247,000 patients were treated with surgical revascularization of lower extremities for atherosclerosis (table 1). Risk-adjusted mortality was 2.8% (95% CI 2.7 to 3.0) in the very high volume quintile versus 3.3% (3.2 to 3.5) in the very low volume quintile (figure 1). Odds of death were reduced in all other quintiles when compared to the very low volume quintile (table 2). The association of volume and outcome persisted when volume was analysed as continuous variable (figure 2) and the minimum volume to achieve a mortality risk below the average of 3.0% was calculated as 123 cases per year. This led to the estimation that among 561 (387 to 1024) patients one additional death was attributable to treatment by a hospital performing less than 123 of such operations (table 3).

In total, more than 22,000 patients receiving open repair of abdominal aortic aneurysm were analysed (table 1). In the very high volume quintile risk-adjusted mortality was 4.7% (95% CI 4.1 to 5.4) versus 7.8% (7.1 to 8.7) in the very low volume quintile (figure 1). When analysed continuously, higher volume was independently associated with lower mortality (figure 2). The calculated minimum volume where risk would fall below the average of 6.0% was 18 cases per year. The resulting PIN was 104 (76 to 166, table 3).

Among the 42,000 patients treated with endovascular repair of abdominal aortic aneurysm (table 1) risk-adjusted mortality was 1.6% (95% CI 1.3 to 1.9) in the very high volume quintile versus 1.7% (1.4 to 2.0) in the very low volume quintile. Highest mortality was observed in the medium volume quintile (2.1%, 1.8 to 2.4, figure 1). Odds of death were not significantly different between volume quintiles (table 2). Analysed as continuous variable no statistically significant effect of hospital volume on mortality was observed (figure 2, table 3).

From 2009 to 2014 about 162,000 patients with carotid endarterectomy were identified (table 1). Risk-adjusted in-hospital mortality was 0.75% (95% CI 0.66 to 0.86) in the very high volume quintile and 0.97% (0.87 to 1.07) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower in-hospital mortality (figure 2). A lower-than-average risk of mortality is expected if hospitals perform at least 93 carotid endarterectomies per year. Under this threshold the estimated PIN was 1646 (886 to 12661, table 3).

Elective low-risk surgery

In three out of the five studied types of elective low-risk surgery higher hospital volume was found to be associated with lower mortality when volume was categorized in quintiles. In two types of elective low-risk surgery this relation persisted when volume was analysed as a continuous variable.

From 2009 to 2014 nearly 889,000 inpatient cholecystectomies for cholelithiasis were performed in German hospitals (table 1). Risk-adjusted mortality differed not significantly between volume quintiles (figure 1), as well as risk-adjusted odds of death (table 2). Continuous increment of hospital volume was not associated with mortality (table 3).

Among the 897,000 inpatient inguinal or femoral hernia repairs (table 1) mortality in the very high volume quintile was lower (0.07%, 95% CI 0.06 to 0.08) than in the very low volume quintile (0.10%, 0.09 to 0.12, figure 1). Yet, the independent effect of continuous increment of hospital volume was not statistically significant (table 3).

The analysis of more than 881,000 primary hip replacements for arthrosis or arthritis (table 1) revealed a constant association of hospital volume and mortality when patients were stratified by volume quintiles. Risk-adjusted in-hospital mortality was 0.10% (95% CI 0.08 to 0.11) in the very high volume quintile versus 0.23% (0.21 to 0.25) in the very low volume quintile (figure 1). In comparison to the very low volume quintile odds of death were significantly reduced in all other volume quintiles (table 2). Within the analysis of continuous increment of hospital volume an independent effect on mortality was observed (figure 2). A minimum volume of 252 cases per year was calculated to achieve a risk of mortality below the average of 0.17%. The PIN resulting from this threshold was 2747 (2186 to 3701, table 3).

Overall 843,000 patients with primary knee replacement for arthrosis or arthritis were identified (table 1). Risk-adjusted mortality was 0.06% (95% CI 0.05 to 0.07) in the very high volume quintile versus 0.13% (0.11 to 0.14) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower mortality (figure 2) and 228 annual cases were calculated as the minimum volume where risk of mortality would fall below the average of 0.10%. This minimum volume threshold resulted in an estimation of one preventable death among 4729 (3513 to 7269) primary knee replacement patients if all hospitals would perform at least 228 such operations per year (table3).

In total, 434,000 patients with transurethral resection of prostate were studied (table 1). No statistically significant differences in in-hospital mortality were found when patients were stratified by hospital volume quintiles (figure 1, table 2) and there was no significant association of hospital volume and mortality when volume was analysed continuously (table 3).

Sensitivity analysis

Within the sensitivity analysis hospital volume was determined more widely by considering all those treatments or procedures, which could be regarded as technically similar to the specific treatment for which outcome was measured. The specific restrictions for the purpose of outcome measurement were applied after determining volume. Using this divergent volume definition results remained substantially unchanged in 23 out of the 25 studied types of treatments.

Different findings were observed regarding isolated coronary bypass graft, where the relation of volume and mortality was more pronounced when all related procedures (i.e., coronary bypass grafts in patients with acute myocardial infarction or combined with other heart surgery instead of elective isolated coronary operations only) were considered for determination of hospital volume. Different from the findings in the main analysis higher volume was constantly associated with lower mortality when patients were stratified by these volume quintiles.

The volume-outcome association in colorectal resections for diverticulosis diminished when hospital volume was determined by considering all colorectal resections, regardless from medical indication. In contrast to the results of the main analysis, no statistically significant relation between volume and outcome was observed under this approach.

Discussion

Lower in-hospital mortality in association with higher hospital volume was observed in 20 out of the 25 studied types of treatment when volume was categorized in quintiles, and persisted in 17 types of treatment when volume was analysed as a continuous variable. While a volume-outcome relationship was not found in all studied emergency conditions and low-risk procedures, it was more consistently present regarding complex surgical procedures. The potential benefit of a centralisation according to the calculated minimum volume thresholds varied depending on the treatment-specific risk of death and the strength of the association between volume and mortality.

The analysis included every patient who underwent one of the studied types of inpatient treatment in a German acute care hospital during the observation period. Limitations occur from the limited information available in administrative data, including lack of information on appropriateness of patient selection for procedures. Although types of treatment and covariates for risk adjustment were defined in a sophisticated way, it is possible that unmeasured differences in disease severity, comorbidity, or appropriateness may partly explain the association between volume and outcome. However, it should be considered that the more severe patients should intentionally not be treated by low-volume hospitals. The analyses could focus hospital volume only because physician volumes are not available in German administrative data. Regarding the determination of hospital volume, a possible misclassification of multi-campus hospitals as high volume providers must be taken into account, resulting in a possible underestimation of the association between hospital volume and mortality.[28]

Inpatient treatments for emergency conditions revealed mixed results. Associations between higher hospital volume and lower mortality were found for treatment of acute myocardial infarction, heart failure, ischemic stroke, and chronic obstructive pulmonary disease. These results are similar to findings of previous studies from other countries. [6-7, 29-34] Regarding the treatment of patients with pneumonia the analysis revealed higher mortality in hospitals with higher volumes. A similar finding has been reported by one previous US study,[35] while another more recent US study found higher hospital volume being associated with lower mortality.[6] No constant relation between volume and outcome was observed in hip fracture patients, similar to findings from a recent US study.[36] However, a previous German study, which was based on national discharge data as well, but focussed an earlier time period and surgically treated hip fracture patients only, found lower mortality related to higher hospital volumes.[18] An Italian study observed a volume-outcome relation in hip fracture patients, too.[34]

An association of lower mortality and higher hospital volume was observed for each studied type of elective heart and thoracic surgery. These findings correspond to those from several European and US studies. [3, 5, 14, 34, 37-39] As well, the findings of an volume-outcome relation in all studied types of major visceral surgery are supported by international findings which point to the same direction.[3, 11-12, 17, 30, 40-44] In the case of vascular surgery, the analyses demonstrated lower mortality in association with higher hospital volume for lower extremity revascularization, carotid endarterectomy and open repair of abdominal aortic aneurysm, in accordance to findings from the international literature. [3, 5, 34, 45-46] A volume-outcome relation for abdominal aortic aneurysm repair (open or endovascular) had been demonstrated by a previous German study based on national discharge data.[18] In the present study, however, endovascular repair of abdominal aortic aneurysm was analysed separately and no significant relationship between volume and mortality was observed. This finding is in contrast to one study from the US.[47]

Among the studied types of elective low-risk surgery lower mortality associated with higher volume was found for primary knee and hip replacement, supported by international findings.[8, 48-51] However, no such relation was observed for cholecystectomy, similar to one study from England,[52] but in contrast to studies from Italy and Scotland, which found a modest association between volume and outcome in cholecystectomy patients.[34, 53] The effect of volume on mortality observed in patients undergoing inguinal or femoral hernia repair was small. Studies from the US and Sweden reported a volume-outcome relation for hernia repair, but focussed different outcomes (hernia recurrence or reoperation rates) and determined volume rather on the surgeon level.[54-55] Regarding transurethral resection of prostate no association between hospital volume and mortality was found. This confirms the findings of a Japanese study which found an association regarding complication and blood transfusion rates, but not regarding mortality.[56]

Overall, the results of the present study seem plausible in view of the current literature. Discrepancies to findings from other studies might be caused by differences in completeness of data or alternative methodological approaches, e.g. regarding case definitions, or volume determination. However, it is also possible that an association between volume and outcome is more or less existent in different countries, depending on characteristics of a health care system and hospital market structures.[37]

Minimum volume thresholds were calculated for those treatments, in which the association of volume and mortality persisted when volume was analysed as a continuous variable, which provides a strong indication that such an association truly exists. The potential for improvement by centralisation according to the thresholds might appear small in the case of treatments with a basically low risk of mortality. However, one should consider that risk of mortality is likely correlated with the occurrence of non-lethal adverse events, in particular with regard to low-risk procedures. Thus, possible improvements of patient safety by centralisation might reach beyond effects on mortality.

Yet, this retrospective observational study cannot provide evidence that an application of the calculated thresholds as minimum volumes would actually improve quality of care. Therefore, the threshold values are meant to serve as basic orientation points for policy decisions in Germany and as hypothesis-generating landmarks for further research in other countries. Although estimated rather conservatively, roughly 80 to 90% of hospitals providing a specific treatment performed annual volumes below the respective threshold, and between 50% (acute myocardial infarction) and 70% (pancreatic resection for carcinoma) of patients were treated by those hospitals. Policy decisions on centralisation of services cannot rely on testing a statistical association upon observational data, alone. As well, the regional availability and accessibility of inpatient services must be considered, in particular regarding emergency treatments. Centralisation should be pushed primarily in oversupplied geographic regions.

Experiences from the Netherlands have demonstrated that centralisation of inpatient services improved national outcome.[57] A previous German study concluded that full implementation of the existing minimum volume regulation could improve the quality of hospital care in Germany.[23] In addition to this, the present study identified further areas where centralisation could provide a benefit for patients, and quantified the possible impact of centralisation efforts by using complete national hospital discharge data. These findings might support future policy decisions in Germany.

Author's contribution

Ulrike Nimptsch designed the study, conducted the analysis, interpreted the data and drafted the manuscript. Thomas Mansky contributed to the study design, to the interpretation of data and to revising the manuscript critically for important intellectual content. Both authors gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table 1 No. of patients and hospitals by volume quintile

		Hospital volume quintile									
		Very low		Low		Medium		High		Very high	
COMMON EMERGENCY CONDITIONS											
Acute myocardial infarction	No. of patients		219,178		219,291		219,189		219,778		220,805
	No. of hospitals		763		198		121		88		54
	Median annual volume *(IQR)*	43	*(20 - 71)*	184	*(154 - 215)*	303	*(274 - 331)*	412	*(387 - 450)*	594	*(534 - 732)*
Heart failure	No. of patients		463,352		463,883		463,283		464,586		465,401
	No. of hospitals		608		263		184		136		87
	Median annual volume *(IQR)*	139	*(63 - 189)*	290	*(260 - 321)*	418	*(374 - 461)*	570	*(518 - 613)*	804	*(703 - 950)*
Ischemic stroke	No. of patients		244,125		244,272		244,299		243,725		246,858
	No. of hospitals		915		155		96		70		42
	Median annual volume *(IQR)*	28	*(10 - 62)*	259	*(213 - 310)*	427	*(383 - 471)*	577	*(542 - 625)*	865	*(766 - 1028)*
Pneumonia	No. of patients		258,016		257,688		258,010		258,051		259,391
	No. of hospitals		630		255		186		140		84
	Median annual volume *(IQR)*	73	*(25 - 107)*	167	*(150 - 183)*	229	*(211 - 249)*	304	*(279 - 331)*	447	*(396 - 523)*
Chronic obstructive pulmonary disease	No. of patients		230,629		230,793		231,093		230,258		232,476
	No. of hospitals		612		264		182		125		61
	Median annual volume *(IQR)*	67	*(33 - 92)*	144	*(126 - 163)*	209	*(187 - 233)*	299	*(262 - 337)*	546	*(455 - 702)*
Hip fracture	No. of patients		142,041		142,082		141,910		141,658		143,271
	No. of hospitals		609		232		172		133		88
	Median annual volume *(IQR)*	43	*(6 - 64)*	101	*(93 - 110)*	137	*(128 - 146)*	176	*(164 - 190)*	244	*(221 - 283)*
ELECTIVE HEART AND THORACIC SURGERY											
Isolated surgical aortic valve replacement	No. of patients		10,275		10,238		10,627		10,066		11,397
	No. of hospitals		33		17		14		10		7
	Median annual volume *(IQR)*	54	*(37 - 71)*	100,5	*(93 - 108)*	132	*(124 - 138)*	172	*(159 - 188)*	246	*(227 - 283)*
Transcatheter aortic valve replacement	No. of patients		9,915		10,009		9,926		9,935		10,980
	No. of hospitals		48		17		12		9		6
	Median annual volume *(IQR)*	31	*(12 - 50)*	98	*(69 - 123)*	141	*(99 - 161)*	169	*(142 - 228)*	286	*(233 - 328)*
Isolated coronary artery bypass graft	No. of patients		35,648		36,967		36,047		37,221		37,807
	No. of hospitals		48		18		14		11		8
	Median annual volume *(IQR)*	120	*(1 - 230)*	353	*(318 - 375)*	436	*(407 - 465)*	561	*(518 - 585)*	729	*(669 - 824)*
Partial lung resection for carcinoma	No. of patients		14,655		14,766		14,626		14,872		15,064
	No. of hospitals		260		48		27		17		9
	Median annual volume *(IQR)*	5	*(2 - 14)*	49	*(43 - 59)*	89	*(79 - 98)*	137	*(122 - 160)*	272	*(208 - 313)*
ELECTIVE MAJOR VISCERAL SURGERY											
Colorectal resection for carcinoma	No. of patients		66,058		66,089		66,119		66,185		66,451
	No. of hospitals		492		218		153		112		71
	Median annual volume *(IQR)*	23	*(14 - 32)*	50	*(45 - 55)*	72	*(66 - 78)*	97	*(91 - 105)*	141	*(126 - 165)*
Colorectal resection for diverticulosis	No. of patients		35,828		35,821		35,810		35,872		36,032
	No. of hospitals		487		215		154		114		73
	Median annual volume *(IQR)*	13	*(7 - 18)*	28	*(25 - 30)*	39	*(36 - 42)*	52	*(48 - 56)*	74	*(68 - 86)*
Total nephrectomy for carcinoma	No. of patients		13,582		13,569		13,570		13,600		13,766
	No. of hospitals		307		90		65		47		31
	Median annual volume *(IQR)*	5	*(2 - 13)*	25	*(23 - 27)*	35	*(33 - 37)*	48	*(45 - 52)*	67	*(60 - 76)*
Cystectomy for carcinoma	No. of patients		8,706		8,702		8,761		8,734		8,832
	No. of hospitals		177		78		56		39		24
	Median annual volume *(IQR)*	9	*(5 - 12)*	18	*(17 - 20)*	26	*(24 - 28)*	36	*(34 - 40)*	57	*(51 - 68)*
Complex oesophageal surgery for carcinoma	No. of patients		3,625		3,625		3,639		3,550		3,769
	No. of hospitals		228		71		43		23		10
	Median annual volume *(IQR)*	2	*(1 - 4)*	8	*(7 - 10)*	14	*(12 - 16)*	25	*(21 - 29)*	54	*(42 - 67)*
Pancreatic resection for carcinoma	No. of patients		6,886		6,915		6,880		6,854		7,020
	No. of hospitals		322		117		71		41		17
	Median annual volume *(IQR)*	3	*(2 - 5)*	10	*(9 - 11)*	16	*(14 - 18)*	27	*(23 - 33)*	57	*(46 - 72)*
ELECTIVE VASCULAR SURGERY											
Surgical lower extremity revascularization for atherosclerosis	No. of patients		49,239		49,385		49,467		49,086		49,997
	No. of hospitals		348		113		79		57		37
	Median annual volume *(IQR)*	21	*(7 - 39)*	72	*(65 - 80)*	102	*(95 - 112)*	143	*(131 - 158)*	210	*(185 - 243)*
Open repair of abdominal aortic aneurysm	No. of patients		4,422		4,425		4,430		4,420		4,530
	No. of hospitals		239		81		50		33		18
	Median annual volume *(IQR)*	3	*(1 - 4)*	9	*(7 - 10)*	15	*(13 - 17)*	21	*(19 - 25)*	39	*(33 - 46)*
Endovascular repair of abdominal aortic aneurysm	No. of patients		8,281		8,338		8,288		8,309		8,462
	No. of hospitals		219		81		52		34		20
	Median annual volume *(IQR)*	6	*(3 - 9)*	17	*(15 - 19)*	26	*(24 - 30)*	40	*(36 - 45)*	64	*(57 - 75)*
Carotid endarterectomy	No. of patients		32,345		32,267		32,460		32,017		33,081
	No. of hospitals		317		101		67		47		30
	Median annual volume *(IQR)*	16	*(6 - 27)*	52	*(46 - 59)*	80	*(73 - 87)*	113	*(104 - 123)*	165	*(148 - 195)*

Table 1 (continued)

ELECTIVE LOW-RISK SURGERY											
Cholecystectomy for cholelithiasis	No. of patients		177,346		177,411		177,835		177,199		178,752
	No. of hospitals		450		232		178		140		94
	Median annual volume *(IQR)*	71	*(44 - 91)*	128	*(118 - 137)*	166	*(157 - 176)*	210	*(196 - 224)*	286	*(264 - 331)*
Inguinal or femoral hernia repair	No. of patients		178,992		179,169		179,285		179,338		179,911
	No. of hospitals		471		247		186		142		84
	Median annual volume *(IQR)*	68	*(45 - 86)*	120	*(111 - 129)*	160	*(150 - 171)*	208	*(194 - 224)*	312	*(274 - 377)*
Primary hip replacement for arthrosis or arthritis	No. of patients		175,918		175,797		176,313		175,834		177,287
	No. of hospitals		608		226		135		82		42
	Median annual volume *(IQR)*	49	*(25 - 71)*	128	*(111 - 146)*	213	*(190 - 242)*	351	*(314 - 388)*	619	*(522 - 768)*
Primary knee replacement for arthrosis or arthritis	No. of patients		168,312		168,479		168,415		168,015		169,623
	No. of hospitals		517		222		143		94		51
	Median annual volume *(IQR)*	56	*(36 - 75)*	125	*(112 - 140)*	195	*(176 - 215)*	291,5	*(267 - 324)*	477	*(421 - 632)*
Transurethral resection of prostate	No. of patients		86,404		86,934		86,199		86,967		87,412
	No. of hospitals		247		104		77		59		40
	Median annual volume *(IQR)*	60	*(23 - 92)*	139	*(128 - 150)*	186	*(172 - 199)*	243	*(227 - 262)*	331	*(303 - 380)*

No. of hospitals: Mean number of hospitals in quintile per year providing the respective inpatient service; IQR: interquartile range within the quintile (due to data protection regulations the minimum and maximum values cannot be displayed).

