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Einfluss des Versorgungs- und Versorgerkontexts auf die Patient:innensicherheit am Beispiel der Geburtshilfe, kolorektalen Chirurgie und Dekubitus

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Zusammenfassung

Hintergrund

Patient:innensicherheit nimmt als ethischer Grundpfeiler medizinischen Handelns sowie als Gut öffentlichen Interesses eine Schlüsselposition in der Gesundheitsversorgung ein. Die Patient:innensicherheit der stationären Akutversorgung soll unter anderem durch legislativ verbindliche Qualitätssicherung und -indikatoren sowie mittels Durchsetzung leistungsberechtigender Mindestfallmengen bei komplexen medizinischen Fällen gewährt und kontinuierlich verbessert werden. Medizinische Fälle unterscheiden sich in ihrer Komplexität im Hinblick auf Alter, Geschlecht und Komorbiditäten. Das stationäre Versorgungssetting unterscheidet sich beispielsweise im Aufnahmezeitpunkt und Aufnahmeanlass, durchgeführter (chirurgischer) Prozedur und der Anzahl an der Versorgung beteiligten Stationen. Stationäre Versorger selbst weisen Unterschiede unter anderem hinsichtlich Versorgungsfähigkeit und -auftrag, Trägerschaft, Bettengröße, Personalschlüssel und -qualifikation sowie Fallmenge auf. Fallindividuell werden in der Qualitätssicherung und in Fallmenge-Outcome-Analysen die Risikofaktoren Alter, Geschlecht und Komorbiditäten statistisch berücksichtigt, jedoch nicht das rahmengebende Versorgungs- oder Versorgersetting.

Fragestellung / Hypothese

Das Ziel dieser Dissertation war es, den Einfluss von Versorger- und Versorgungsvariablen auf multiple Patient:innensicherheitsoutcomes mehrerer stationär behandelter Indikationen unter Nutzung unterschiedlicher Daten und Methoden zu analysieren. Für den stationären Versorgungskontext steht der Aufnahmeanlass als Surrogatvariable für die Akuität des Falls (Forschungsziel 1) im Fokus. Für die stationären Versorger sollte aufgrund der legislativen Implikation der Einfluss der Fallmenge untersucht werden (Forschungsziel 2). Aus diesen zwei Forschungszielen wurden drei Einzelfragestellungen abgeleitet, analysiert und im Rahmen von drei Publikationen beantwortet:

(1) Ist das Geburtsoutcome bei Niedrigrisiko-Geburten mit der Fallmenge des Krankenhauses assoziiert?

(2) Welche Zusammenhänge bestehen zwischen Versorger- und Versorgungsvariablen bei der Patient:innensicherheit kolorektaler Resektionen?

(3) Welche Rolle nimmt der Versorgungskontext als Risikofaktor bei der Inzidenz von Dekubitalulcera ein?

Material und Methoden

Publikation (1) - Systematisches Review

Publikation (1) wurde als systematisches Review konzipiert. Zu den Einschlusskriterien gehörten die Analyse von Einflüssen der Fallmenge (Exposition/ Vergleichsgröße) auf die Mortalität (primäres Outcome), Komplikationen/ Kaiserschnitten (sekundäres Outcome) bei Mutter und Kind bei Niedrigrisiko-Geburten (Population) in analytisch ausgewerteten Primärstudien (Studientyp). Vor dem Hintergrund internationaler Vergleichbarkeit musste die Studie in einem Land mit Neonatalmortalität <5/1000 gemäß UN Child Mortality Report durchgeführt, in englischer oder deutscher Sprache verfasst und ab dem 01. Januar 2000 veröffentlicht worden sein. Das systematische Review wurde gemäß den Berichts- und Qualitätsstandards der „Preferred Reporting Items for Systematic Reviews and Meta-Analyses“ (PRISMA) und der zweiten Version des „A MeaSurement Tool to Assess systematic Reviews“ (AMSTAR 2) Instrumentes durchgeführt. Es wurde a priori ein Reviewprotokoll im International Prospective Register of Systematic Reviews (PROSPERO) veröffentlicht. Die Identifikation relevanter Literatur beinhaltete eine maschinelle Suche in Medline und Excerpta Medica Database (EMBASE) via OVID, eine Handsuche referenzierter und referenzierender Artikel in den eingeschlossenen Studien sowie den Einbezug klinischer Experten. Einschluss, Extraktion und Qualitätsbewertung wurden doppelt unabhängig durchgeführt.