Table 2 Odds ratios of in-hospital death according to volume quintile

		Hospital volume quintile								
		Very low	Low		Medium		High		Very high	
COMMON EMERGENCY CONDITIONS										
Acute myocardial infarction	Crude OR	1.00	0.82		0.74		0.72		0.71	
	Adjusted OR *(95% CI)*	1.00	* 0.84	*(0.81 to 0.87)*	* 0.75	*(0.72 to 0.78)*	* 0.73	*(0.7 to 0.76)*	* 0.69	*(0.66 to 0.72)*
Heart failure	Crude OR	1.00	0.95		0.89		0.87		0.81	
	Adjusted OR *(95% CI)*	1.00	0.99	*(0.96 to 1.01)*	* 0.96	*(0.93 to 0.99)*	* 0.95	*(0.92 to 0.98)*	* 0.91	*(0.88 to 0.94)*
Ischemic stroke	Crude OR	1.00	0.77		0.70		0.70		0.72	
	Adjusted OR *(95% CI)*	1.00	* 0.90	*(0.87 to 0.94)*	* 0.87	*(0.83 to 0.9)*	* 0.94	*(0.91 to 0.98)*	* 0.94	*(0.91 to 0.98)*
Pneumonia	Crude OR	1.00	1.09		1.16		1.12		1.08	
	Adjusted OR *(95% CI)*	1.00	1.10	*(1.07 to 1.13)*	1.17	*(1.14 to 1.21)*	1.13	*(1.09 to 1.16)*	1.08	*(1.04 to 1.11)*
Chronic obstructive pulmonary disease	Crude OR	1.00	1.06		1.04		0.91		0.66	
	Adjusted OR *(95% CI)*	1.00	1.09	*(1.06 to 1.14)*	1.08	*(1.04 to 1.12)*	* 0.94	*(0.90 to 0.98)*	* 0.70	*(0.65 to 0.75)*
Hip fracture	Crude OR	1.00	1.06		1.06		1.07		1.00	
	Adjusted OR *(95% CI)*	1.00	1.07	*(1.03 to 1.12)*	1.07	*(1.03 to 1.11)*	1.10	*(1.06 to 1.15)*	1.01	*(0.97 to 1.06)*
ELECTIVE HEART AND THORACIC SURGERY										
Isolated surgical aortic valve replacement	Crude OR	1.00	0.90		0.80		0.74		0.74	
	Adjusted OR *(95% CI)*	1.00	0.87	*(0.69 to 1.10)*	* 0.78	*(0.62 to 0.99)*	* 0.69	*(0.54 to 0.87)*	* 0.77	*(0.61 to 0.97)*
Transcatheter aortic valve replacement	Crude OR	1.00	0.97		0.90		0.78		0.64	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.69 to 1.1)*	* 0.87	*(0.62 to 0.99)*	* 0.79	*(0.54 to 0.87)*	* 0.65	*(0.61 to 0.97)*
Isolated coronary artery bypass graft	Crude OR	1.00	0.93		1.03		0.73		0.70	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.81 to 1.17)*	1.08	*(0.90 to 1.28)*	* 0.82	*(0.68 to 0.99)*	0.92	*(0.76 to 1.11)*
Partial lung resection for carcinoma	Crude OR	1.00	0.71		0.68		0.52		0.37	
	Adjusted OR *(95% CI)*	1.00	* 0.77	*(0.67 to 0.90)*	* 0.73	*(0.63 to 0.85)*	* 0.58	*(0.50 to 0.69)*	* 0.49	*(0.41 to 0.58)*
ELECTIVE MAJOR VISCERAL SURGERY										
Complex oesophageal surgery for carcinoma	Crude OR	1.00	0.83		0.81		0.62		0.51	
	Adjusted OR *(95% CI)*	1.00	* 0.81	*(0.68 to 0.96)*	0.85	*(0.72 to 1.01)*	* 0.67	*(0.56 to 0.82)*	* 0.47	*(0.38 to 0.58)*
Pancreatic resection for carcinoma	Crude OR	1.00	0.76		0.66		0.52		0.46	
	Adjusted OR *(95% CI)*	1.00	* 0.80	*(0.71 to 0.92)*	* 0.68	*(0.59 to 0.77)*	* 0.54	*(0.46 to 0.62)*	* 0.46	*(0.39 to 0.54)*
Colorectal resection for carcinoma	Crude OR	1.00	0.92		0.77		0.72		0.63	
	Adjusted OR *(95% CI)*	1.00	0.97	*(0.91 to 1.02)*	* 0.85	*(0.80 to 0.90)*	* 0.83	*(0.78 to 0.88)*	* 0.75	*(0.70 to 0.80)*
Colorectal resection for diverticulosis	Crude OR	1.00	0.86		0.77		0.65		0.60	
	Adjusted OR *(95% CI)*	1.00	* 0.87	*(0.80 to 0.95)*	* 0.87	*(0.79 to 0.95)*	* 0.80	*(0.72 to 0.88)*	* 0.74	*(0.67 to 0.82)*
Total nephrectomy for carcinoma	Crude OR	1.00	0.92		0.87		0.75		0.80	
	Adjusted OR *(95% CI)*	1.00	0.95	*(0.79 to 1.13)*	0.89	*(0.75 to 1.06)*	* 0.78	*(0.64 to 0.94)*	* 0.80	*(0.67 to 0.97)*
Cystectomy for carcinoma	Crude OR	1.00	0.85		0.89		0.80		0.70	
	Adjusted OR *(95% CI)*	1.00	* 0.85	*(0.73 to 0.98)*	0.86	*(0.74 to 1.00)*	* 0.80	*(0.69 to 0.93)*	* 0.69	*(0.58 to 0.82)*
ELECTIVE VASCULAR SURGERY										
Surgical lower extremity revas-cularization for atherosclerosis	Crude OR	1.00	0.86		0.80		0.73		0.75	
	Adjusted OR *(95% CI)*	1.00	* 0.88	*(0.81 to 0.96)*	* 0.85	*(0.78 to 0.94)*	* 0.82	*(0.75 to 0.9)*	* 0.82	*(0.75 to 0.91)*
Open repair of abdominal aortic aneurysm	Crude OR	1.00	0.67		0.73		0.62		0.52	
	Adjusted OR *(95% CI)*	1.00	* 0.71	*(0.59 to 0.84)*	* 0.76	*(0.63 to 0.91)*	* 0.60	*(0.50 to 0.72)*	* 0.55	*(0.45 to 0.68)*
Endovascular repair of abdominal aortic aneurysm	Crude OR	1.00	0.77		1.17		0.80		0.82	
	Adjusted OR *(95% CI)*	1.00	0.81	*(0.63 to 1.04)*	1.26	*(1.00 to 1.59)*	0.93	*(0.72 to 1.19)*	0.91	*(0.68 to 1.21)*
Carotid endarterectomy	Crude OR	1.00	0.85		0.81		0.82		0.66	
	Adjusted OR *(95% CI)*	1.00	0.92	*(0.77 to 1.09)*	0.89	*(0.75 to 1.05)*	0.90	*(0.76 to 1.06)*	* 0.77	*(0.64 to 0.93)*
ELECTIVE LOW-RISK SURGERY										
Cholecystectomy for cholelithiasis	Crude OR	1.00	0.97		1.00		0.98		0.84	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.87 to 1.09)*	1.06	*(0.95 to 1.19)*	1.07	*(0.95 to 1.19)*	0.95	*(0.85 to 1.08)*
Inguinal or femoral hernia repair	Crude OR	1.00	0.88		0.75		0.66		0.43	
	Adjusted OR *(95% CI)*	1.00	0.94	*(0.77 to 1.14)*	0.90	*(0.72 to 1.11)*	0.83	*(0.66 to 1.04)*	* 0.66	*(0.51 to 0.86)*
Transurethral resection of prostate	Crude OR	1.00	1.11		1.18		1.13		0.92	
	Adjusted OR *(95% CI)*	1.00	1.06	*(0.89 to 1.25)*	1.11	*(0.93 to 1.32)*	1.08	*(0.90 to 1.28)*	0.98	*(0.82 to 1.18)*
Primary hip replacement for arthrosis or arthritis	Crude OR	1.00	0.78		0.56		0.48		0.27	
	Adjusted OR *(95% CI)*	1.00	* 0.87	*(0.75 to 1.00)*	* 0.70	*(0.60 to 0.82)*	* 0.67	*(0.56 to 0.79)*	* 0.41	*(0.33 to 0.51)*
Primary knee replacement for arthrosis or arthritis	Crude OR	1.00	0.79		0.68		0.59		0.35	
	Adjusted OR *(95% CI)*	1.00	0.84	*(0.69 to 1.02)*	* 0.76	*(0.62 to 0.94)*	* 0.68	*(0.54 to 0.85)*	* 0.45	*(0.34 to 0.58)*

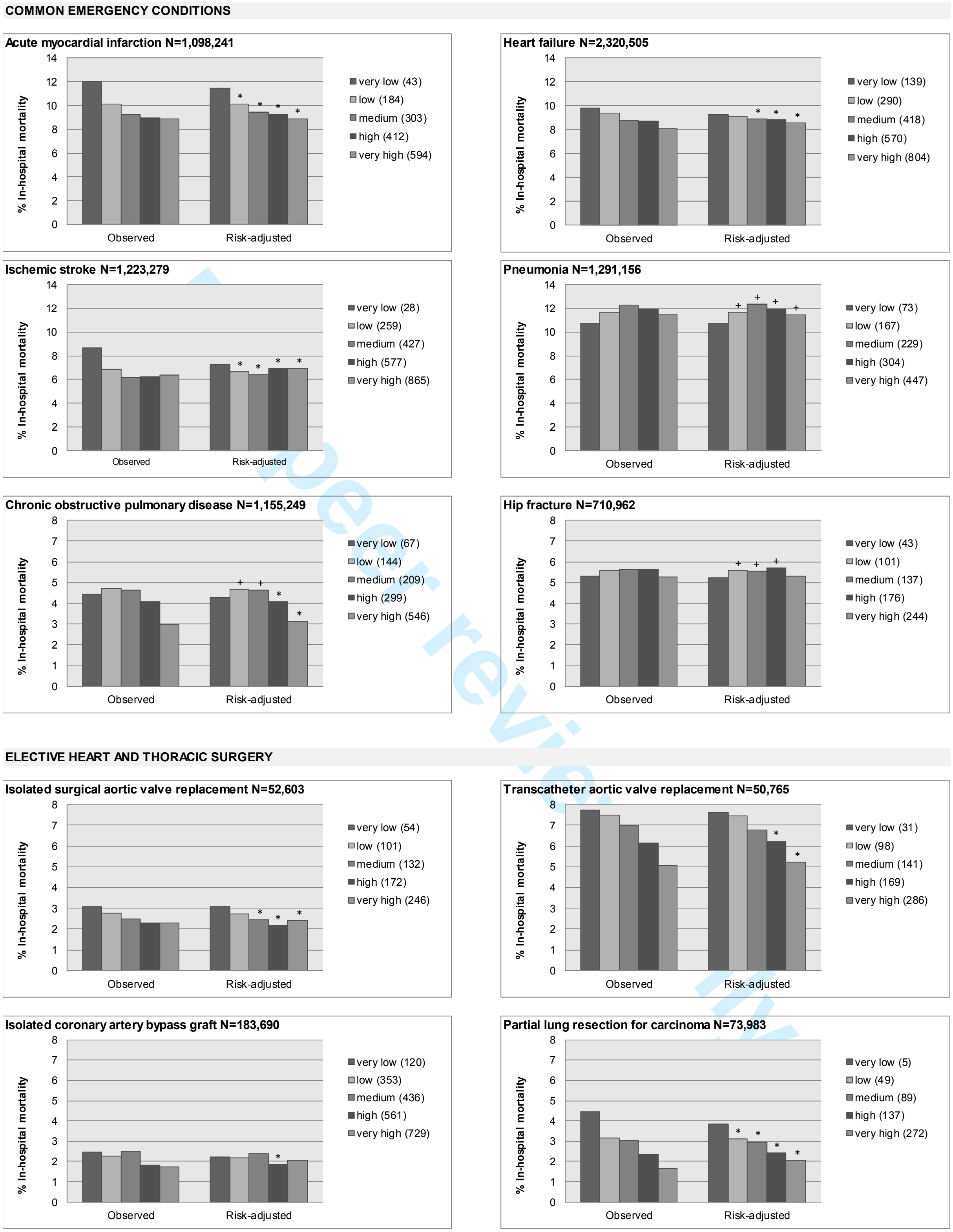
* Statistically significant lower than reference category (very low volume).
Covariates used for risk adjustment are displayed in Appendix table 3.

Table 3 Minimum volume threshold estimation and assessment of population impact

	Logistic regression coefficients of hospital volume				VARL Minimum volume threshold (95% CI)		Average mortality in population	Adjusted mortality if volume ≥ VARL (95% CI)		PRD Population-based risk difference (95% CI)		PIN Population impact number (95% CI)	
	Simple model		Full model										
	β	p	β	p									
COMMON EMERGENCY CONDITIONS													
Acute myocardial infarction	-0.0003	<.001	-0.0003	<.001	309	(288 to 330)	9.8%	9.1%	(9.0 to 9.2)	0.7%	(0.7 to 0.8)	137	(127 to 149)
Heart failure	-0.0001	0.001	0.0000	0.358	-		8.9%						
Ischemic stroke	-0.0002	0.000	0.0000	0.025	-		6.9%						
Pneumonia	0.0000	0.003	0.0000	<.001	-		11.6%						
Chronic obstructive pulmonary disease	-0.0003	0.039	-0.0002	0.026	271	(240 to 301)	4.2%	3.6%	(3.5 to 3.6)	0.6%	(0.5 to 0.6)	170	(158 to 185)
Hip fracture	0.0000	0.138	0.0000	0.828	-		5.5%						
ELECTIVE HEART AND THORACIC SURGERY													
Isolated surgical aortic valve replacement	-0.0014	0.001	-0.0010	0.039	147	(111 to 182)	2.6%	2.4%	(2.2 to 2.6)	0.2%	(0.0 to 0.3)	516	(288 to 2589)
Transcatheter aortic valve replacement	-0.0024	<.001	-0.0017	<.001	157	(142 to 171)	6.6%	5.8%	(5.5 to 6.2)	0.8%	(0.5 to 1.0)	133	(101 to 193)
Isolated coronary artery bypass graft	-0.0007	<.001	-0.0003	0.024	475	(430 to 521)	2.1%	2.0%	(1.9 to 2.1)	0.2%	(0.1 to 0.2)	658	(445 to 1271)
Partial lung resection for carcinoma	-0.0034	<.001	-0.0025	<.001	108	(95 to 120)	2.9%	2.3%	(2.1 to 2.5)	0.6%	(0.5 to 0.7)	168	(137 to 217)
ELECTIVE MAJOR VISCERAL SURGERY													
Colorectal resection for carcinoma	-0.0023	<.001	-0.0014	<.001	82	(76 to 88)	6.0%	5.4%	(5.3 to 5.5)	0.5%	(0.4 to 0.6)	197	(167 to 241)
Colorectal resection for diverticulosis	-0.0049	<.001	-0.0025	0.003	44	(38 to 49)	3.5%	3.2%	(3.1 to 3.4)	0.3%	(0.2 to 0.4)	364	(269 to 564)
Total nephrectomy for carcinoma	-0.0032	0.012	-0.0029	0.047	40	(24 to 56)	2.1%	1.9%	(1.7 to 2.0)	0.2%	(0.1 to 0.3)	459	(295 to 1056)
Cystectomy for carcinoma	-0.0054	<.001	-0.0055	<.001	31	(23 to 39)	4.7%	4.3%	(4.0 to 4.6)	0.4%	(0.2 to 0.7)	227	(150 to 480)
Complex oesophageal surgery for carcinoma	-0.0105	<.001	-0.0111	<.001	22	(17 to 28)	8.5%	6.3%	(5.7 to 6.9)	2.1%	(1.6 to 2.6)	47	(38 to 62)
Pancreatic resection for carcinoma	-0.0049	<.001	-0.0045	0.001	29	(21 to 37)	8.8%	6.6%	(6.2 to 7.2)	2.2%	(1.7 to 2.6)	46	(39 to 58)
ELECTIVE VASCULAR SURGERY													
Surgical lower extremity revascularization for atherosclerosis	-0.0011	<.001	-0.0007	<.001	123	(102 to 144)	3.0%	2.8%	(2.7 to 2.9)	0.2%	(0.1 to 0.3)	561	(387 to 1024)
Open repair of abdominal aortic aneurysm	-0.0129	<.001	-0.0112	<.001	18	(14 to 23)	6.0%	5.0%	(4.6 to 5.5)	1.0%	(0.6 to 1.3)	104	(76 to 166)
Endovascular repair of abdominal aortic aneurysm	-0.0031	0.014	-0.0028	0.069	-		1.7%						
Carotid endarterectomy	-0.0021	<.001	-0.0014	<.001	93	(69 to 116)	0.87%	0.81%	(0.74 to 0.88)	0.06%	(0.01 to 0.11)	1646	(886 to 12661)
ELECTIVE LOW-RISK SURGERY													
Cholecystectomy for cholelithiasis	-0.0003	0.008	-0.0001	0.425	-		0.43%						
Inguinal or femoral hernia repair	-0.0019	0.009	-0.0007	0.212	-		0.09%						
Primary hip replacement for arthrosis or arthritis	-0.0020	<.001	-0.0013	<.001	252	(227 to 278)	0.17%	0.13%	(0.12 to 0.14)	0.04%	(0.03 to 0.05)	2747	(2186 to 3701)
Primary knee replacement for arthrosis or arthritis	-0.0020	<.001	-0.0016	<.001	228	(190 to 265)	0.10%	0.07%	(0.07 to 0.08)	0.02%	(0.01 to 0.03)	4729	(3513 to 7269)
Transurethral resection of prostate	-0.0003	0.130	-0.0001	0.740	-		0.36%						

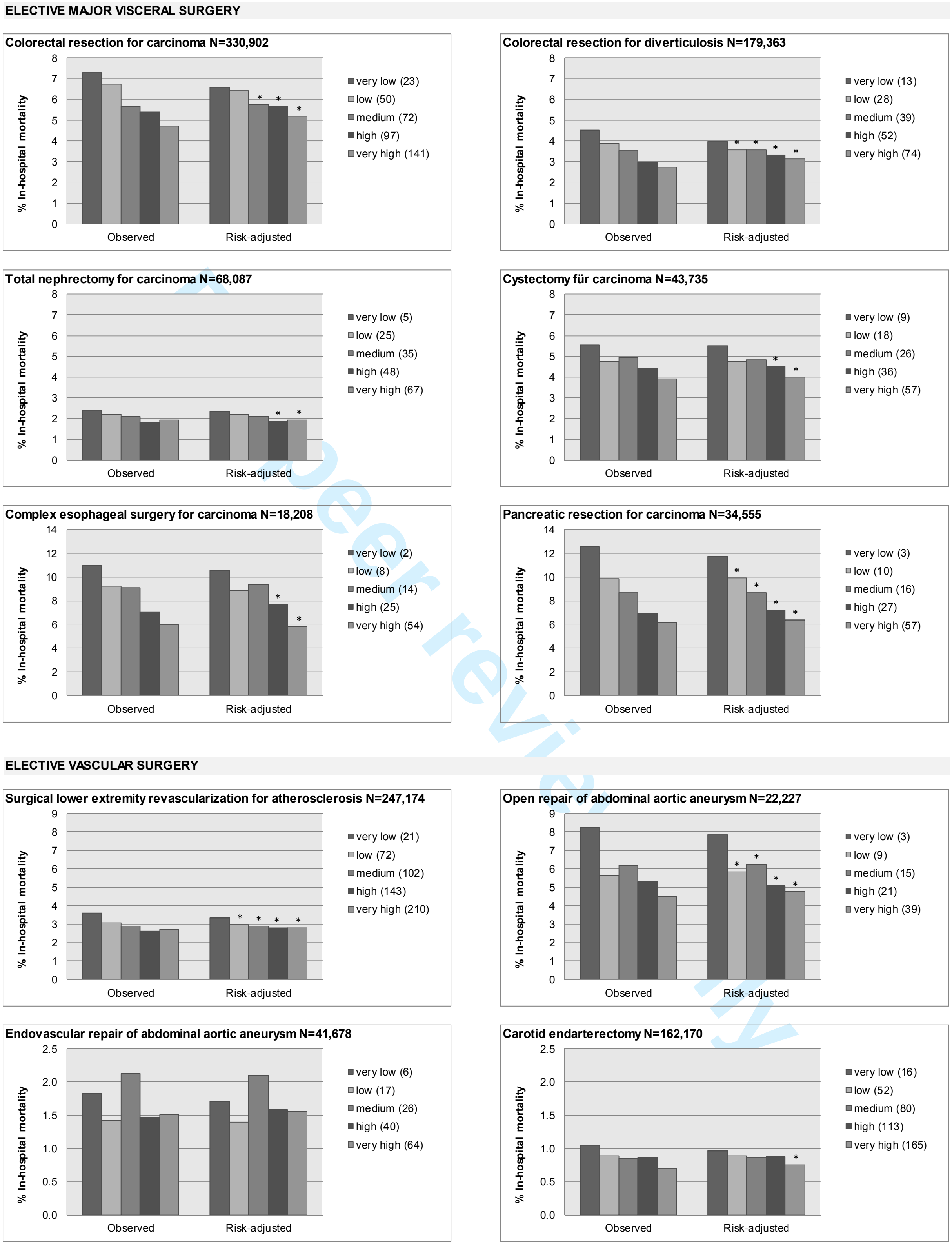
Logistic regression coefficients of hospital volume relate to an increment of 1 case per year. CI: Confidence interval.
VARL: Value of acceptable risk limit (Bender 1999), calculated from the logistic regression coefficient of the simple model. It estimates a minimum volume threshold to achieve a risk of in-hospital mortality which is lower than a predefined acceptable risk. The acceptable risk for each treatment was set to the average mortality in the respective patient population during the observation period.
The population impact number PIN is the reciprocal of the difference between the average mortality in the patient population and the adjusted mortality in those patients treated by hospitals with volumes above the threshold (population-based risk difference PRD). It can be interpreted as average number of the entire patient population among whom one death is attributable to treatment by a below-threshold volume hospital. Covariates used for risk adjustment are displayed in Appendix table 3.

Figure 1 Observed and risk-adjusted in-hospital mortality by hospital volume quintile



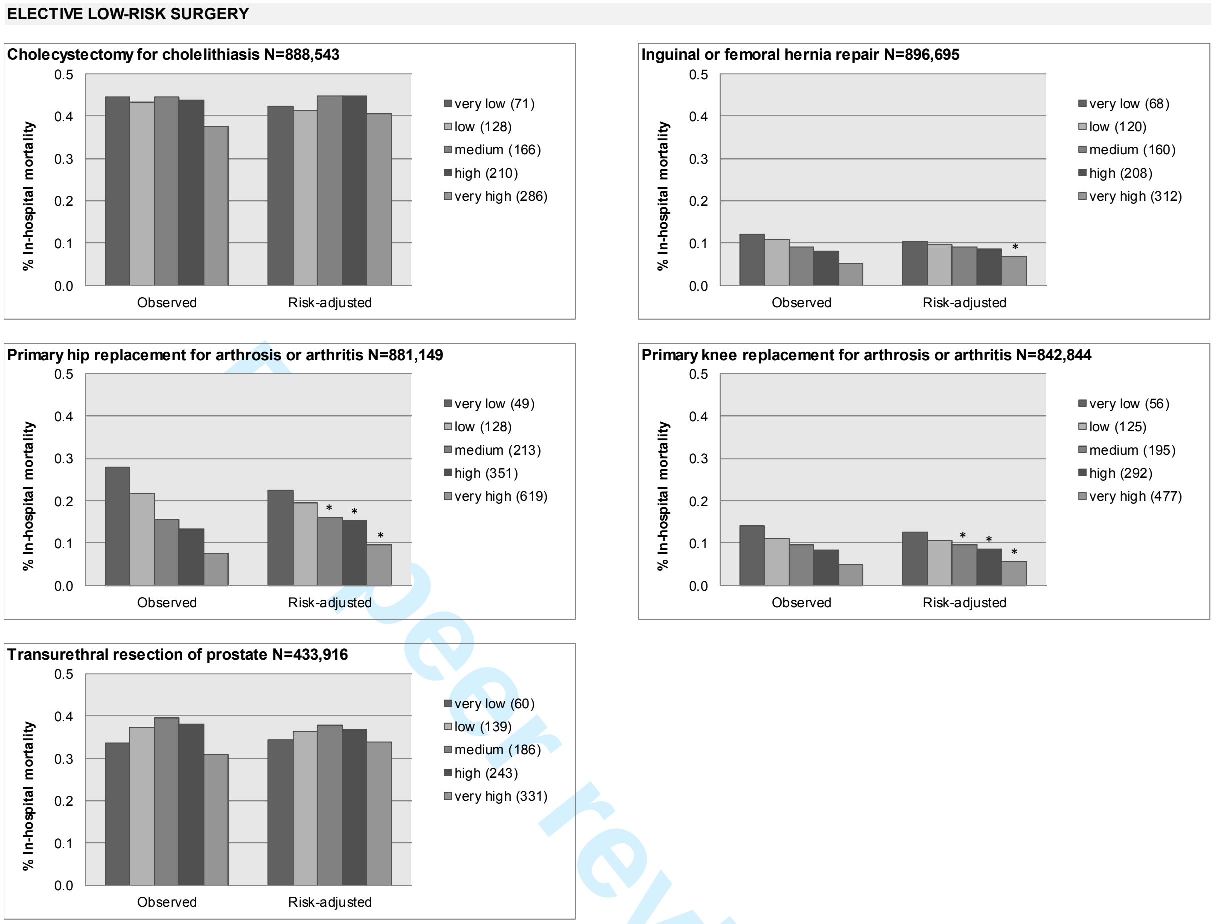
* Statistically significant lower than very low volume quintile. + Statistically significant higher than very low volume quintile.
Numbers displayed in the legend of each graph denote the median annual hospital volume within the respective volume quintile.
Covariates used for risk adjustment are displayed in Appendix table 3.

Figure 1 (continued)



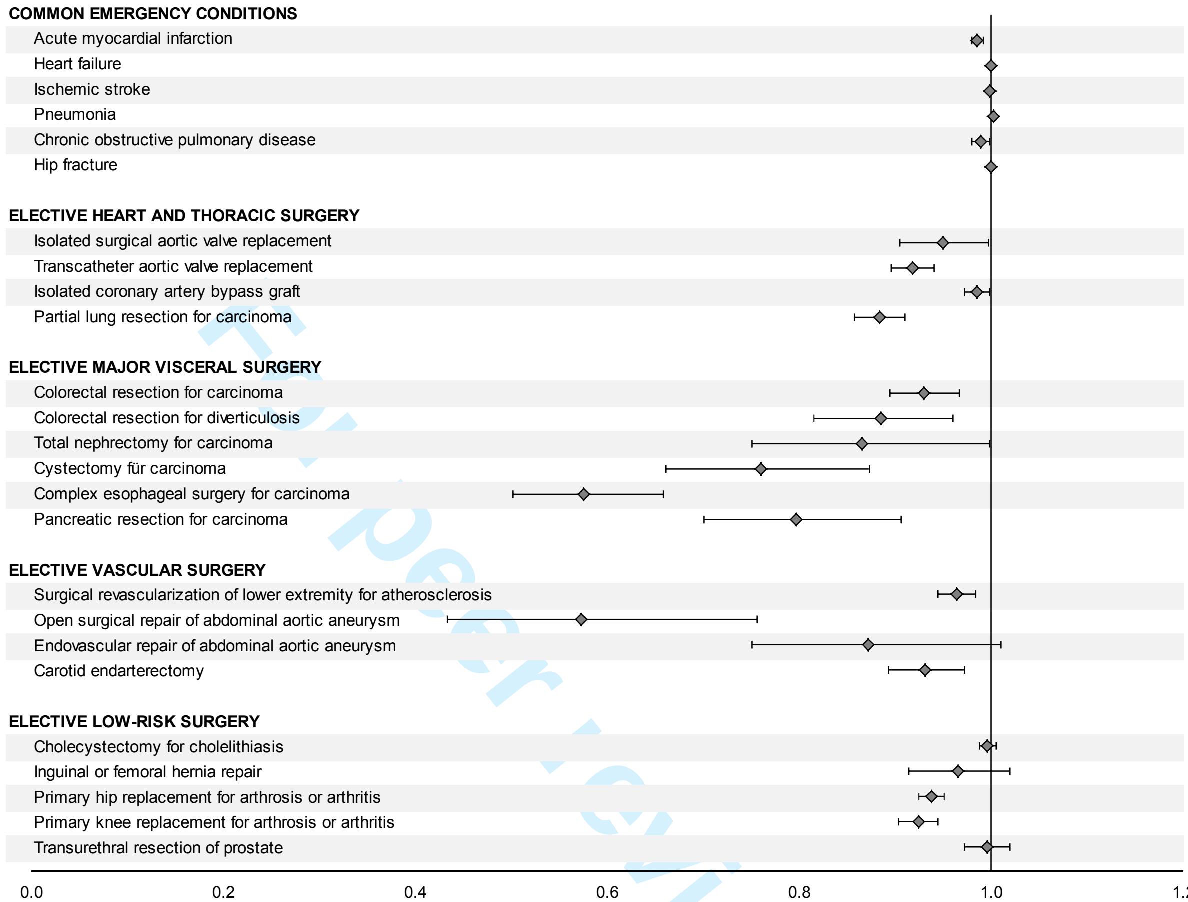
* Statistically significant lower than very low volume quintile. + Statistically significant higher than very low volume quintile.
Numbers displayed in the legend of each graph denote the median annual hospital volume within the respective volume quintile.
Covariates used for risk adjustment are displayed in Appendix table 3.

Figure 1 (continued)



* Statistically significant lower than very low volume quintile. + Statistically significant higher than very low volume quintile.
Numbers displayed in the legend of each graph denote the median annual hospital volume within the respective volume quintile.
Covariates used for risk adjustment are displayed in Appendix table 3.

Figure 2 Adjusted odds ratios of in-hospital death according to an increment of hospital volume of 50 cases per year



Whiskers indicate 95% confidence interval. Covariates used for risk-adjustment are displayed in Appendix table 3.