Publikation (2) und (3) - Querschnittstudien

Für die explorativen Fragestellungen der Publikationen (2) und (3) wurde jeweils ein Querschnittdesign mit unterschiedlichen Datenquellen angwendet.

Publikation (2) untersuchte explorativ unter anderem die Assoziationen zwischen Aufnahmeanlass sowie Fallmenge und Mortalität, postoperativem Lungenversagen, Nierenversagen und postoperativen Wundinfektionen nach kolorektalen Resektionen in 232 Krankenhäusern. Zur Analyse konnten Abrechnungsdaten nach §21 Krankenhaus-entgeltgesetz (KHEntgG) aus den Jahren 2016 - 2018 verwendet werden. Für eine korrekte Definition kolorektaler Resektionen (German Inpatient Quality Indicators), Komorbiditäten (Elixhauser Comorbidity Index) und den nicht letalen Patient:innensicherheitsoutcomes des postoperativen Lungenversagens, Nierenversagens und postoperativen Wundinfektionen konnten validierte und publizierte Definitionen herangezogen werden. Die statistische Analyse erfolgte mit einer Mehrebenenregression zur Abbildung der verschiedenen Ebenen zwischen individuellem Fall, Versorgungs- und Versorgersetting.

Publikation (3) untersuchte in einem monozentrischen Setting mit gematchten klinischen Daten und Abrechnungsdaten nach §21 KHEntgG des Universitätsklinikums Dresden (2014 - 2018) die Assoziationen zwischen Dekubitusinzidenz und beispielsweise Aufnahmeanlass, Anästhesiedauer Anzahl behandlungsbeteiligter Stationen. Mit dem zusätzlichen Ziel, die Prädiktierbarkeit inzidenten Dekubitus auf Grundlage der assoziierten Risikofaktoren zu analysieren, kam mit Bayesian Additive Regression Trees (BART) ein Machine-Learning-Ansatz zum Einsatz.

Ergebnisse

In *Publikation (1)* zeigten die nach einem Title-Abstract-Screening mit 7.955 Einträgen 13 eingeschlossenen Beobachtungs- und Registerstudien eine akzeptable Studienqualität. Eine quantitative Auswertung (Meta-Analyse) wurde aufgrund heterogener Definitionen bei Population, Fallschwellen, Outcomes und statistischer Methodik nicht durchgeführt. Die Fallmenge war protektiv mit der perinatalen Mortalität in der Mehrheit der Studien assoziiert. Für die weiteren Outcomes Totgeburt, Neonatalmortalität, maternale Mortalität, Kaiserschnitte oder Komplikationen bei Mutter oder Kind zeigte das Review keinen über die Mehrheit der Studien konsistenten Fallmengeneffekt.

Die Analyse von 54.168 Kolonresektionen (209 Versorger) und 20.395 Rektumresektionen (200 Versorger) in *Publikation (2)* identifizierte Aufnahmen als Notfall oder Zuverlegung und Wochenendchirurgie als durchgehend signfikanten Risikofaktor für die Patient:innensicherheit (Mortalität, postoperatives Lungenversagen, Nierenversagen und postoperative Wundinfektionen) bei Kolon- sowie Rektumresektionen. Fallmenge und Patient:innensicherheit waren mehrheitlich insignifikant mit Kolonresektionen und protektiv mit Rektumresektionen assoziiert.

In der Auswertung von insgesamt 149.006 stationär behandelten Fällen, inklusive 4.663 inzidenten Dekubitusfällen aus *Publikation (3),* war Dekubitus mit der Aufnahme als Notfall oder Zuverlegung und einer OP-Dauer >50 Minuten assoziiert. Die Prädiktierbarkeit erwies sich aufgrund einer hohen Anzahl von falsch-negativen Werten als eingeschränkt.