Appendix table 1 Inclusion and exclusion criteria for case definition

	Inclusion	Exclusion
COMMON EMERGENCY CONDITIONS		
Acute myocardial infarction	PD I21 I22; direct admission	
Heart failure	PD I50 I110 I130 I132; direct admission	
Ischemic stroke	PD I63; direct admission	
Pneumonia	PD A481 J100 J110 J12 J13 J14 J15 J16 J17 J18; direct admission	SD U6900 (nosocomial acquired pneumonia)
Chronic obstructive pulmonary disease	PD J44; direct admission	
Hip fracture	PD S720 S721; direct admission	
ELECTIVE HEART AND THORACIC SURGERY		
Isolated surgical aortic valve replacement	OPS 53510	OPS 53502 53503 53504 53505 53506 53507 5350x 5350y 53511 53512 53513 53514 5351x 5351y 53521 53522 53523 5352y 53531 53532 53533 53534 53535 5353x 5353y 53541 53542 53543 53544 5354y 53581 53582 53583 53584 53585 5358x 5358y 536 538a0 538a1 538233 53823x 53845 53846 53847 5384x 5384y 538a7 538a8 538230 538232 538401 538402 53840x 538411 538412 53841x 538421 538422 53842x 538431 538432 53843x 53844 5355 5356 5357 5359 5371 53725 53732 53733 53734 53735 53736 53737 53738 5373x 5373y 5375 537a (other heart surgery); OPS 535a0 (transcatheter aortic valve replacement); PD I33 I38 I39 (endocarditis)
Transcatheter aortic valve replacement	OPS 535a0	
Isolated coronary artery bypass graft	OPS 536	OPS 5350 5351 5352 5353 5354 5358 535a 5379a 5379b 538a0 538a1 538233 53823x 53845 53846 53847 5384x 5384y 538a7 538a8 538230 538232 538401 538402 53840x 538411 538412 53841x 538421 538422 53842x 538431 538432 53843x 53844 5355 5356 5357 5359 5371 53725 53732 53733 53734 53735 53736 53737 53738 5373x 5373y 5375 537a (other heart surgery); PD I21, I22 (acute myocardial infarction)
Partial lung resection for carcinoma	OPS 5321 5322 5323 5324 5325; PD or SD C34 D022	OPS 5327 5328 (pneumonectomy)
ELECTIVE MAJOR VISCERAL SURGERY		
Colorectal resection for carcinoma	OPS 5455 5456 5458 5484 5485; PD or SD C18 C19 C20 C218 D010 D011 D012	
Colorectal resection for diverticulosis	OPS 5455 5456 5458 5484 5485; PD K572 K573 K574 K575 K578 K579	SD C18 C19 C20 C218 D010 D011 D012 (colorectal carcinoma)
Total nephrectomy for carcinoma	OPS 55544 55545 55546 55547 5554a 5554b 5554x 5554y; PD or SD C64 C65 C66	OPS 55547 55549 5555 (post mortem resection, graft resection, donor resection or transplantation of kidney)
Cystectomy for carcinoma	OPS 5576 56870 56872 56873; PD or SD C67 D090 D414	
Complex oesophageal surgery for carcinoma	OPS 5423 5424 5425 5426 54270 54271 54380 54381 5438x; PD or SD C15 C160	
Pancreatic resection for carcinoma	OPS 5521 5522 5523 5524 5525; PD or SD C25 C241	OPS 55253 55254 5528 (post mortem resection, graft resection, or transplantation of pancreas)
ELECTIVE VASCULAR SURGERY		
Open repair of unruptured abdominal aortic aneurysm	OPS 538233 53823x 53845 53846 53847 5384x 5384y; PD or SD I7100 I7101 I7102 I7103 I712 I714 I716 I719	PD or SD I7104 I7105 I7106 I7107 I711 I713 I715 I718 (ruptured aortic aneurysm); OPS 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab (surgical repair of thoracic aortic aneurysm); OPS 538a0 538a1 (endovascular repair of abdominal aortic aneurysm)
Endovascular repair of unruptured abdominal aortic aneurysm	OPS 538a0 538a1; PD or SD I7100 I7101 I7102 I7103 I712 I714 I716 I719	PD or SD I7104 I7105 I7106 I7107 I711 I713 I715 I718 (ruptured aortic aneurysm); OPS 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab (surgical repair of thoracic aortic aneurysm)
Surgical lower extremity revascularization for atherosclerosis	OPS 53805 53807 53808 53815 53817 53818 538253 538254 538255 53825x 53827 53828 538352 538353 538354 538355 53835x 53837 53838 539333 539335 539336 539338 539341 539342 539343 539344 539345 539346 539347 53934x 53935 53936 53937 539552 539553 539554 539555 53955x 53957 53958 53965 53967 53968 53975 53977 53978; PD or SD I7020 I7021 I7022 I7023 I7024	OPS 538233 53823x 53845 53846 53847 5384x 5384y 538a0 538a1 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab 5335 5375 5504 5528 5555 (repair of aortic aneurysm, solid organ transplantation); PD or SD I723 I724 I728 I729 I74 T823 T824 T825 T827 T828 T829 (arterial dissection, aneurysm or embolism, complication of stent prosthesis)
Carotid endarterectomy	OPS 53800 53810 53820 53830 538c01 53950 53970	OPS 535 536 5370 5371 5372 5373 5374 5375 53791 53796 53797 53798 53799 5379a 5379b 5379c 537620 537621 537630 537631 537640 537641 537650 537651 537660 537661 537670 537671 537680 537681 537690 537691 537694 537a 538233 53823x 53845 53846 53847 5384x 5384y 538a0 538a1 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab 53805 53807 53808 53815 53817 53818 538253 538254 538255 53825x 53827 53828 538352 538353 538354 538355 53835x 53837 53838 539332 539333 539335 539336 539338 53933x 539341 539342 539343 539344 539345 539346 539347 53934x 53935 53936 53937 539552 539553 539554 539555 53955x 53957 53958 53965 53967 53968 53975 53977 53978 5864 5865 (heart surgery, aortic aneurysm repair, lower extremity revascularization, lower limb amputation); PD or SD C00 C01 C02 C03 C04 C05 C06 C07 C08 C09 C10 C11 C12 C13 C14 C15 (neoplasm of ear, nose or throat)

Appendix table 1 (continued)

ELECTIVE LOW-RISK SURGERY		
Cholecystectomy for cholelithiasis	OPS 55110 55111 55112 5511x 5511y; PD K80	SD C D0 (malign neoplasm); OPS 55113 55114 55115 (extended or simultaneously performed cholecystectomy)
Inguinal or femoral hernia repair	OPS 5530 5531; PD K40 K41	OPS 5451 5452 5453 5454 5455 5456 5458 5459 5460 5461 5462 5463 5464 5465 5466 5467 5468 5469 5484 5485 55304 55308 55314 55318 (other intestinal surgery)
Primary hip replacement for arthrosis or arthritis	OPS 582000 582001 582002 582010 582011 582012 582020 582021 582022 582030 582031 582040 582041 582060 582061 582080 582081 582082 582092 582093 582094 582095 582096 5820x0 5820x1 5820x2; PD M05 M06 M07 M08 M160 M161 M162 M163 M166 M167 M169 M87	OPS 5829c 5829g 5829n 57854d 582810 582840 582860 5829k 5829m (replacement for malign neoplasm, modular prosthesis, two-stage revision); SD M8005 M8085 M8415 M8445 M8485 M8495 M8505 M8545 M8555 M8565 M9075 M9688 Q650 Q651 S324 (osteoporosis, other osteopathy, hip fracture, congenital deformity of hip)
Primary knee replacement for arthrosis or arthritis	OPS 58221 58222 58223 58224 58226 58227 58229 5822a 5822b 5822d 5822e 5822g 5822h 5822j 5822k 582200 582201 582202; PD M05 M06 M07 M08 M170 M171 M174 M175 M179 M87	OPS 5829c 5829g 5829n 57854d 582810 582840 582860 5829k 5829m (replacement for malign neoplasm, modular prosthesis, two-stage revision); SD M8000 M8005 M8080 M8085 M8400 M8405 M8406 M8505 M8506 M8545 M8546 M8555 M8556 M8565 M8566 (osteoporosis or other osteopathy)
Transurethral resection of prostate	OPS 5601	

PD: principal diagnosis (ICD-10-GM); SD: secondary diagnosis (ICD-10-GM); OPS: procedure classification code [Operationen- und Prozedurenschlüssel]; direct admission: patient was not transferred-in from another acute care hospital.
Official classifications according to the German Institute of Medical Documentation and Information (DIMDI): http://www.dimdi.de/static/en/klassi/icd-10-gm/index.htm (ICD-10-GM); http://www.dimdi.de/static/en/klassi/ops/index.htm (OPS).
The case definitions rely on previous work on hospital quality indicators: Mansky T, Nimptsch U, Cools A, Hellerhoff F. G-IQI | German Inpatient Quality Indicators. Version 5.0. - Band 2: Definitionshandbuch für das Datenjahr 2016. Berlin: Universitätsverlag der TU Berlin. https://depositonce.tu-berlin.de/handle/11303/5819

Appendix table 2 Definition of covariates used for risk adjustment

Covariate	Definition
Calendar year of treatment	2009, 2010, 2011, 2012, 2013, 2014
Demographics	
Age	5-year age groups
Female sex	
Comorbidity	
Cardiac arrhythmia	PD or SD I442 I48 Z450 Z950
Heart failure or cardiomyopathy	PD or SD I50 I110 I130 I132 I420 I426 I427 I428 I429
Chronic ischemic heart disease	PD or SD I25
Hypertension (without heart or renal failure)	PD or SD I10 I119 I129 I139 I15
Valvular disease	PD or SD I340 I342 I350 I351 I352 I050 I051 I052 I060 I061 I062 Q231 Q232 Q233
Atherosclerosis of peripheral arteries	PD or SD I702
Sequelae of cerebrovascular disease	PD or SD I69
Chronic pulmonary disease	PD or SD J41 J42 J44 J45 J47
Mucoviscidosis	PD or SD E84
Chronic liver disease	PD or SD B18 I864 I982 K70 K73 K74 K760 K761 K765 K766 K767 Q446 Q447
Chronic pancreatitis	PD or SD K860 K861
Severe renal disease or chronic renal failure	PD or SD I120 I131 I132 N03 N04 N05 N07 N08 N11 N12 N14 N15 N16 N18 N19 Z992
Diabetes mellitus	PD or SD E10 E11 E12 E13 E14
Obesity	PD or SD E66
Cachexia or malnutrition	PD or SD R64 R634 E43 E44
Coagulopathy	PD or SD D66 D67 D680 D681 D682 D684 D685 D686 D688 D689 D691 D693 D694
Malign neoplasm	PD or SD C00-C97
Metastatic cancer	PD or SD C77 C78 C79
Specific risk factors	
ST-elevation myocardial infarction	PD I210 I211 I212 I213
Cardiogenic shock	PD or SD R570
Subsequent myocardial infarction	PD I22
Heart failure NYHA classification stage IV	PD I5014
Chronic obstructive pulmonary disease FEV1 <35%	PD J4400 J4410 J4480 J4490
Fracture of neck of femur	PD S720
Complex disease of intestine	PD or SD K55 K56 K593 K630 K631
Peripheral vascular disease stage	PD or SD I + II: I7020 I7021; III: I7022; IV: I7023 I7024
Acute cholecystitis	PD K800 K810
Trans-apical aortic valve replacement	OPS 535a01 535a02
Extended colorectal resection	OPS 5458 54540 54541 54542 54543 54544 54545 54546 5501 5502 5437 5436 5454x 5454y
Resection of visceral organs other than pancreas	OPS 5437 5436 5502 5501 5455 5456 54540 54541 54542 54543 54544 54545 54546 5454x 5454y

PD: principal diagnosis (ICD-10-GM); SD: secondary diagnosis (ICD-10-GM); OPS: procedure classification system [Operationen- und Prozedurenschlüssel]. Official classifications according to the German Institute of Medical Documentation and Information (DIMDI): http://www.dimdi.de/static/en/klassi/icd-10-gm/index.htm (ICD-10-GM); http://www.dimdi.de/static/en/klassi/ops/index.htm (OPS).

Appendix table 3 Application of covariates used to estimate risk-adjusted in-hospital mortality

	Calendar year of treatment	5-year age groups	Female sex	Cardiac arrhythmia	Heart failure or cardiomyopathy	Chronic ischemic heart disease	Hypertension (without heart or renal failure)	Valvular disease	Atherosclerosis of peripheral arteries	Sequelae of cerebrovascular disease	Chronic pulmonary disease	Mucoviscidosis	Chronic liver disease	Chronic pancreatitis	Severe renal disease or chronic renal failure	Diabetes mellitus	Obesity	Cachexia or malnutrition	Coagulopathy	Malign neoplasm	Metastatic cancer	ST-elevation myocardial infarction	Cardiogenic shock	Subsequent myocardial infarction	Heart failure NYHA classification stage IV	Chronic obstructive pulmonary disease FEV1 <35%	Fracture of neck of femur	Complex disease of intestine	Peripheral vascular disease stage	Acute cholecystitis	Trans-apical aortic valve replacement	Extended colorectal resection	Resection of visceral organs other than pancreas	**Area under the curve** (c-statistic)
COMMON EMERGENCY CONDITIONS																																		
Acute myocardial infarction	x	x	x				x	x	x		x		x		x	x	x	x	x	x		x	x	x										0,827
Heart failure	x	x	x	x		x		x	x	x	x		x		x	x	x	x	x	x					x									0,729
Ischemic stroke	x	x	x		x	x	x	x	x		x		x		x	x	x	x	x	x														0,743
Pneumonia	x	x	x	x	x	x	x	x	x			x	x		x	x	x	x	x	x														0,715
Chronic obstructive pulmonary disease	x	x	x	x	x	x	x	x	x				x		x	x	x	x	x	x						x								0,716
Hip fracture	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x							x							0,782
ELECTIVE HEART AND THORACIC SURGERY																																		
Isolated surgical aortic valve replacement	x	x	x	x	x	x	x		x		x		x		x	x	x	x	x	x														0,772
Transcatheter aortic valve replacement	x	x	x	x	x	x	x		x		x		x		x	x	x	x	x	x											x			0,710
Isolated coronary artery bypass graft	x	x	x	x	x		x	x	x		x		x		x	x	x	x	x	x														0,786
Partial lung resection for carcinoma	x	x	x	x	x	x	x	x	x				x		x	x	x	x	x		x													0,782
ELECTIVE MAJOR VISCERAL SURGERY																																		
Colorectal resection for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x							x				x		0,825
Colorectal resection for diverticulosis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x									x				x		0,908
Total nephrectomy for carcinoma	x	x	x	x	x	x	x	x	x		x		x			x	x	x	x		x													0,826
Cystectomy for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x													0,765
Complex oesophageal surgery for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x													0,751
Pancreatic resection for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x												x	0,776
ELECTIVE VASCULAR SURGERY																																		
Surgical lower extremity revascularization for atherosclerosis	x	x	x	x	x	x	x	x			x		x		x	x	x	x	x	x									x					0,853
Open repair of abdominal aortic aneurysm	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,771
Endovascular repair of abdominal aortic aneurysm	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,814
Carotid endarterectomy	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,758
ELECTIVE LOW-RISK SURGERY																																		
Cholecystectomy for cholelithiasis	x	x	x	x	x	x	x	x	x		x		x	x	x	x	x	x	x											x				0,943
Inguinal or femoral hernia repair	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,938
Primary hip replacement for arthrosis or arthritis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,869
Primary knee replacement for arthrosis or arthritis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,820
Transurethral resection of prostate	x	x		x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,868

Hospital volume and mortality for 25 types of inpatient treatment in German hospitals – Observational study using complete national data from 2009 to 2014

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Hospital volume and mortality for 25 types of inpatient treatment in German hospitals – Observational study using complete national data from 2009 to 2014

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Abstract

Objectives To explore the existence and strength of a relationship between hospital volume and mortality, to estimate minimum-volume thresholds and to assess the potential benefit of centralisation of services.

Design Observational population-based study using complete German hospital discharge data (Diagnosis-Related Group Statistics [DRG Statistics]).

Setting All acute care hospitals in Germany.

Participants All adult patients hospitalised for one out of 25 common or medically important types of inpatient treatment from 2009 to 2014.

Main outcome measure Risk-adjusted in-hospital mortality.

Results Lower in-hospital mortality in association with higher hospital volume was observed in 20 out of the 25 studied types of treatment when volume was categorized in quintiles, and persisted in 17 types of treatment when volume was analysed as a continuous variable. Such a relationship was found in some of the studied emergency conditions and low-risk procedures. It was more consistently present regarding complex surgical procedures. For example, about 22,000 patients receiving open repair of abdominal aortic aneurysm were analysed. In very high volume hospitals risk-adjusted mortality was 4.7% (95% CI 4.1 to 5.4) compared to 7.8% (7.1 to 8.7) in very low volume hospitals. The minimum volume above which risk of death would fall below the average mortality was estimated as 18 cases per year. If all hospitals providing this service would perform at least 18 cases per year one death among 104 (76 to 166) patients could potentially be prevented.

Conclusions Based on complete national hospital discharge data the results confirmed volume-outcome relationships for many complex surgical procedures, as well as for some emergency conditions and low-risk procedures. Following these findings, the study identified areas where centralisation would provide a benefit for patients undergoing the specific type of treatment in German hospitals and quantified the possible impact of centralisation efforts.

Keywords

Volume-outcome relationship, hospital discharge data, in-hospital mortality, Germany

Strengths and limitations of the study

- The strength of this study is the use of current and complete national hospital discharge data, covering virtually every patient who underwent one out of the studied types of treatment during the study period.
- As hospital volumes vary widely among German acute care hospitals this is a proper setting to study volume-outcome relationships.
- In contrast to most other volume-outcome studies, the present approach includes the calculation of minimum volume thresholds along with an assessment of the possible impact of centralization efforts on the population.
- Within this observational retrospective study the statistical association between volume and outcome was tested upon administrative data.
- As information available from administrative data is limited, it is possible that unmeasured differences in disease severity, comorbidity, or appropriateness of patient selection may partly explain the association between volume and outcome.
- This study did not consider hospital characteristics like teaching status, type of ownership, or location.

Introduction

The relationship between hospital volume and patient outcomes has been widely studied. For many inpatient treatments a higher volume was found to be associated with better outcomes, such as for high-risk surgical procedures, medical conditions or elective low-risk surgery.[1-10] Systematic reviews and meta analyses were conducted to aggregate results into a broader frame of knowledge.[11-14] However, the heterogeneity of methods used impairs conclusions from meta analyses. In particular, the categorisation of high volume hospitals varies according to the geographical context.[15-16] Moreover, many studies include only samples of patients or are restricted to patients with a specific type of insurance or within a delimited geographic area. Therefore, it is often uncertain if the association of volume and outcome found in one study may be generalizable to the whole population affected, or even to populations in other countries with different health care systems. Finally, studies reporting better outcome in relation to higher volume often lack an assessment of the clinical and policy significance of their findings.[16]

To date, the volume-outcome relationship in Germany has been studied only for few inpatient services, such as pancreatic resection, abdominal aortic aneurysm repair, hip fracture, or treatment of very low birthweight infants.[17-20] The German acute care hospital market is characterized by a relative overcapacity of hospital beds and high hospitalization rates.[21] Volumes of inpatient treatments vary widely among the about 1,600 German acute care hospitals.[22] In 2004, minimum volume thresholds for specific types of inpatient treatment were established. However, it has been found that many hospitals did not adhere to this regulation, and the debate about the underlying evidence remains controversial.[23-25]

Efforts to improve quality of care by centralisation of services need to rely on evidence that higher volume is associated with better outcome. Therefore, this study aimed to explore the relation of hospital volume and outcome in the German hospital market by using complete national hospital discharge data. For a broad range of common or medically important inpatient services the existence and strength of a relationship between volume and mortality was analysed. Where lower mortality in relation to higher volume was observed minimum volume thresholds, above which mortality would be reduced, were estimated. Impact measures were calculated to assess the potential benefit of centralisation efforts.

Methods

Data

German acute care hospitals are obliged to submit their inpatient discharge data annually to a nationwide database, which is available for research purposes. This database (Diagnosis-Related Group Statistics [DRG Statistics] provided by the Research Data Centres of the Federal Statistical Office and the statistical offices of the 'Länder') contains discharge information on every inpatient episode, covering patients of all types of insurance. Principal and secondary diagnoses are coded according to the German adaptation of the International Classification of Diseases (ICD-10-GM). Procedures are coded according to the German procedure coding system (OPS, Operationen- und Prozedurenschlüssel). Information on sex, age, source of admission, discharge disposition, and length of stay are also included. Based on an anonymized hospital identifier every inpatient episode can be assigned to the treating hospital.[26] The analyses included data of the years 2009 to 2014. Data were accessed via controlled remote data analysis.

Patient population

To study a broad range of hospital services five groups of inpatient treatments comprising 25 single conditions or procedures were analysed:

- Common emergency conditions (6)
- Elective heart and thoracic surgery (4)
- Elective major visceral surgery (6)
- Elective vascular surgery (4)
- Elective low-risk surgery (5)

Each type of treatment was defined by specific inclusion and exclusion criteria in order to minimize confounding by differences in case-mix. Treatments for emergency conditions (e.g. acute myocardial infarction) were restricted to direct admissions by excluding patients who had been transferred-in from another acute care hospital. Elective surgical treatments were defined by restriction to certain medical indications (e.g. colorectal resection for carcinoma) or exclusion of complicated constellations (e.g. aortic valve replacement excluding combined other heart surgery). All definitions refer to adult patients aged 20 years and older. Inclusion and exclusion criteria are listed in Appendix Table 1.

Hospital volume

Volume of patients treated by a hospital was calculated for each year of observation corresponding to the respective definition of a studied type of treatment. Aiming to compare results in the context of the current literature, hospitals were ranked into quintiles of approximately equal case numbers according to their annual volume. This ranking was done separately for each year for observation, allowing the rank of one hospital to change from one year to another, if volume changed over time. Additionally, annual hospital volume was analysed as a continuous variable.

Within a sensitivity analysis hospital volume was additionally determined on the basis of wider case definitions in order to fully consider all treatments which might enhance a hospital's experience regarding a specific condition or procedure (e.g., all colorectal resections regardless from medical indication). This approach led to a higher estimation of annual volume per hospital in most cases and resulted in a slightly different ranking of hospitals. Within this analysis restrictions in case definition, as described above, were subsequently applied for outcome measurement.

Outcome measure, risk adjustment and statistical analysis

In-hospital mortality, defined as death before discharge, was studied as outcome measure. Observed and risk-adjusted mortality were stratified by volume quintiles.

Risk-adjusted mortality for each volume quintile was calculated by using generalized estimating equations (GEE) with a logit link function, accounting for clustering of patients within hospitals. Using the pooled data of the entire observation period one GEE model was fitted for each studied treatment. Depending on the type of treatment, models included comorbidities, which most likely have been present on admission (e.g. diabetes, chronic liver disease), specific indicators of disease severity (e.g. ST-elevation myocardial infarction), or extension of surgery (e.g. concomitant resection of other visceral organs in patients with pancreatic resection). 5-year age groups, sex, and calendar year of treatment were considered within each model. The definitions and treatment-specific applications of covariates for risk adjustment are displayed in Appendix tables 2 and 3.

In order to estimate the independent impact of hospital volume on in-hospital mortality, hospital volume was subsequently entered into each model, taken as a categorically variable. Odds ratios for in-hospital death by hospital volume quintile were calculated.

To further explore the relationship between volume and outcome GEE models with volume as a continuous variable were fitted for each treatment. In a first step, hospital volume was taken as the only predictor (simple model). In a second step the treatment-specific covariates, as described above, were entered into the model (full model) and odds ratios for in-hospital death according to an increment of one case, as well as of 50 cases per year were calculated.

Where the regression coefficient of a one-case increment of hospital volume remained statistically significant after consideration of covariates, minimum volume thresholds were estimated from the simple model using Benders Value of Acceptable Risk Limit.[27] This value is calculated from the function of the logistic regression coefficient of hospital volume. It denotes the threshold where mortality is expected to fall below a predefined acceptable risk. The acceptable risk was set to the average mortality of the respective treatment during the observation period.

The clinical relevance of thresholds was assessed by the population impact number (PIN). The PIN was calculated as reciprocal of the difference between the average mortality risk in the entire patient population and the adjusted risk among patients treated by hospitals with volumes above the threshold (population-based risk difference PRD).[28] In the context of this study, the PIN can be interpreted as average number of patients within a treatment group among whom one death is attributable to treatment by a below-threshold volume hospital, due to excess risk of mortality in these hospitals. In other words, among this number of patients one death could hypothetically be prevented if all hospitals providing the respective inpatient service had annual volumes equal or higher than the threshold.

The level of statistical significance was set to .05. The analyses were conducted using SAS Version 9.3 (SAS Institute Inc., Cary, NC, USA).

Reporting guideline

Reporting of this analysis adheres to the RECORD (REporting of studies Conducted using Observational Routinely-collected health Data) Statement.[29]

Results

Common emergency conditions

Lower in-hospital mortality in association with higher hospital volume was observed in four out of the six studied types of common emergency treatment when volume was categorized in quintiles and persisted in two types of treatment when volume was analysed as a continuous variable.

From 2009 to 2014 nearly 1.1 million patients were treated for acute myocardial infarction (table 1). Risk-adjusted mortality was 8.9% (95% CI 8.8 to 9.0) in the very high volume quintile versus 11.4% (11.3 to 11.6) in the very low volume quintile (figure 1). Adjusted odds ratios of in-hospital death were significantly reduced in the low to very high volume quintiles when compared to the very low volume quintile (table 2). A statistically significant effect of volume on mortality was also observed when volume was analysed as a continuous variable. An increment of 50 cases per year was associated with reduced odds of death (figure 2). The minimum hospital volume where risk of mortality would fall below the average mortality of 9.8% was calculated as 309 cases per year. Stratification by this threshold resulted in a population-based risk difference (PRD) of 0.7% (0.7 to 0.8) and a population impact number (PIN) of 137 (127 to 149, table 3). This means that out of 137 patients hospitalized for acute myocardial infarction one death would be prevented if annual volumes in treating hospitals were at least 309.

In total, 2.3 million patients treated for heart failure were studied. Risk-adjusted mortality was 8.5% (95% CI 8.4 to 8.6) in the very high volume quintile versus 9.2% (9.1 to 9.3) in the very low volume quintile (figure 1). For volume as a continuous variable no association was found after consideration of covariates (table 3).

During the observation period 1.2 million patients were hospitalized for ischemic stroke (table 1). Adjusted mortality in the very high volume quintile was 6.9% (95% CI 6.8 to 7.0) versus 7.3% (7.2 to 7.4) in the very low volume quintile (figure 1). After consideration of covariates no measurable effect of hospital volume as a continuous variable was observed (table 3).

Among the 1.3 million patients treated for pneumonia (table 1) higher hospital volume was associated with higher in-hospital mortality. Adjusted mortality was 11.5% (95% CI 11.3 to 11.6) in the very high volume quintile, 12.3% (12.2 to 12.5) in the medium volume quintile and 10.8% (10.7 to 10.9) in the very low volume quintile (figure 1), and the odds ratios were higher in the low to very high volume quintiles when compared to the very low volume quintile (table 2). When considered as a continuous variable hospital volume was not associated with mortality (table 3).

For the more than 1.15 million patients with chronic obstructive pulmonary disease (COPD, table 1) adjusted mortality was 3.1% (95% CI 3.0 to 3.2) in the very high volume quintile and 4.3% (4.2 to 4.4) in the very low volume quintile (figure 1). Hospital volume as a continuous variable had an independent effect on mortality (figure 2) and the minimum volume to achieve a lower-than-average risk of death was calculated as 271 patients per year. This threshold was estimated to prevent one death among 170 (158 to 185) COPD patients (table 3).

The analysis of 711,000 patients hospitalized for hip fracture (table 1) revealed slightly higher mortality in low to high volume quintiles when compared to the very low volume quintile (figure 1). Hospital volume as a continuous variable had no effect on mortality (table 3).

Elective heart and thoracic surgery

For each out of the four studied types of heart and thoracic surgery lower in-hospital mortality in association with higher hospital volume was observed.

From 2009 to 2014 about 52,600 patients were treated with isolated surgical aortic valve replacement (table 1). Adjusted mortality was 2.4% (95% CI 2.1 to 2.7) in the very high volume quintile versus 3.1% (2.8 to 3.4%) in the very low volume quintile (figure 1). Reduced odds of death were found in the medium to very high volume quintiles when compared to the very low volume quintile (table 2). As a continuous variable hospital volume demonstrated an independent effect on mortality (figure 2). The minimum volume to achieve a lower-than-average risk of death was calculated as 147 annual treatments. This threshold resulted in a non-significant PRD of 0.2% (-0.02 to 0.3) and a PIN of 516 (288 to 2589, table 3).

In-hospital mortality of the 50,800 patients treated with transcatheter aortic valve replacement (table 1) was 5.2% (95% CI 4.8 to 5.7) in the very high volume quintile versus 7.6% (7.1 to 8.2) in the very low volume quintile (figure 1). Hospital volume as a continuous variable revealed an independent effect on mortality (figure 2) and the minimum volume to fall below the average mortality of 6.6% was calculated as 157 cases per year. Application of this threshold was estimated to prevent one death among 133 (101 to 193) patients (table 3). This means that among 133 patients with transcatheter aortic valve replacement one death would be prevented if all providing hospitals would perform this treatment at least 157 times per year.

184,000 patients were treated with an isolated coronary artery bypass graft (table 1). According to hospital quintiles no constant association of volume and mortality was found (figure 1, table 2). However, an independent effect of hospital volume on mortality was observed when volume was analysed as a continuous variable (figure 2) and the minimum volume to achieve a risk of death below the average of 2.1% was calculated as 475 cases per year. This threshold led to a PIN of 658 (445 to 1271, table 3).

In total, 74,000 patients with partial lung resection for carcinoma were studied (table 1). In the very high volume quintile adjusted mortality was 2.0% (95% CI 1.8 to 2.3) versus 3.8% (3.6 to 4.1) in the very low volume quintile (figure 1). The observed independent effect of hospital volume when analysed continuously resulted in a minimum volume of 108 cases per year. This threshold was estimated to prevent one death among 168 (137 to 217) patients (table 3).

Elective major visceral surgery

Lower mortality associated with higher hospital volume was found for all six studied types of elective visceral surgery.

During the observation period 331,000 colorectal resections for carcinoma were performed in German hospitals (table 1). Mortality was 5.2% (95% CI 5.0 to 5.4) in the very high volume quintile and 6.6% (6.4 to 6.8) in the very low volume quintile (figure 1). In comparison to the very low volume quintile odds of death were statistically significantly reduced in the medium to very high volume quintiles (table 2). Hospital volume as a continuous variable had an independent effect on mortality (figure 2). The minimum volume to achieve a risk of death below the average of 6.0% was calculated as 82 annual treatments, associated with a PIN of 197 (167 to 241, table 3).

179,000 colorectal resections were performed for diverticulosis (table 1). Adjusted mortality was 3.1% (95% CI 2.9 to 3.3) in the very high volume quintile versus 3.9% (3.8 to 4.1) in the very low volume quintile (figure1). Hospital volume as a continuous variable had an independent effect on mortality and a minimum volume of 44 was calculated to achieve a risk of death below the average of 3.5%. This threshold was associated with a PIN of 364 (269 to 564, table 3).

During the observation period 68,000 patients with total nephrectomy for carcinoma were identified (table 1). In the very high volume quintile adjusted mortality was 1.9% (95% CI 1.7 to 2.2) and in the very low volume quintile 2.3% (2.1 to 2.6). The independent effect of hospital volume as a continuous variable demonstrated borderline statistical significance (figure 2) and the minimum volume to achieve lower-than-average mortality was calculated as 40 cases per year. Application of this threshold would prevent one death among 459 (295 to 1056) nephrectomy patients (table 3).

Adjusted mortality among the 44,000 patients receiving cystectomy for carcinoma (table 1) was 4.0% (95% CI 3.6 to 4.4) in the very high volume quintile versus 5.5% (5.0 to 6.0) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower mortality (figure 2). This relation of volume and outcome resulted in a minimum volume of 31 cases per year to fall below the average mortality of 4.7%. Application of this threshold was associated a PIN of 227 (150 to 480, table 3).

Among the 18,000 patients with complex oesophageal surgery for carcinoma adjusted mortality was 5.8% (95% CI 5.1 to 6.6) in the very high volume quintile versus 10.5% (9.5 to 11.6) in the very low volume quintile. As a continuous variable hospital volume had an independent effect on mortality and the minimum volume to fall below the average mortality of 8.5% was calculated as 22 cases per year. If all hospitals would perform at least 22 complex oesophageal surgeries per year one death among 47 (38 to 62) patients could be prevented (table 3).

A pancreatic resection for carcinoma was performed in 35,000 patients in total (table 1). Adjusted mortality was 6.4% (95% CI 5.8 to 7.0) in the very high volume quintile versus 11.7% (10.9 to 12.5) in the very low volume quintile (figure 1). Continuous increment of hospital volume was associated with lower mortality and the minimum volume where risk of death would fall below the average mortality of 8.8% was calculated as 29 cases per year. This threshold resulted in a PIN of 46 (39 to 58, table 3).

Elective vascular surgery

In three out of the four studied types of elective vascular surgery higher hospital volume was associated with lower in-hospital mortality.

During the observation period 247,000 patients were treated with surgical revascularization of lower extremities for atherosclerosis (table 1). Risk-adjusted mortality was 2.8% (95% CI 2.7 to 3.0) in the very high volume quintile versus 3.3% (3.2 to 3.5) in the very low volume quintile (figure 1). Odds of death were reduced in all other quintiles when compared to the very low volume quintile (table 2). The association of volume and outcome persisted when volume was analysed as continuous variable (figure 2) and the minimum volume to achieve a mortality risk below the average of 3.0% was calculated as 123 cases per year. This led to the estimation that among 561 (387 to 1024) patients one additional death was attributable to treatment by a hospital performing less than 123 of such operations (table 3).

In total, more than 22,000 patients receiving open repair of abdominal aortic aneurysm were analysed (table 1). In the very high volume quintile risk-adjusted mortality was 4.7% (95% CI 4.1 to 5.4) versus 7.8% (7.1 to 8.7) in the very low volume quintile (figure 1). When analysed continuously, higher volume was independently associated with lower mortality (figure 2). The calculated minimum volume where risk would fall below the average of 6.0% was 18 cases per year. The resulting PIN was 104 (76 to 166, table 3).

Among the 42,000 patients treated with endovascular repair of abdominal aortic aneurysm (table 1) risk-adjusted mortality was 1.6% (95% CI 1.3 to 1.9) in the very high volume quintile versus 1.7% (1.4 to 2.0) in the very low volume quintile. Highest mortality was observed in the medium volume quintile (2.1%, 1.8 to 2.4, figure 1).

Odds of death were not significantly different between volume quintiles (table 2). Analysed as continuous variable no statistically significant effect of hospital volume on mortality was observed (figure 2, table 3).

From 2009 to 2014 about 162,000 patients with carotid endarterectomy were identified (table 1). Risk-adjusted in-hospital mortality was 0.75% (95% CI 0.66 to 0.86) in the very high volume quintile and 0.97% (0.87 to 1.07) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower in-hospital mortality (figure 2). A lower-than-average risk of mortality is expected if hospitals perform at least 93 carotid endarterectomies per year. Under this threshold the estimated PIN was 1646 (886 to 12661, table 3).

Elective low-risk surgery

In three out of the five studied types of elective low-risk surgery higher hospital volume was found to be associated with lower mortality when volume was categorized in quintiles. In two types of elective low-risk surgery this relation persisted when volume was analysed as a continuous variable.

From 2009 to 2014 nearly 889,000 inpatient cholecystectomies for cholelithiasis were performed in German hospitals (table 1). Risk-adjusted mortality differed not significantly between volume quintiles (figure 1), as well as risk-adjusted odds of death (table 2). Continuous increment of hospital volume was not associated with mortality (table 3).

Among the 897,000 inpatient inguinal or femoral hernia repairs (table 1) mortality in the very high volume quintile was lower (0.07%, 95% CI 0.06 to 0.08) than in the very low volume quintile (0.10%, 0.09 to 0.12, figure 1). Yet, the independent effect of continuous increment of hospital volume was not statistically significant (table 3).

The analysis of more than 881,000 primary hip replacements for arthrosis or arthritis (table 1) revealed a constant association of hospital volume and mortality when patients were stratified by volume quintiles. Risk-adjusted in-hospital mortality was 0.10% (95% CI 0.08 to 0.11) in the very high volume quintile versus 0.23% (0.21 to 0.25) in the very low volume quintile (figure 1). In comparison to the very low volume quintile odds of death were significantly reduced in all other volume quintiles (table 2). Within the analysis of continuous increment of hospital volume an independent effect on mortality was observed (figure 2). A minimum volume of 252 cases per year was calculated to achieve a risk of mortality below the average of 0.17%. The PIN resulting from this threshold was 2747 (2186 to 3701, table 3).

Overall 843,000 patients with primary knee replacement for arthrosis or arthritis were identified (table 1). Risk-adjusted mortality was 0.06% (95% CI 0.05 to 0.07) in the very high volume quintile versus 0.13% (0.11 to 0.14) in the very low volume quintile (figure 1). Continuous increment of hospital volume was independently associated with lower mortality (figure 2) and 228 annual cases were calculated as the minimum volume where risk of mortality would fall below the average of 0.10%. This minimum volume threshold resulted in an estimation of one preventable death among 4729 (3513 to 7269) primary knee replacement patients if all hospitals would perform at least 228 such operations per year (table3).