Schlussfolgerungen

Die Ergebnisse der publizierten Analysen dieser Arbeit weisen darauf hin, dass der Aufnahmeanlass als Teil des Versorgungssettings trotz umfassender Adjustierung durchgängig als Risikofaktor mit der Patient:innensicherheit assoziiert war. Bezüglich

dem Einfluss der Fallmenge auf die Patient:innensicherheit zeigten sowohl das systematische Review (*Publikation (1)*) zur Niedrigrisiko-Geburtshilfe als auch die Querschnittstudie zur Patient:innensicherheit kolorektaler Resektionen (*Publikation (2)*) heterogene Ergebnisse. Im Rahmen der Untersuchung von Fallmenge-Outcome-Vergleichen konnten unter anderem die Risikoadjustierung, die Definitionen von Populationen und Outcomes sowie die Detailtiefe des verwendeten Datensatzes als zu berücksichtigende Faktoren identifiziert werden und unterstreichen die Notwendigkeit umfassender und gründlicher Risikoadjustierungen.

Qualitätssicherung und Mindestmengen besitzen eine hohe versorgungs- und gesundheitswirtschaftliche Relevanz. Im Sinne Evidenzbasierter Medizin sind entsprechende Ansätze oftmals auf die Beforschung durch Beobachtungsstudien als bestverfügbare Evidenz angewiesen. Gemessen an der skizzierten Relevanz von externer Qualitätssicherung und Mindestmengen definiert diese Arbeit auf Grundlage einer umfassenden inhaltlichen und statistischen Analyseplanung die Notwendigkeit einer gründlichen (risikoadjustierten) Analyse von Fall-, Versorgungs- und Versorgervariablen als relevante Risikofaktoren der Patient:innensicherheit.

Summary

Background

Patient safety is an ethical principle of medical care, a matter of public interest and therefore, a central goal in healthcare. Quality assurance and its indicators or minimum volume thresholds in treating complex cases as obligate programs aim at assurance and continuous improvement of patient safety in inpatient care. Medical cases differ in age, sex and comorbidities. Inpatient care differs in admission time, reason, performed procedures, or the number of care-involved wards. Hospitals differ in ownership, bed size, or caseload. Quality assurance programs usually adjust for case variables (e.g. age, sex, comorbidities). They do not adjust for variables of care or hospital and highlight the need for a comprehensive analysis of the different risk factor sets case, care, and hospital.

Aim and hypotheses

The aim of this work was to analyze relationships between care and hospital variables and multiple patient safety outcomes of differing indications using multiple data sources and methods. Referring to the care context this work analyzed the associations between admission reasons) and patient safety outcomes *(research goal 1)*. Referring to the hospital context this work analyzed the associations between hospital case volume and patient safety due to the political relevance of (minimum) case volume thresholds *(research goal 2)*.

The research goals of this work were derived into three specific questions and publications:

1) *Are birth outcomes in low risk birth cohorts related to hospital birth volumes?*
2) *Are multiple patient safety outcomes related to healthcare and hospital-related risk factors in colorectal resection cases?*
3) *Is the incidence of inpatient pressure ulers related to inpatient care setting?*

Material and methods

Publication (1) Systematic review

Publication (1) was a systematic review. The inclusion criteria were the analysis of relationships between hospital birth volume (exposition) and mortality (primary outcome) and complications/cesarean sections (secondary outcomes) in all births or a pre-defined low-risk birth cohort (population) analyzed in primary studies (study type). Concerning comparability, the study needed to be conducted in a country with a neonatal mortality

below 5 per 1000 births. Additional criteria were English or German language of the article and a publication after 01/01/2000.The systematic review followed the reporting and quality standards of the „Preferred Reporting Items for Systematic Reviews and Meta-Analyses“ (PRISMA) and the second version of „A MeaSurement Tool to Assess systematic Reviews“ (AMSTAR 2). A review protocol has been prospectively registered in the „International Prospective Register of Systematic Reviews“ (PROSPERO). The literature search contained a database search in Medline and EMBASE supported by hand search and clinical experts highlighting relevant literature. Two independent reviewers conducted screening, extraction and critical appraisal.

Publication (2) and (3) Cross-sectional design

A cross-sectional design was applied for both explorative questions of *publication (2)* and *(3)* using different data sources. Publication (2) exploratively analyzed associations between admission reason, case volume along with other variables and mortality, postoperative lung failure, renal failure, and postoperative wound infections of colorectal resections in 232 hospitals. For the analysis, accounting data by §21 Krankenhausentgeltgesetz (KHEntgG) covering the years 2016 - 2018 were used. Colorectal resections were determined using the definitions of the German Inpatient Quality Indicators (GIQI). Comorbidities (Elixhauser Comorbidity Index) and the non-lethal patient safety outcomes postoperative respiratory failure, renal failure, and postoperative wound infections were defined by published and validated sets. The different levels between case, care, and hospital were captured using multilevel logistic regression models.