In total, 434,000 patients with transurethral resection of prostate were studied (table 1). No statistically significant differences in in-hospital mortality were found when patients were stratified by hospital volume quintiles (figure 1, table 2) and there was no significant association of hospital volume and mortality when volume was analysed continuously (table 3).

Sensitivity analysis

Within the sensitivity analysis hospital volume was determined more widely by considering all those treatments or procedures, which could be regarded as technically similar to the specific treatment for which outcome was measured. The specific restrictions for the purpose of outcome measurement were applied after determining volume. Using this divergent volume definition results remained substantially unchanged in 23 out of the 25 studied types of treatments.

Different findings were observed regarding isolated coronary artery bypass graft, where the relation of volume and mortality was more pronounced when all related procedures (i.e., coronary bypass grafts in patients with acute myocardial infarction or combined with other heart surgery instead of elective isolated coronary operations only) were considered for determination of hospital volume. Different from the findings in the main analysis higher volume was constantly associated with lower mortality when patients were stratified by these volume quintiles.

The volume-outcome association in colorectal resections for diverticulosis diminished when hospital volume was determined by considering all colorectal resections, regardless from medical indication. In contrast to the results of the main analysis, no statistically significant relation between volume and outcome was observed under this approach.

Discussion

Lower in-hospital mortality in association with higher hospital volume was observed in 20 out of the 25 studied types of treatment when volume was categorized in quintiles, and persisted in 17 types of treatment when volume was analysed as a continuous variable. While a volume-outcome relationship was not found in all studied emergency conditions and low-risk procedures, it was more consistently present regarding complex surgical procedures. The potential benefit of a centralisation according to the calculated minimum volume thresholds varied depending on the treatment-specific risk of death and the strength of the association between volume and mortality.

The analysis included every patient who underwent one of the studied types of inpatient treatment in a German acute care hospital during the observation period. Limitations occur from the limited information available in administrative data, including lack of information on appropriateness of patient selection for procedures. Although types of treatment and covariates for risk adjustment were defined in a sophisticated way, it is possible that unmeasured differences in disease severity, comorbidity, or appropriateness may partly explain the association between volume and outcome. However, it should be considered that the more severe patients should intentionally not be treated by low-volume hospitals. Elective types of treatment were either defined by exclusion of patients with diagnoses pointing to an emergency admission, or potential emergency diagnoses were considered within the risk adjustment models. However, this approach might not have fully separated elective admissions. The analyses could focus hospital volume only because physician volumes are not available in German administrative data. Regarding the determination of hospital volume, a possible misclassification of multi-campus hospitals as high volume providers must be taken into account, resulting in a possible underestimation of the association between hospital volume and mortality.[30] Finally, this study did not consider hospital characteristics like teaching status, type of ownership, or location.

Inpatient treatments for emergency conditions revealed mixed results. Associations between higher hospital volume and lower mortality were found for treatment of acute myocardial infarction, heart failure, ischemic stroke, and chronic obstructive pulmonary disease. These results are similar to findings of previous studies from other countries.[6-7, 31-36] Regarding the treatment of patients with pneumonia the analysis revealed higher mortality in hospitals with higher volumes. A similar finding has been reported by one previous US study,[37] while another more recent US study found higher hospital volume being associated with lower mortality.[6] No constant relation between volume and outcome was observed in hip fracture patients, similar to findings from a recent US study.[38] However, a previous German study, which was based on national discharge data as well, but focussed an earlier time period and surgically treated hip fracture patients only, found lower mortality related to higher hospital volumes.[19] An Italian study observed a volume-outcome relation in hip fracture patients, too.[36]

An association of lower mortality and higher hospital volume was observed for each studied type of elective heart and thoracic surgery. These findings correspond to those from several European and US studies.[3, 5, 14, 36, 39-41] In the present study, a more pronounced volume-outcome association was found for lung resection than for the studied types of heart surgery. This might be explained by an already quite high degree of centralization of heart surgery services in Germany.

The analysis of major visceral surgery treatments revealed the most pronounced associations between volume and mortality, e.g. regarding oesophageal surgery, cystectomy, or pancreatic resection for carcinoma. These results are well-supported by international evidence of a strong volume-outcome association in complex visceral surgery.[3, 11-12, 17-18, 42-46]

In the case of vascular surgery, the analyses demonstrated lower mortality in association with higher hospital volume for lower extremity revascularization, carotid endarterectomy and open repair of abdominal aortic aneurysm, in accordance to findings from the international literature.[3, 5, 36, 47-48] A volume-outcome relation for abdominal aortic aneurysm repair (open, endovascular, or totally percutaneous) had been demonstrated by a previous German study based on national discharge data.[19] In the present study, however, endovascular repair of abdominal aortic aneurysm was analysed separately and no significant relationship between volume and mortality was observed. This finding is in contrast to one study from the US,[49] while a more recent US study found no significant association.[5]

Among the studied types of elective low-risk surgery lower mortality associated with higher volume was found for primary knee and hip replacement, supported by international findings.[8, 51-54] However, no such relation was observed for cholecystectomy, similar to one study from England,[55] but in contrast to studies from Italy and Scotland, which found a modest association between volume and outcome in cholecystectomy patients.[36, 10] The effect of volume on mortality observed in patients undergoing inguinal or femoral hernia repair was small. Studies from the US and Sweden reported a volume-outcome relation for hernia repair, but focussed different outcomes (hernia recurrence or reoperation rates) and determined volume rather on the surgeon level.[56-57] Regarding transurethral resection of prostate no association between hospital volume and mortality was found. This confirms the findings of a Japanese study which found an association regarding complication and blood transfusion rates, but not regarding mortality.[58]

Overall, the results of the present study seem plausible in view of the current literature. Discrepancies to findings from other studies might be caused by differences in completeness of data or alternative methodological approaches, e.g. regarding case definitions, or volume determination. However, it is also possible that an association between volume and outcome is more or less existent in different countries, depending on characteristics of a health care system and hospital market structures.[39]

Minimum volume thresholds were calculated for those treatments, in which the association of volume and mortality persisted when volume was analysed as a continuous variable, which provides a strong indication that such an association truly exists. The highest population impact of centralisation according to the calculated thresholds was estimated for oesophageal surgery and pancreatic resection for carcinoma. Compared to this, the potential for improvement might appear small in the case of treatments with a basically low risk of mortality. However, one should consider that risk of mortality is likely correlated with the occurrence of non-lethal adverse events, in particular with regard to low-risk procedures. Thus, possible improvements of patient safety by centralisation might reach beyond effects on mortality.

When interpreting the findings of this study, one should note that observational studies cannot proof a causal volume-outcome relation. In consequence, this retrospective observational study cannot provide evidence that an application of the calculated thresholds as minimum volumes would actually improve quality of care. Therefore, the threshold values are meant to serve as basic orientation points for policy decisions in Germany and as hypothesis-generating landmarks for further research. Although estimated rather conservatively, roughly 80 to 90% of hospitals providing a specific treatment performed annual volumes below the respective threshold, and between 50% (acute myocardial infarction) and 70% (pancreatic resection for carcinoma) of patients were treated by those hospitals. Policy decisions on centralisation of services cannot rely on testing a statistical association upon observational data, alone. As well, the regional availability and accessibility of inpatient services must be considered, in particular regarding emergency treatments. Centralisation should be pushed primarily in oversupplied geographic regions. However, experiences from the Netherlands have demonstrated that centralisation of inpatient services improved national outcome.[59]

A previous German study concluded that full implementation of the existing minimum volume regulation could improve the quality of hospital care in Germany.[24] In addition to this, the present study identified further areas where centralisation could provide a benefit for patients, and quantified the possible impact of centralisation efforts by using complete national hospital discharge data. These findings might support future policy decisions in Germany.

Author's contribution

Ulrike Nimptsch designed the study, conducted the analysis, interpreted the data and drafted the manuscript. Thomas Mansky contributed to the study design, to the interpretation of data and to revising the manuscript critically for important intellectual content. Both authors gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table 1 No. of patients and hospitals by volume quintile

		Hospital volume quintile									
		Very low		Low		Medium		High		Very high	
COMMON EMERGENCY CONDITIONS											
Acute myocardial infarction	No. of patients		219,178		219,291		219,189		219,778		220,805
	No. of hospitals		763		198		121		88		54
	Median annual volume *(IQR)*	43	*(20 - 71)*	184	*(154 - 215)*	303	*(274 - 331)*	412	*(387 - 450)*	594	*(534 - 732)*
Heart failure	No. of patients		463,352		463,883		463,283		464,586		465,401
	No. of hospitals		608		263		184		136		87
	Median annual volume *(IQR)*	139	*(63 - 189)*	290	*(260 - 321)*	418	*(374 - 461)*	570	*(518 - 613)*	804	*(703 - 950)*
Ischemic stroke	No. of patients		244,125		244,272		244,299		243,725		246,858
	No. of hospitals		915		155		96		70		42
	Median annual volume *(IQR)*	28	*(10 - 62)*	259	*(213 - 310)*	427	*(383 - 471)*	577	*(542 - 625)*	865	*(766 - 1028)*
Pneumonia	No. of patients		258,016		257,688		258,010		258,051		259,391
	No. of hospitals		630		255		186		140		84
	Median annual volume *(IQR)*	73	*(25 - 107)*	167	*(150 - 183)*	229	*(211 - 249)*	304	*(279 - 331)*	447	*(396 - 523)*
Chronic obstructive pulmonary disease	No. of patients		230,629		230,793		231,093		230,258		232,476
	No. of hospitals		612		264		182		125		61
	Median annual volume *(IQR)*	67	*(33 - 92)*	144	*(126 - 163)*	209	*(187 - 233)*	299	*(262 - 337)*	546	*(455 - 702)*
Hip fracture	No. of patients		142,041		142,082		141,910		141,658		143,271
	No. of hospitals		609		232		172		133		88
	Median annual volume *(IQR)*	43	*(6 - 64)*	101	*(93 - 110)*	137	*(128 - 146)*	176	*(164 - 190)*	244	*(221 - 283)*
ELECTIVE HEART AND THORACIC SURGERY											
Isolated surgical aortic valve replacement	No. of patients		10,275		10,238		10,627		10,066		11,397
	No. of hospitals		33		17		14		10		7
	Median annual volume *(IQR)*	54	*(37 - 71)*	100,5	*(93 - 108)*	132	*(124 - 138)*	172	*(159 - 188)*	246	*(227 - 283)*
Transcatheter aortic valve replacement	No. of patients		9,915		10,009		9,926		9,935		10,980
	No. of hospitals		48		17		12		9		6
	Median annual volume *(IQR)*	31	*(12 - 50)*	98	*(69 - 123)*	141	*(99 - 161)*	169	*(142 - 228)*	286	*(233 - 328)*
Isolated coronary artery bypass graft	No. of patients		35,648		36,967		36,047		37,221		37,807
	No. of hospitals		48		18		14		11		8
	Median annual volume *(IQR)*	120	*(1 - 230)*	353	*(318 - 375)*	436	*(407 - 465)*	561	*(518 - 585)*	729	*(669 - 824)*
Partial lung resection for carcinoma	No. of patients		14,655		14,766		14,626		14,872		15,064
	No. of hospitals		260		48		27		17		9
	Median annual volume *(IQR)*	5	*(2 - 14)*	49	*(43 - 59)*	89	*(79 - 98)*	137	*(122 - 160)*	272	*(208 - 313)*
ELECTIVE MAJOR VISCERAL SURGERY											
Colorectal resection for carcinoma	No. of patients		66,058		66,089		66,119		66,185		66,451
	No. of hospitals		492		218		153		112		71
	Median annual volume *(IQR)*	23	*(14 - 32)*	50	*(45 - 55)*	72	*(66 - 78)*	97	*(91 - 105)*	141	*(126 - 165)*
Colorectal resection for diverticulosis	No. of patients		35,828		35,821		35,810		35,872		36,032
	No. of hospitals		487		215		154		114		73
	Median annual volume *(IQR)*	13	*(7 - 18)*	28	*(25 - 30)*	39	*(36 - 42)*	52	*(48 - 56)*	74	*(68 - 86)*
Total nephrectomy for carcinoma	No. of patients		13,582		13,569		13,570		13,600		13,766
	No. of hospitals		307		90		65		47		31
	Median annual volume *(IQR)*	5	*(2 - 13)*	25	*(23 - 27)*	35	*(33 - 37)*	48	*(45 - 52)*	67	*(60 - 76)*
Cystectomy for carcinoma	No. of patients		8,706		8,702		8,761		8,734		8,832
	No. of hospitals		177		78		56		39		24
	Median annual volume *(IQR)*	9	*(5 - 12)*	18	*(17 - 20)*	26	*(24 - 28)*	36	*(34 - 40)*	57	*(51 - 68)*
Complex oesophageal surgery for carcinoma	No. of patients		3,625		3,625		3,639		3,550		3,769
	No. of hospitals		228		71		43		23		10
	Median annual volume *(IQR)*	2	*(1 - 4)*	8	*(7 - 10)*	14	*(12 - 16)*	25	*(21 - 29)*	54	*(42 - 67)*
Pancreatic resection for carcinoma	No. of patients		6,886		6,915		6,880		6,854		7,020
	No. of hospitals		322		117		71		41		17
	Median annual volume *(IQR)*	3	*(2 - 5)*	10	*(9 - 11)*	16	*(14 - 18)*	27	*(23 - 33)*	57	*(46 - 72)*
ELECTIVE VASCULAR SURGERY											
Surgical lower extremity revascularization for atherosclerosis	No. of patients		49,239		49,385		49,467		49,086		49,997
	No. of hospitals		348		113		79		57		37
	Median annual volume *(IQR)*	21	*(7 - 39)*	72	*(65 - 80)*	102	*(95 - 112)*	143	*(131 - 158)*	210	*(185 - 243)*
Open repair of abdominal aortic aneurysm	No. of patients		4,422		4,425		4,430		4,420		4,530
	No. of hospitals		239		81		50		33		18
	Median annual volume *(IQR)*	3	*(1 - 4)*	9	*(7 - 10)*	15	*(13 - 17)*	21	*(19 - 25)*	39	*(33 - 46)*
Endovascular repair of abdominal aortic aneurysm	No. of patients		8,281		8,338		8,288		8,309		8,462
	No. of hospitals		219		81		52		34		20
	Median annual volume *(IQR)*	6	*(3 - 9)*	17	*(15 - 19)*	26	*(24 - 30)*	40	*(36 - 45)*	64	*(57 - 75)*
Carotid endarterectomy	No. of patients		32,345		32,267		32,460		32,017		33,081
	No. of hospitals		317		101		67		47		30
	Median annual volume *(IQR)*	16	*(6 - 27)*	52	*(46 - 59)*	80	*(73 - 87)*	113	*(104 - 123)*	165	*(148 - 195)*

Table 1 (continued)

ELECTIVE LOW-RISK SURGERY											
Cholecystectomy for cholelithiasis	No. of patients		177,346		177,411		177,835		177,199		178,752
	No. of hospitals		450		232		178		140		94
	Median annual volume *(IQR)*	71	*(44 - 91)*	128	*(118 - 137)*	166	*(157 - 176)*	210	*(196 - 224)*	286	*(264 - 331)*
Inguinal or femoral hernia repair	No. of patients		178,992		179,169		179,285		179,338		179,911
	No. of hospitals		471		247		186		142		84
	Median annual volume *(IQR)*	68	*(45 - 86)*	120	*(111 - 129)*	160	*(150 - 171)*	208	*(194 - 224)*	312	*(274 - 377)*
Primary hip replacement for arthrosis or arthritis	No. of patients		175,918		175,797		176,313		175,834		177,287
	No. of hospitals		608		226		135		82		42
	Median annual volume *(IQR)*	49	*(25 - 71)*	128	*(111 - 146)*	213	*(190 - 242)*	351	*(314 - 388)*	619	*(522 - 768)*
Primary knee replacement for arthrosis or arthritis	No. of patients		168,312		168,479		168,415		168,015		169,623
	No. of hospitals		517		222		143		94		51
	Median annual volume *(IQR)*	56	*(36 - 75)*	125	*(112 - 140)*	195	*(176 - 215)*	291,5	*(267 - 324)*	477	*(421 - 632)*
Transurethral resection of prostate	No. of patients		86,404		86,934		86,199		86,967		87,412
	No. of hospitals		247		104		77		59		40
	Median annual volume *(IQR)*	60	*(23 - 92)*	139	*(128 - 150)*	186	*(172 - 199)*	243	*(227 - 262)*	331	*(303 - 380)*

No. of hospitals: Mean number of hospitals in quintile per year providing the respective inpatient service; IQR: interquartile range within the quintile (due to data protection regulations the minimum and maximum values cannot be displayed).