Based on a machine learning approach *Publication (3)* analyzed the associations between incident inpatient pressure ulcers and admission reason, length of surgical anesthesia and number of care-involved wards in a mono-centric setting. The analysis used a matched dataset of clinical and accounting data (§21 KHEntgG) on a five year basis (2014 - 2018) of the University hospital Carl Gustav Carus Dresden.

Results and implications

Publication (1) included thirteen studies after the screening of 7955 records with an acceptable study quality. A pooled analysis was not appropriate due to heterogeneously defined populations, volume thresholds, outcomes and statistical methods. A consistent and protective volume-outcome over the majority of the included studies could be shown for perinatal mortality. The included studies did not report a consistent volume-outcome

effect for neonatal and maternal mortality, stillbirths, birth complications and caesarean sections.

The analysis of 54,168 colon (209 hospitals) und 20,395 rectum resections in *publication (2)* (200 hospitals) showed a consistent association of emergency admissions, intransfers from other hospitals and weekend surgery to a poor patient safety outcome (mortality, postoperative respiratory failure, renal failure and postoperative wound infections. The relationships between case volume and patient safety outcomes were insignificant in colon resections and protective in rectum resections.

The analysis of 149,006 inpatient cases including 4,663 incident inpatient pressure ulcers in *publication (3)* was associated to emergency admission, intransfer from other hospitals and a length of anesthesia over 50 minutes.

Implications

This work shows a consistent association of admission reason to patient safety outcomes including fully adjusted statistics. Concerning case volume both the systematic review (*publication (1)* of low-risk births and the cross-sectional analysis of patient safety in colorectal resections show heterogeneous effects. The analysis of case volume strongly depends on risk adjustment, definitions of populations and outcomes and the granularity of the dataset used for analysis. These heterogeneous results indicate a need for well-planned risk adjusted analyses.

Quality assurance and minimum case volume contain a high relevance to care politics and economy due to the relevance to sanctions and possible portfolio of hospitals. Following the principles of Evidence-based medicine, these global interventions can only be analyzed with observational studies as best-available evidence. Concerning the relevance, the three publications conducted for this work proved the relevance of care- and hospital setting and their need for risk adjustment in patient safety research.

Abbildungsverzeichnis

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Abkürzungsverzeichnis

AMSTAR	A MeaSurement Tool to Assess systematic Reviews
APS	Aktionsbündnis Patientensicherheit
AUC	Area under the curve
ÄZQ	Ärztliches Zentrum für Qualität in der Medizin
BÄK	Bundesärztekammer
BART	Bayesian Additive Regression Trees
BMC	BioMed Central
BMJ	British Medical Journal
DRG	Diagnosis-related group
EbM	Evidenzbasierte Medizin
EMBASE	Excerpta Medica Database
G-BA	Gemeinsamer Bundesausschuss
G-IQI	German Inpatient Quality Indicators
GKV	Gesetzliche Krankenversicherung
GQMG	Gesellschaft für Qualität und Management im Gesundheitswesen
ICD	International Classification of Diseases
IOM	Institute of Medicine
IQM	Initiative Qualitätsmedizin
IQTIG	Institut für Qualität und Transparenz im Gesundheitswesen
JCR	Journal Citation Report
KHEntgG	Krankenhausentgeltgesetz
LASSO	Least absolute shrinkage and selection operator
OR	Odds ratio
PICOS	Population, Intervention, Comparator, Outcome, Studientyp
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
ROC	Receiver Operating Curve
SGB	Sozialgesetzbuch
SIGN	Scottish Intercollegiate Network
TEP	Totalendoprothetik
TUD	Technische Universität Dresden
UKD	Universitätsklinikum Carl Gustav Carus Dresden
UN	United Nations

1 Einführung in die Thematik - Begriff und Relevanz der Patient:innensicherheit

Patient:innensicherheit ist ein nicht verhandelbares Gut medizinischen Handelns und wird, mit der Abwesenheit unerwünschter Ereignisse (*adverse events*) definiert. Vor dem Hintergrund vermeidbarer unerwünschter Ereignisse rückt die Patient:innensicherheit als Indikator für die ambulante und insbesondere stationäre Versorgungsqualität zunehmend in den gesundheitspolitischen und versorgungswissenschaftlichen Fokus (Geraedts et al., 2017).