Table 2 Odds ratios of in-hospital death according to volume quintile

		Hospital volume quintile								
		Very low	Low		Medium		High		Very high	
COMMON EMERGENCY CONDITIONS										
Acute myocardial infarction	Crude OR	1.00	0.82		0.74		0.72		0.71	
	Adjusted OR *(95% CI)*	1.00	* 0.84	*(0.81 to 0.87)*	* 0.75	*(0.72 to 0.78)*	* 0.73	*(0.7 to 0.76)*	* 0.69	*(0.66 to 0.72)*
Heart failure	Crude OR	1.00	0.95		0.89		0.87		0.81	
	Adjusted OR *(95% CI)*	1.00	0.99	*(0.96 to 1.01)*	* 0.96	*(0.93 to 0.99)*	* 0.95	*(0.92 to 0.98)*	* 0.91	*(0.88 to 0.94)*
Ischemic stroke	Crude OR	1.00	0.77		0.70		0.70		0.72	
	Adjusted OR *(95% CI)*	1.00	* 0.90	*(0.87 to 0.94)*	* 0.87	*(0.83 to 0.9)*	* 0.94	*(0.91 to 0.98)*	* 0.94	*(0.91 to 0.98)*
Pneumonia	Crude OR	1.00	1.09		1.16		1.12		1.08	
	Adjusted OR *(95% CI)*	1.00	1.10	*(1.07 to 1.13)*	1.17	*(1.14 to 1.21)*	1.13	*(1.09 to 1.16)*	1.08	*(1.04 to 1.11)*
Chronic obstructive pulmonary disease	Crude OR	1.00	1.06		1.04		0.91		0.66	
	Adjusted OR *(95% CI)*	1.00	1.09	*(1.06 to 1.14)*	1.08	*(1.04 to 1.12)*	* 0.94	*(0.90 to 0.98)*	* 0.70	*(0.65 to 0.75)*
Hip fracture	Crude OR	1.00	1.06		1.06		1.07		1.00	
	Adjusted OR *(95% CI)*	1.00	1.07	*(1.03 to 1.12)*	1.07	*(1.03 to 1.11)*	1.10	*(1.06 to 1.15)*	1.01	*(0.97 to 1.06)*
ELECTIVE HEART AND THORACIC SURGERY										
Isolated surgical aortic valve replacement	Crude OR	1.00	0.90		0.80		0.74		0.74	
	Adjusted OR *(95% CI)*	1.00	0.87	*(0.69 to 1.10)*	* 0.78	*(0.62 to 0.99)*	* 0.69	*(0.54 to 0.87)*	* 0.77	*(0.61 to 0.97)*
Transcatheter aortic valve replacement	Crude OR	1.00	0.97		0.90		0.78		0.64	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.69 to 1.1)*	* 0.87	*(0.62 to 0.99)*	* 0.79	*(0.54 to 0.87)*	* 0.65	*(0.61 to 0.97)*
Isolated coronary artery bypass graft	Crude OR	1.00	0.93		1.03		0.73		0.70	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.81 to 1.17)*	1.08	*(0.90 to 1.28)*	* 0.82	*(0.68 to 0.99)*	0.92	*(0.76 to 1.11)*
Partial lung resection for carcinoma	Crude OR	1.00	0.71		0.68		0.52		0.37	
	Adjusted OR *(95% CI)*	1.00	* 0.77	*(0.67 to 0.90)*	* 0.73	*(0.63 to 0.85)*	* 0.58	*(0.50 to 0.69)*	* 0.49	*(0.41 to 0.58)*
ELECTIVE MAJOR VISCERAL SURGERY										
Complex oesophageal surgery for carcinoma	Crude OR	1.00	0.83		0.81		0.62		0.51	
	Adjusted OR *(95% CI)*	1.00	* 0.81	*(0.68 to 0.96)*	0.85	*(0.72 to 1.01)*	* 0.67	*(0.56 to 0.82)*	* 0.47	*(0.38 to 0.58)*
Pancreatic resection for carcinoma	Crude OR	1.00	0.76		0.66		0.52		0.46	
	Adjusted OR *(95% CI)*	1.00	* 0.80	*(0.71 to 0.92)*	* 0.68	*(0.59 to 0.77)*	* 0.54	*(0.46 to 0.62)*	* 0.46	*(0.39 to 0.54)*
Colorectal resection for carcinoma	Crude OR	1.00	0.92		0.77		0.72		0.63	
	Adjusted OR *(95% CI)*	1.00	0.97	*(0.91 to 1.02)*	* 0.85	*(0.80 to 0.90)*	* 0.83	*(0.78 to 0.88)*	* 0.75	*(0.70 to 0.80)*
Colorectal resection for diverticulosis	Crude OR	1.00	0.86		0.77		0.65		0.60	
	Adjusted OR *(95% CI)*	1.00	* 0.87	*(0.80 to 0.95)*	* 0.87	*(0.79 to 0.95)*	* 0.80	*(0.72 to 0.88)*	* 0.74	*(0.67 to 0.82)*
Total nephrectomy for carcinoma	Crude OR	1.00	0.92		0.87		0.75		0.80	
	Adjusted OR *(95% CI)*	1.00	0.95	*(0.79 to 1.13)*	0.89	*(0.75 to 1.06)*	* 0.78	*(0.64 to 0.94)*	* 0.80	*(0.67 to 0.97)*
Cystectomy for carcinoma	Crude OR	1.00	0.85		0.89		0.80		0.70	
	Adjusted OR *(95% CI)*	1.00	* 0.85	*(0.73 to 0.98)*	0.86	*(0.74 to 1.00)*	* 0.80	*(0.69 to 0.93)*	* 0.69	*(0.58 to 0.82)*
ELECTIVE VASCULAR SURGERY										
Surgical lower extremity revas-cularization for atherosclerosis	Crude OR	1.00	0.86		0.80		0.73		0.75	
	Adjusted OR *(95% CI)*	1.00	* 0.88	*(0.81 to 0.96)*	* 0.85	*(0.78 to 0.94)*	* 0.82	*(0.75 to 0.9)*	* 0.82	*(0.75 to 0.91)*
Open repair of abdominal aortic aneurysm	Crude OR	1.00	0.67		0.73		0.62		0.52	
	Adjusted OR *(95% CI)*	1.00	* 0.71	*(0.59 to 0.84)*	* 0.76	*(0.63 to 0.91)*	* 0.60	*(0.50 to 0.72)*	* 0.55	*(0.45 to 0.68)*
Endovascular repair of abdominal aortic aneurysm	Crude OR	1.00	0.77		1.17		0.80		0.82	
	Adjusted OR *(95% CI)*	1.00	0.81	*(0.63 to 1.04)*	1.26	*(1.00 to 1.59)*	0.93	*(0.72 to 1.19)*	0.91	*(0.68 to 1.21)*
Carotid endarterectomy	Crude OR	1.00	0.85		0.81		0.82		0.66	
	Adjusted OR *(95% CI)*	1.00	0.92	*(0.77 to 1.09)*	0.89	*(0.75 to 1.05)*	0.90	*(0.76 to 1.06)*	* 0.77	*(0.64 to 0.93)*
ELECTIVE LOW-RISK SURGERY										
Cholecystectomy for cholelithiasis	Crude OR	1.00	0.97		1.00		0.98		0.84	
	Adjusted OR *(95% CI)*	1.00	0.98	*(0.87 to 1.09)*	1.06	*(0.95 to 1.19)*	1.07	*(0.95 to 1.19)*	0.95	*(0.85 to 1.08)*
Inguinal or femoral hernia repair	Crude OR	1.00	0.88		0.75		0.66		0.43	
	Adjusted OR *(95% CI)*	1.00	0.94	*(0.77 to 1.14)*	0.90	*(0.72 to 1.11)*	0.83	*(0.66 to 1.04)*	* 0.66	*(0.51 to 0.86)*
Transurethral resection of prostate	Crude OR	1.00	1.11		1.18		1.13		0.92	
	Adjusted OR *(95% CI)*	1.00	1.06	*(0.89 to 1.25)*	1.11	*(0.93 to 1.32)*	1.08	*(0.90 to 1.28)*	0.98	*(0.82 to 1.18)*
Primary hip replacement for arthrosis or arthritis	Crude OR	1.00	0.78		0.56		0.48		0.27	
	Adjusted OR *(95% CI)*	1.00	* 0.87	*(0.75 to 1.00)*	* 0.70	*(0.60 to 0.82)*	* 0.67	*(0.56 to 0.79)*	* 0.41	*(0.33 to 0.51)*
Primary knee replacement for arthrosis or arthritis	Crude OR	1.00	0.79		0.68		0.59		0.35	
	Adjusted OR *(95% CI)*	1.00	0.84	*(0.69 to 1.02)*	* 0.76	*(0.62 to 0.94)*	* 0.68	*(0.54 to 0.85)*	* 0.45	*(0.34 to 0.58)*

* Statistically significant lower than reference category (very low volume).
Covariates used for risk adjustment are displayed in Appendix table 3.

Table 3 Minimum volume threshold estimation and assessment of population impact

	Logistic regression coefficients of hospital volume: Simple model β	Simple model p	Full model β	Full model p	VARL Minimum volume threshold	(95% CI)	Average mortality in population	Adjusted mortality if volume ≥ VARL	(95% CI)	PRD Population-based risk difference	(95% CI)	PIN Population impact number	(95% CI)
COMMON EMERGENCY CONDITIONS													
Acute myocardial infarction	-0.0003	<.001	-0.0003	<.001	309	(288 to 330)	9.8%	9.1%	(9.0 to 9.2)	0.7%	(0.7 to 0.8)	137	(127 to 149)
Heart failure	-0.0001	0.001	0.0000	0.358	-		8.9%						
Ischemic stroke	-0.0002	0.000	0.0000	0.025	-		6.9%						
Pneumonia	0.0000	0.003	0.0000	<.001	-		11.6%						
Chronic obstructive pulmonary disease	-0.0003	0.039	-0.0002	0.026	271	(240 to 301)	4.2%	3.6%	(3.5 to 3.6)	0.6%	(0.5 to 0.6)	170	(158 to 185)
Hip fracture	0.0000	0.138	0.0000	0.828	-		5.5%						
ELECTIVE HEART AND THORACIC SURGERY													
Isolated surgical aortic valve replacement	-0.0014	0.001	-0.0010	0.039	147	(111 to 182)	2.6%	2.4%	(2.2 to 2.6)	0.2%	(0.0 to 0.3)	516	(288 to 2589)
Transcatheter aortic valve replacement	-0.0024	<.001	-0.0017	<.001	157	(142 to 171)	6.6%	5.8%	(5.5 to 6.2)	0.8%	(0.5 to 1.0)	133	(101 to 193)
Isolated coronary artery bypass graft	-0.0007	<.001	-0.0003	0.024	475	(430 to 521)	2.1%	2.0%	(1.9 to 2.1)	0.2%	(0.1 to 0.2)	658	(445 to 1271)
Partial lung resection for carcinoma	-0.0034	<.001	-0.0025	<.001	108	(95 to 120)	2.9%	2.3%	(2.1 to 2.5)	0.6%	(0.5 to 0.7)	168	(137 to 217)
ELECTIVE MAJOR VISCERAL SURGERY													
Colorectal resection for carcinoma	-0.0023	<.001	-0.0014	<.001	82	(76 to 88)	6.0%	5.4%	(5.3 to 5.5)	0.5%	(0.4 to 0.6)	197	(167 to 241)
Colorectal resection for diverticulosis	-0.0049	<.001	-0.0025	0.003	44	(38 to 49)	3.5%	3.2%	(3.1 to 3.4)	0.3%	(0.2 to 0.4)	364	(269 to 564)
Total nephrectomy for carcinoma	-0.0032	0.012	-0.0029	0.047	40	(24 to 56)	2.1%	1.9%	(1.7 to 2.0)	0.2%	(0.1 to 0.3)	459	(295 to 1056)
Cystectomy for carcinoma	-0.0054	<.001	-0.0055	<.001	31	(23 to 39)	4.7%	4.3%	(4.0 to 4.6)	0.4%	(0.2 to 0.7)	227	(150 to 480)
Complex oesophageal surgery for carcinoma	-0.0105	<.001	-0.0111	<.001	22	(17 to 28)	8.5%	6.3%	(5.7 to 6.9)	2.1%	(1.6 to 2.6)	47	(38 to 62)
Pancreatic resection for carcinoma	-0.0049	<.001	-0.0045	0.001	29	(21 to 37)	8.8%	6.6%	(6.2 to 7.2)	2.2%	(1.7 to 2.6)	46	(39 to 58)
ELECTIVE VASCULAR SURGERY													
Surgical lower extremity revascularization for atherosclerosis	-0.0011	<.001	-0.0007	<.001	123	(102 to 144)	3.0%	2.8%	(2.7 to 2.9)	0.2%	(0.1 to 0.3)	561	(387 to 1024)
Open repair of abdominal aortic aneurysm	-0.0129	<.001	-0.0112	<.001	18	(14 to 23)	6.0%	5.0%	(4.6 to 5.5)	1.0%	(0.6 to 1.3)	104	(76 to 166)
Endovascular repair of abdominal aortic aneurysm	-0.0031	0.014	-0.0028	0.069	-		1.7%						
Carotid endarterectomy	-0.0021	<.001	-0.0014	<.001	93	(69 to 116)	0.87%	0.81%	(0.74 to 0.88)	0.06%	(0.01 to 0.11)	1646	(886 to 12661)
ELECTIVE LOW-RISK SURGERY													
Cholecystectomy for cholelithiasis	-0.0003	0.008	-0.0001	0.425	-		0.43%						
Inguinal or femoral hernia repair	-0.0019	0.009	-0.0007	0.212	-		0.09%						
Primary hip replacement for arthrosis or arthritis	-0.0020	<.001	-0.0013	<.001	252	(227 to 278)	0.17%	0.13%	(0.12 to 0.14)	0.04%	(0.03 to 0.05)	2747	(2186 to 3701)
Primary knee replacement for arthrosis or arthritis	-0.0020	<.001	-0.0016	<.001	228	(190 to 265)	0.10%	0.07%	(0.07 to 0.08)	0.02%	(0.01 to 0.03)	4729	(3513 to 7269)
Transurethral resection of prostate	-0.0003	0.130	-0.0001	0.740	-		0.36%						

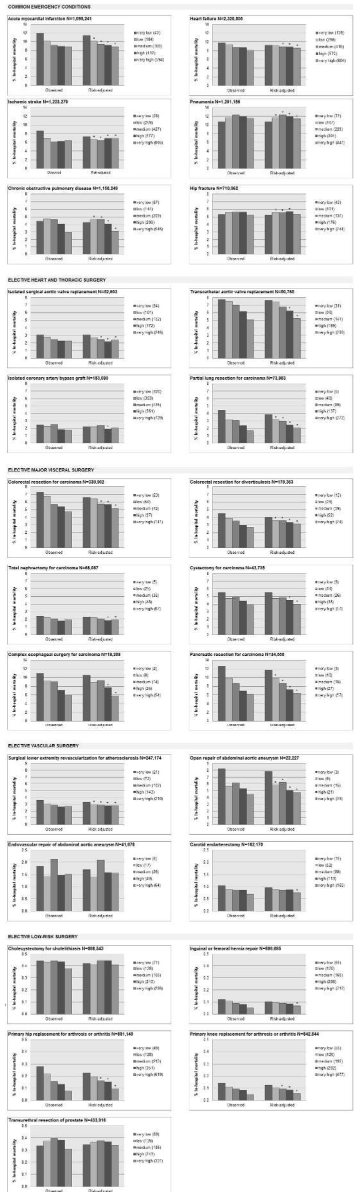
Logistic regression coefficients of hospital volume relate to an increment of 1 case per year. CI: Confidence interval.
VARL: Value of acceptable risk limit (Bender 1999), calculated from the logistic regression coefficient of the simple model. It estimates a minimum volume threshold to achieve a risk of in-hospital mortality which is lower than a predefined acceptable risk. The acceptable risk for each treatment was set to the average mortality in the respective patient population during the observation period.
The population impact number PIN is the reciprocal of the difference between the average mortality in the patient population and the adjusted mortality in those patients treated by hospitals with volumes above the threshold (population-based risk difference PRD). It can be interpreted as average number of the entire patient population among whom one death is attributable to treatment by a below-threshold volume hospital. Covariates used for risk adjustment are displayed in Appendix table 3.

Figure 1 Observed and risk-adjusted in-hospital mortality by hospital volume quintile

* Statistically significant lower than very low volume quintile. + Statistically significant higher than very low volume quintile. Numbers displayed in the legend of each graph denote the median annual hospital volume within the respective volume quintile. Covariates used for risk adjustment are displayed in Appendix table 3.

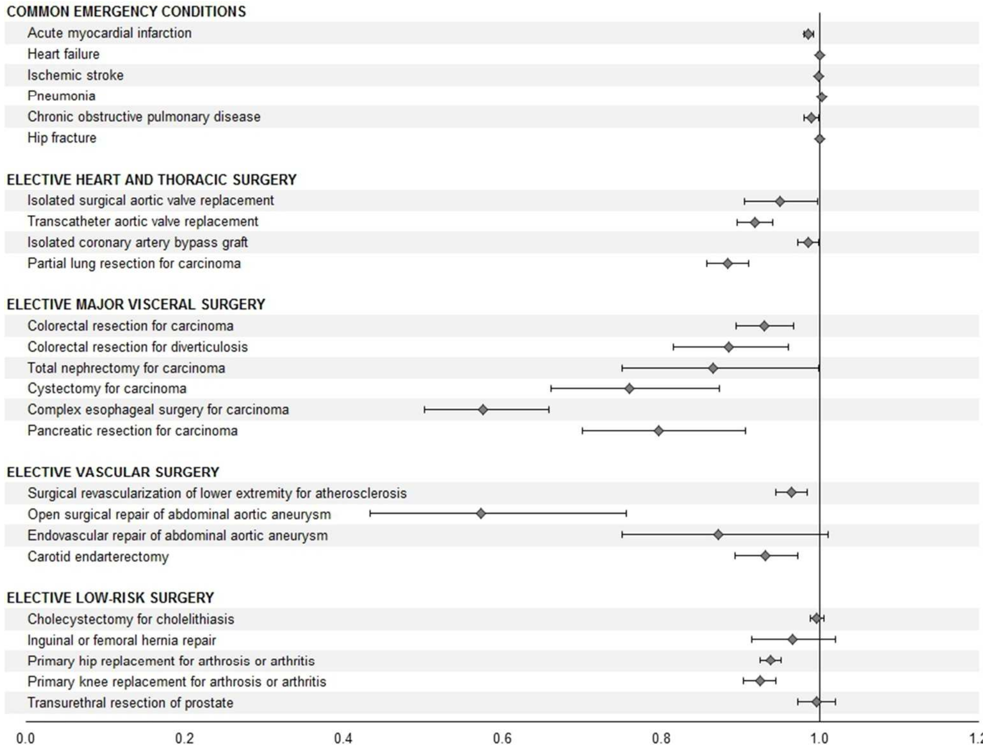
Figure 2 Adjusted odds ratios of in-hospital death according to an increment of hospital volume of 50 cases per year

Whiskers indicate 95% confidence interval. Covariates used for risk-adjustment are displayed in Appendix table 3.