Zu solchen Ereignissen zählen beispielsweise im stationären Versorgungsprozess erworbene (sog. nosokomiale) Infektionen, durch Mobilisierung vermeidbare und während der stationären Versorgung auftretende Druckgeschwüre (Dekubitus) oder die Mortalität bei Versorgungsprozessen mit niedrigem Sterberisiko, wie zum Beispiel die maternale perinatale Mortalität (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2020a, 2020b).

Jeder medizinische Fall wird unter unterschiedlichen Ausgangsbedingungen versorgt. Diese umfassen, neben fallindividuellen Faktoren wie Alter, Geschlecht und Grunderkrankungen, sowohl den Zugang zur stationären Versorgung als auch das versorgende Krankenhaus (Versorger) selbst. In der Bundesrepublik Deutschland wird das über die Gesetzliche Krankenversicherung (GKV) abrechenbare Leistungsgeschehen der stationären Versorgung im Rahmen der Selbstverwaltung durch den Gemeinsamen Bundesausschuss (G-BA) gesteuert (Kapitel 1.1) und durch die Landeskrankenhauspläne der einzelnen Bundesländer sichergestellt (Bäcker et al., 2020; Zimmermann, 2011). Der Zugang zur stationären Versorgung erfolgt entweder durch die Einweisung eines ambulanten Versorgers, wie Hausarzt:ärztin oder Facharzt:ärztin, als Notfall beispielsweise durch den Rettungsdienst oder zwischen einzelnen stationären Versorgern als Zu- oder Wegverlegung (Bäcker et al., 2020). Nach Diagnostik und Therapie erfolgen Entlassung, fallpauschalenbezogene Abrechnung (über diagnosis-related group - DRG) und für ein Teil der Behandlungen die Berichtlegung in Form der verpflichtenden (externen) Qualitätssicherung (Kapitel 1.2).

Abbildung 1 zeigt, dass zu **fall**individuellen (Risiko-)Faktoren (u.a. Alter, Geschlecht, Komorbiditäten) der **Versorgung**srahmen (u.a. Aufnahmeanlass, Aufnahmezeitpunkt) (Chen et al., 2019; Hernandez-Boussard et al., 2017; Honeyford et al., 2018; McCallum

et al., 2016; Mueller et al., 2019; O'Leary et al., 2019; Pauls et al., 2017; Sharp et al., 2017) und der individuelle **Versorger** (u.a. Bettengröße, Trägerschaft, Fallmenge) als Risikofaktoren sowohl für das klinische als auch Patient:innensicherheitsrelevante Ergebnis zu berücksichtigen sind (Karalis et al., 2016; Kolfschoten et al., 2014; Lake et al., 2016; Link et al., 2017; Liu et al., 2015; Shah et al., 2015; Shahian & Normand, 2003; The UK Neonatal Staffing Study Group, 2002; Trenner et al., 2020; Wirth et al., 2022; Yoo et al., 2019; Yoshii & Fushimi, 2006).

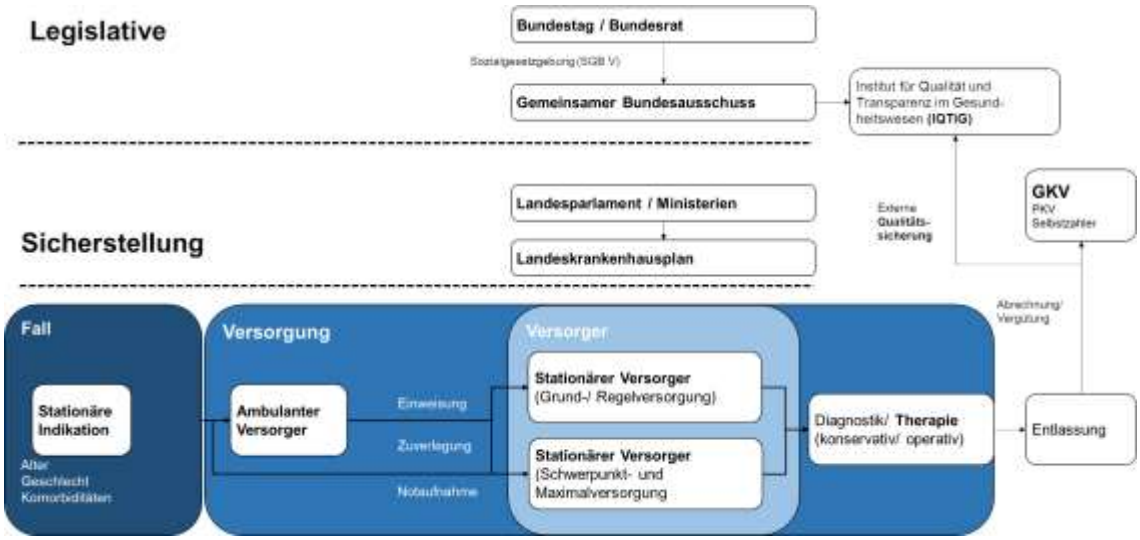

Abbildung 1 - Stationäre Versorgung nach Bäcker, Hensen & Zimmermann (Bäcker et al., 2020; Hensen, 2019; Zimmermann, 2011) (eigene Darstellung)

Im Jahr 2000 veröffentlichte das *Committee on Quality of Health Care in America* des *Institute of Medicine* (IOM) mit „To err is human" einen umfassenden Bericht zur Patient:innensicherheit in der Gesundheitsversorgung (Institute of Medicine Committee on Quality of Health Care in America, 2000). Das IOM definiert Patient:innensicherheit als „Freiheit unbeabsichtigter Verletzungen" (*freedom of accidental injury)* und formulierte mit dem Nachfolgewerk „Crossing the Quality Chasm: A New Health System for the 21st Century" gesundheits- und wissenschaftspolitische Vorschläge, um die Gesundheitsversorgung stärker an Qualität und insbesondere an Patient:innensicherheit auszurichten. Hierzu gehörten eine stärkere politische Priorisierung einer (patienten-)sicheren Gesundheitsversorgung, eine legislativ verbindliche Identifikation und Monitoring von Risikobereichen/ -indikationen, Vergütungsoptionen bei Interventionen zur Verbesserung der Patient:innensicherheit, die Anwendung evidenzbasierter Therapiekonzepte, höhere Transparenz in Behandlung und Reporting sowie eine

allgemeine patientenzentrierte und evidenzbasierte Gesundheitsversorgung (Institute of Medicine Committee on Quality of Health Care in America, 2000, 2001).

Die Evidenzbasierte Medizin (EbM) beabsichtigt, Entscheidungen zu Gesundheitsversorgung und Therapie anhand der nachgewiesenen Wirksamkeit bzw. Studienlage und patientenzentriert zu treffen. Die Verknüpfung von klinischer Expertise und wissenschaftlicher Kompetenz, insbesondere im Hinblick auf die Qualität und Aussagekraft klinischer Studien („critical appraisal“) soll so zu einer empirisch belegbaren individualisierten und folglich qualitativ hochwertigen Gesundheitsversorgung führen (Guyatt et al., 1992; Sackett, 1969; Sackett et al., 1996). Der Fokus auf evidenzbasierte Therapiekonzepte unterstreicht das Ziel einer verbesserten Versorgungsqualität durch die gestärkte Transparenz von Strukturen und Prozessen und einer erleichterten Adaption von „best-practice“-Strategien. Diesem Konzept sich anschließend sollen mit einer auf Transparenz und Evidenz fußenden Sicherheitskultur in Strukturen und Prozessen sollen (unerwünschte) Schadensereignisse bei der Gesundheitsversorgung minimiert, bestenfalls gänzlich verhindert und die Versorgungsqualität erhöht werden (Institute of Medicine Committee on Quality of Health Care in America, 2000).

Generell beschreibt „Qualität“ die Eigenschaften eines Produktes oder eine Dienstleistung. Durch die Verknüpfung mit konkreten Anforderungen und/ oder einem Endpunkt lässt sich somit, wenn auch uneinheitlich definiert, die Güte einer medizinischen Versorgungsleistung bestimmen (Eberlein-Gonska, 2011; Geraedts et al., 2017; Petzold et al., 2018).