Observed and risk-adjusted in-hospital mortality by hospital volume quintile

104x337mm (300 x 300 DPI)



Adjusted odds ratios of in-hospital death according to an increment of hospital volume of 50 cases per year

80x61mm (300 x 300 DPI)

Hospital volume and mortality for 25 types of inpatient treatment in German hospitals – Observational study using complete national data from 2009 to 2014

Appendix table 1 Inclusion and exclusion criteria for case definition

	Inclusion	Exclusion
COMMON EMERGENCY CONDITIONS		
Acute myocardial infarction	PD I21 I22; direct admission	
Heart failure	PD I50 I110 I130 I132; direct admission	
Ischemic stroke	PD I63; direct admission	
Pneumonia	PD A481 J100 J110 J12 J13 J14 J15 J16 J17 J18; direct admission	SD U6900 (nosocomial acquired pneumonia)
Chronic obstructive pulmonary disease	PD J44; direct admission	
Hip fracture	PD S720 S721; direct admission	
ELECTIVE HEART AND THORACIC SURGERY		
Isolated surgical aortic valve replacement	OPS 53510	OPS 53502 53503 53504 53505 53506 53507 5350x 5350y 53511 53512 53513 53514 5351x 5351y 53521 53522 53523 5352y 53531 53532 53533 53534 53535 5353x 5353y 53541 53542 53543 53544 5354y 53581 53582 53583 53584 53585 5358x 5358y 536 538a0 538a1 538233 53823x 53845 53846 53847 5384x 5384y 538a7 538a8 538230 538232 538401 538402 53840x 538411 538412 53841x 538421 538422 53842x 538431 538432 53843x 53844 5355 5356 5357 5359 5371 53725 53732 53733 53734 53735 53736 53737 53738 5373x 5373y 5375 537a (other heart surgery); OPS 535a0 (transcatheter aortic valve replacement); PD I33 I38 I39 (endocarditis)
Transcatheter aortic valve replacement	OPS 535a0	
Isolated coronary artery bypass graft	OPS 536	OPS 5350 5351 5352 5353 5354 5358 535a 5379a 5379b 538a0 538a1 538233 53823x 53845 53846 53847 5384x 5384y 538a7 538a8 538230 538232 538401 538402 53840x 538411 538412 53841x 538421 538422 53842x 538431 538432 53843x 53844 5355 5356 5357 5359 5371 53725 53732 53733 53734 53735 53736 53737 53738 5373x 5373y 5375 537a (other heart surgery); PD I21, I22 (acute myocardial infarction)
Partial lung resection for carcinoma	OPS 5321 5322 5323 5324 5325; PD or SD C34 D022	OPS 5327 5328 (pneumonectomy)
ELECTIVE MAJOR VISCERAL SURGERY		
Colorectal resection for carcinoma	OPS 5455 5456 5458 5484 5485; PD or SD C18 C19 C20 C218 D010 D011 D012	
Colorectal resection for diverticulosis	OPS 5455 5456 5458 5484 5485; PD K572 K573 K574 K575 K578 K579	SD C18 C19 C20 C218 D010 D011 D012 (colorectal carcinoma)
Total nephrectomy for carcinoma	OPS 55544 55545 55546 55547 5554a 5554b 5554x 5554y; PD or SD C64 C65 C66	OPS 55547 55549 5555 (post mortem resection, graft resection, donor resection or transplantation of kidney)
Cystectomy for carcinoma	OPS 5576 56870 56872 56873; PD or SD C67 D090 D414	
Complex oesophageal surgery for carcinoma	OPS 5423 5424 5425 5426 54270 54271 54380 54381 5438x; PD or SD C15 C160	
Pancreatic resection for carcinoma	OPS 5521 5522 5523 5524 5525; PD or SD C25 C241	OPS 55253 55254 5528 (post mortem resection, graft resection, or transplantation of pancreas)
ELECTIVE VASCULAR SURGERY		
Open repair of unruptured abdominal aortic aneurysm	OPS 538233 53823x 53845 53846 53847 5384x 5384y; PD or SD I7100 I7101 I7102 I7103 I712 I714 I716 I719	PD or SD I7104 I7105 I7106 I7107 I711 I713 I715 I718 (ruptured aortic aneurysm); OPS 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab (surgical repair of thoracic aortic aneurysm); OPS 538a0 538a1 (endovascular repair of abdominal aortic aneurysm)
Endovascular repair of unruptured abdominal aortic aneurysm	OPS 538a0 538a1; PD or SD I7100 I7101 I7102 I7103 I712 I714 I716 I719	PD or SD I7104 I7105 I7106 I7107 I711 I713 I715 I718 (ruptured aortic aneurysm); OPS 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab (surgical repair of thoracic aortic aneurysm)
Surgical lower extremity revascularization for atherosclerosis	OPS 53805 53807 53808 53815 53817 53818 538253 538254 538255 53825x 53827 53828 538352 538353 538354 538355 53835x 53837 53838 539333 539335 539336 539338 539341 539342 539343 539344 539345 539346 539347 53934x 53935 53936 53937 539552 539553 539554 539555 53955x 53957 53958 53965 53967 53968 53975 53977 53978; PD or SD I7020 I7021 I7022 I7023 I7024	OPS 538233 53823x 53845 53846 53847 5384x 5384y 538a0 538a1 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab 5335 5375 5504 5528 5555 (repair of aortic aneurysm, solid organ transplantation); PD or SD I723 I724 I728 I729 I74 T823 T824 T825 T827 T828 T829 (arterial dissection, aneurysm or embolism, complication of stent prosthesis)
Carotid endarterectomy	OPS 53800 53810 53820 53830 538c01 53950 53970	OPS 535 536 5370 5371 5372 5373 5374 5375 53791 53796 53797 53798 53799 5379a 5379b 5379c 537620 537621 537630 537631 537640 537641 537650 537651 537660 537661 537670 537671 537680 537681 537690 537691 537694 537a 538233 53823x 53845 53846 53847 5384x 5384y 538a0 538a1 538230 538232 53840 53841 53842 53843 53844 53848 538a7 538a8 538aa 538ab 53805 53807 53808 53815 53817 53818 538253 538254 538255 53825x 53827 53828 538352 538353 538354 538355 53835x 53837 53838 539332 539333 539335 539336 539338 53933x 539341 539342 539343 539344 539345 539346 539347 53934x 53935 53936 53937 539552 539553 539554 539555 53955x 53957 53958 53965 53967 53968 53975 53977 53978 5864 5865 (heart surgery, aortic aneurysm repair, lower extremity revascularization, lower limb amputation); PD or SD C00 C01 C02 C03 C04 C05 C06 C07 C08 C09 C10 C11 C12 C13 C14 C15 (neoplasm of ear, nose or throat)

Appendix table 1 (continued)

ELECTIVE LOW-RISK SURGERY		
Cholecystectomy for cholelithiasis	OPS 55110 55111 55112 5511x 5511y; PD K80	SD C D0 (malign neoplasm); OPS 55113 55114 55115 (extended or simultaneously performed cholecystectomy)
Inguinal or femoral hernia repair	OPS 5530 5531; PD K40 K41	OPS 5451 5452 5453 5454 5455 5456 5458 5459 5460 5461 5462 5463 5464 5465 5466 5467 5468 5469 5484 5485 55304 55308 55314 55318 (other intestinal surgery)
Primary hip replacement for arthrosis or arthritis	OPS 582000 582001 582002 582010 582011 582012 582020 582021 582022 582030 582031 582040 582041 582060 582061 582080 582081 582082 582092 582093 582094 582095 582096 5820x0 5820x1 5820x2; PD M05 M06 M07 M08 M160 M161 M162 M163 M166 M167 M169 M87	OPS 5829c 5829g 5829n 57854d 582810 582840 582860 5829k 5829m (replacement for malign neoplasm, modular prosthesis, two-stage revision); SD M8005 M8085 M8415 M8445 M8485 M8495 M8505 M8545 M8555 M8565 M9075 M9688 Q650 Q651 S324 (osteoporosis, other osteopathy, hip fracture, congenital deformity of hip)
Primary knee replacement for arthrosis or arthritis	OPS 58221 58222 58223 58224 58226 58227 58229 5822a 5822b 5822d 5822e 5822g 5822h 5822j 5822k 582200 582201 582202; PD M05 M06 M07 M08 M170 M171 M174 M175 M179 M87	OPS 5829c 5829g 5829n 57854d 582810 582840 582860 5829k 5829m (replacement for malign neoplasm, modular prosthesis, two-stage revision); SD M8000 M8005 M8080 M8085 M8400 M8405 M8406 M8505 M8506 M8545 M8546 M8555 M8556 M8565 M8566 (osteoporosis or other osteopathy)
Transurethral resection of prostate	OPS 5601	

PD: principal diagnosis (ICD-10-GM); SD: secondary diagnosis (ICD-10-GM); OPS: procedure classification code [Operationen- und Prozedurenschlüssel]; direct admission: patient was not transferred-in from another acute care hospital.
Official classifications according to the German Institute of Medical Documentation and Information (DIMDI): http://www.dimdi.de/static/en/klassi/icd-10-gm/index.htm (ICD-10-GM); http://www.dimdi.de/static/en/klassi/ops/index.htm (OPS).
The case definitions rely on previous work on hospital quality indicators which were modified for the purpose of this analysis: Mansky T, Nimptsch U, Cools A, Hellerhoff F. G-IQI | German Inpatient Quality Indicators. Version 5.0. - Band 2: Definitionshandbuch für das Datenjahr 2016. Berlin: Universitätsverlag der TU Berlin. https://depositonce.tu-berlin.de/handle/11303/5819

Appendix table 2 Definition of covariates used for risk adjustment

Covariate	Definition
Calendar year of treatment	2009, 2010, 2011, 2012, 2013, 2014
Demographics	
Age	5-year age groups
Female sex	
Comorbidity	
Cardiac arrhythmia	PD or SD I442 I48 Z450 Z950
Heart failure or cardiomyopathy	PD or SD I50 I110 I130 I132 I420 I426 I427 I428 I429
Chronic ischemic heart disease	PD or SD I25
Hypertension (without heart or renal failure)	PD or SD I10 I119 I129 I139 I15
Valvular disease	PD or SD I340 I342 I350 I351 I352 I050 I051 I052 I060 I061 I062 Q231 Q232 Q233
Atherosclerosis of peripheral arteries	PD or SD I702
Sequelae of cerebrovascular disease	PD or SD I69
Chronic pulmonary disease	PD or SD J41 J42 J44 J45 J47
Mucoviscidosis	PD or SD E84
Chronic liver disease	PD or SD B18 I864 I982 K70 K73 K74 K760 K761 K765 K766 K767 Q446 Q447
Chronic pancreatitis	PD or SD K860 K861
Severe renal disease or chronic renal failure	PD or SD I120 I131 I132 N03 N04 N05 N07 N08 N11 N12 N14 N15 N16 N18 N19 Z992
Diabetes mellitus	PD or SD E10 E11 E12 E13 E14
Obesity	PD or SD E66
Cachexia or malnutrition	PD or SD R64 R634 E43 E44
Coagulopathy	PD or SD D66 D67 D680 D681 D682 D684 D685 D686 D688 D689 D691 D693 D694
Malign neoplasm	PD or SD C00-C97
Metastatic cancer	PD or SD C77 C78 C79
Specific risk factors	
ST-elevation myocardial infarction	PD I210 I211 I212 I213
Cardiogenic shock	PD or SD R570
Subsequent myocardial infarction	PD I22
Heart failure NYHA classification stage IV	PD I5014
Chronic obstructive pulmonary disease FEV1 <35%	PD J4400 J4410 J4480 J4490
Fracture of neck of femur	PD S720
Complex disease of intestine	PD or SD K55 K56 K593 K630 K631
Peripheral vascular disease stage	PD or SD I + II: I7020 I7021; III: I7022; IV: I7023 I7024
Acute cholecystitis	PD K800 K810
Trans-apical aortic valve replacement	OPS 535a01 535a02
Extended colorectal resection	OPS 5458 54540 54541 54542 54543 54544 54545 54546 5501 5502 5437 5436 5454x 5454y
Resection of visceral organs other than pancreas	OPS 5437 5436 5502 5501 5455 5456 54540 54541 54542 54543 54544 54545 54546 5454x 5454y

PD: principal diagnosis (ICD-10-GM); SD: secondary diagnosis (ICD-10-GM); OPS: procedure classification system [Operationen- und Prozedurenschlüssel]. Official classifications according to the German Institute of Medical Documentation and Information (DIMDI): http://www.dimdi.de/static/en/klassi/icd-10-gm/index.htm (ICD-10-GM); http://www.dimdi.de/static/en/klassi/ops/index.htm (OPS).

Appendix table 3 Application of covariates used to estimate risk-adjusted in-hospital mortality

	Calendar year of treatment	5-year age groups	Female sex	Cardiac arrhythmia	Heart failure or cardiomyopathy	Chronic ischemic heart disease	Hypertension (without heart or renal failure)	Valvular disease	Atherosclerosis of peripheral arteries	Sequelae of cerebrovascular disease	Chronic pulmonary disease	Mucoviscidosis	Chronic liver disease	Chronic pancreatitis	Severe renal disease or chronic renal failure	Diabetes mellitus	Obesity	Cachexia or malnutrition	Coagulopathy	Malign neoplasm	Metastatic cancer	ST-elevation myocardial infarction	Cardiogenic shock	Subsequent myocardial infarction	Heart failure NYHA classification stage IV	Chronic obstructive pulmonary disease FEV1 <35%	Fracture of neck of femur	Complex disease of intestine	Peripheral vascular disease stage	Acute cholecystitis	Trans-apical aortic valve replacement	Extended colorectal resection	Resection of visceral organs other than pancreas	**Area under the curve** (c-statistic)
COMMON EMERGENCY CONDITIONS																																		
Acute myocardial infarction	x	x	x				x	x	x		x		x		x	x	x	x	x	x		x	x	x										0,827
Heart failure	x	x	x	x		x		x	x	x	x		x		x	x	x	x	x	x					x									0,729
Ischemic stroke	x	x	x		x	x	x	x	x		x		x		x	x	x	x	x	x														0,743
Pneumonia	x	x	x	x	x	x	x	x	x			x	x		x	x	x	x	x	x														0,715
Chronic obstructive pulmonary disease	x	x	x	x	x	x	x	x	x				x		x	x	x	x	x	x						x								0,716
Hip fracture	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x							x							0,782
ELECTIVE HEART AND THORACIC SURGERY																																		
Isolated surgical aortic valve replacement	x	x	x	x	x	x	x		x		x		x		x	x	x	x	x	x														0,772
Transcatheter aortic valve replacement	x	x	x	x	x	x	x		x		x		x		x	x	x	x	x	x											x			0,710
Isolated coronary artery bypass graft	x	x	x	x	x		x	x	x		x		x		x	x	x	x	x	x														0,786
Partial lung resection for carcinoma	x	x	x	x	x	x	x	x	x				x		x	x	x	x	x		x													0,782
ELECTIVE MAJOR VISCERAL SURGERY																																		
Colorectal resection for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x							x				x		0,825
Colorectal resection for diverticulosis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x									x				x		0,908
Total nephrectomy for carcinoma	x	x	x	x	x	x	x	x	x		x		x			x	x	x	x		x													0,826
Cystectomy for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x													0,765
Complex oesophageal surgery for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x													0,751
Pancreatic resection for carcinoma	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x		x												x	0,776
ELECTIVE VASCULAR SURGERY																																		
Surgical lower extremity revascularization for atherosclerosis	x	x	x	x	x	x	x	x			x		x		x	x	x	x	x	x									x					0,853
Open repair of abdominal aortic aneurysm	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,771
Endovascular repair of abdominal aortic aneurysm	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,814
Carotid endarterectomy	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,758
ELECTIVE LOW-RISK SURGERY																																		
Cholecystectomy for cholelithiasis	x	x	x	x	x	x	x	x	x		x		x	x	x	x	x	x	x											x				0,943
Inguinal or femoral hernia repair	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,938
Primary hip replacement for arthrosis or arthritis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,869
Primary knee replacement for arthrosis or arthritis	x	x	x	x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,820
Transurethral resection of prostate	x	x		x	x	x	x	x	x		x		x		x	x	x	x	x	x														0,868

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title and abstract Title and abstract Not applicable
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			Introduction (p. 3)
Objectives	3	State specific objectives, including any prespecified hypotheses			Introduction (p. 3)
Methods					
Study Design	4	Present key elements of study design early in the paper			Introduction (p. 3)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Methods (p. 4-5)

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Appendix table 1 Not applicable Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Appendix tables 2 and 3
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			Methods (p. 4-6)
Bias	9	Describe any efforts to address potential sources of bias			Methods (p. 4-6)

Study size	10	Explain how the study size was arrived at			Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			Methods (p. 5)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			Methods (p. 5-6) Not applicable Not applicable Not applicable Methods (p. 5)
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Methods (p. 4) Not applicable

Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Not applicable
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods (p. 4) and appendix table 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			Table 1 Not applicable
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			Table 1

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Figure 1 and 2, tables 2 and 3 Table 1, figure 1 Table 3
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			Results (p. 13)
Discussion					
Key results	18	Summarise key results with reference to study objectives			Discussion (p. 14)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion (p. 14)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			Discussion (p. 15-17)
Generalisability	21	Discuss the generalisability (external validity) of the study results			Discussion (p. 16)

Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			Title page
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Not applicable

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.