Der Fokus auf Transparenz und Evidenz medizinischer Versorgung geht auf das Struktur-, Prozess- und Ergebnisqualitätsmodell von Avedis Donabedian zurück. Diesem liegt die Annahme zugrunde, dass Strukturen und Prozesse das klinische Ergebnis (Outcome) beeinflussen und aktiv zu gestalten sind (Donabedian, 1988; Donabedian, 2005). Aus diesen Erläuterungen ist Patient:innensicherheit zwei Bereichen zuordenbar:

1. Patient:innensicherheit ist durch die Messung unbeabsichtigter Schadensereignisse ein quantifizierbares Qualitätsattribut der Gesundheitsversorgung eines Versorgers (bspw. Krankenhaus) und eines Gesundheitssystems im Gesamten.
2. Patient:innensicherheit als Prinzip der Schadensvermeidung ist ein übergeordnetes Ziel eines jeden Gesundheitssystems und formuliert eine eigene (wissenschaftliche) Disziplin, mit dem Ziel, ein Gesundheitssystem durch Patient:innensicherheitsforschung vertrauenswürdiger zu gestalten und zu verbessern (Emanuel et al., 2009).

1.1 Patient:innensicherheit und Qualität im deutschen Gesundheitswesen

Patient:innensicherheit und Qualität sind in der deutschen Gesundheitsversorgung ein Gut des öffentlichen Interesses. Qualitätssicherung ist im Rahmen von §135a Sozialgesetzbuch V (SGB) als ein Bestandteil der Sozialgesetzgebung verankert (Sozialgesetzbuch V, 2022a). Sowohl die Legislative als auch relevante Organe des deutschen Gesundheitswesens, wie beispielsweise die Bundesärztekammer (BÄK), das Aktionsbündnis Patient:innensicherheit (APS), die Gesellschaft für Qualität und Management im Gesundheitswesen (GQMG) oder das Ärztliche Zentrum für Qualität in der Medizin (ÄZQ) und nicht zuletzt der Gemeinsame Bundesausschuss (G-BA) nehmen Patient:innensicherheit als Kernziel medizinischen Handelns in den Fokus (Geraedts et al., 2017).

Nach § 92 SGB V verabschiedet der G-BA Richtlinien unter anderem zur Qualitätssicherung und -management, um die legislativen Vorgaben des SGB V rechtsverbindlich umzusetzen (Zimmermann, 2011). Die Aufgaben des G-BA zur Qualitätssicherung in der stationären Akutversorgung umfassen nach §136b SGB V Beschlüsse zu

- verbindlichen Fortbildungsnachweisen bei Fachärzt:innen sowie psychologischen Psychotherapeut:innen,
- Mindestmengen für planbare Leistungen, bei denen die Qualität des Behandlungsergebnisses nachweislich von der erbrachten Leistungsmenge abhängt,
- Vorgaben zur Veröffentlichung eines strukturierten Qualitätsberichts sowie
- die Benennung von mindestens vier Leistungsbereichen mit einem Anreizsystem zur Erfüllung besonderer Qualitätsanforderungen (Sozialgesetzbuch V, 2022b).

1.2 Patient:innensicherheit im Rahmen der (externen) Qualitätssicherung

Mit der Verabschiedung des GKV-Gesundheitsreformgesetzes im Jahr 2000 wurden verpflichtende Maßnahmen zur (externen) Qualitätssicherung und die Einführung eines einrichtungsinternen Qualitätsmanagements gesetzlich vorgeschrieben (Hensen, 2019).

Die Hauptverantwortung für die bundesweite Darstellung und methodische Weiterentwicklung der Versorgungsqualität und der externen Qualitätssicherung als Bestandteil einer obligaten Berichtlegung und Quantifizierung selbiger liegt nach §137a SGB V bei dem Institut für Qualität und Transparenz im Gesundheitswesen (IQTIG) (Sozialgesetzbuch V, 2022c).

Das IQTIG ist das hauptverantwortliche Institut für die legislativ vorgeschriebene Qualitätssicherung und wurde durch den G-BA nach §137b SGBV mit der Entwicklung von Maßnahmen der Qualitätssicherung und Verbesserung der Transparenz ambulanter und stationärer Versorgung beauftragt (Sozialgesetzbuch V, 2022d). Die Patient:innensicherheit gehört neben Wirksamkeit, Angemessenheit, Rechtzeitigkeit/ Verfügbarkeit, Koordination/ Kontinuität und Ausrichtung der Versorgungsgestaltung an den Patient:innen zum Rahmenkonzept Qualität des IQTIG. Das IQTIG orientiert sich in der Definition von Patient:innensicherheit an der bestehenden Definition des IOM als „Abwesenheit unerwünschter, schädlicher Ereignisse im Rahmen der Versorgung“ (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2022). Ein Schlüsselelement der Arbeit des IQTIG ist die „externe Qualitätssicherung“ (eQS). Die stationären Versorger sind verpflichtet, die medizinische Versorgungsqualität anhand von Struktur-, Prozess- und teilweise risikoadjustierten Ergebnisqualitätsindikatoren durch derzeit 15 Qualitätssicherungsverfahren beispielsweise in der Perinatalmedizin, bei Dekubitus oder nosokomialen Infektionen fallindividuell zu berichten. Das IQTIG wertet die von jedem stationären Akutversorger verbindlich zu sendenden fallindividuellen Qualitätssicherungsbögen jahresweise aus und kann bei Verdacht auf qualitative Mängel die Leistungserbringer zu Stellungnahmen auffordern und sanktionieren (u.a. Vergütungsabschläge) (Gemeinsamer Bundesausschuss, 2022; Geraedts & de Cruppé, 2022).

Wie in Kapitel 1 beschrieben, beschreibt Qualität mit einem Abgleich zwischen (Soll-) Anforderungen und (Ist-) Erfüllungsgrad die Güte einer Leistung. Der Qualitätsindikator operationalisiert diesen Abgleich zwischen Anforderung und Erfüllungsgrad (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2022) und hat in der Folge die Aufgabe, die Qualität anhand vordefinierter Referenzwerte messbar abzubilden (Geraedts et al., 2017). Die Anforderung an medizinische Qualitätsindikatoren ist dabei die statistische Berücksichtigung fallindividueller und durch die Versorger nicht beeinflussbarer Risiken (Risikoadjustierung). Neben fallindividuellen Risikofaktoren wie Alter, Geschlecht und Komorbiditäten fungieren beispielsweise die Umstände der Versorgung (u.a. Aufnahmeanlass, Eingriffszeitpunkt) oder die Komplexität der Therapien als Indikator für die Akuität eines Falls (Braithwaite, 2018). Der Risikoadjustierung kommt dabei aufgrund der Fallkomplexität medizinischer Versorgung eine besondere Rolle zu (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2022).

Neben legislativ verbindlichen externen Qualitätssicherungsverfahren analysieren in Deutschland freiwillige Initiativen verschiedene Qualitätsindikatoren stationärer Versorgung. Dabei stützen sich Verfahren wie beispielsweise die Initiative Qualitätsmedizin (IQM) (Mansky et al., 2017), die Qualitätsindikatoren kirchlicher Krankenhäuser (Stausberg et al., 2011) oder die Qualitätssicherung mit Routinedaten (QSR) (Günster et al., 2013) gänzlich auf bereits bestehende, sogenannte Sekundärdaten (Schach, 1981) beziehungsweise mittlerweile versorgungsnahen Daten wie etwa Abrechnungs- oder Versicherungsdaten der Gesetzlichen Krankenversicherung (Klinkhammer-Schalke et al., 2020).

1.3 Mindestmengen als Instrument der Patient:innensicherheit

Wie unter Kapitel 1.2 aufgeführt, gehört zur Qualitätssicherung im deutschen Gesundheitswesen die Identifikation und Definition von Leistungsbereichen, bei denen erst ab einer bestimmten (Mindest-)Menge behandelter Fälle die Versorgung zulässig ist (§136b SGB V) (Sozialgesetzbuch V, 2022b). In Deutschland gelten für Transplantationen (Leber, Niere, Stammzellen), komplexe chirurgische Eingriffe (Speiseröhre, Bauchspeicheldrüse, Hüft- und Knie-Totalendprothesen, Brustkrebs) und die Frühgeborenenversorgung (<1250g Geburtsgewicht) quantifizierte Mindestmengen als obligate Operationalisierung der Erfahrung eines Versorgers (Gemeinsamer Bundesausschuss, 2020). Erstmalig in der Viszeral- und onkologischen Chirurgie beschrieben (Begg et al., 1998; Luft et al., 1979), folgen Mindestmengen dem Prinzip von protektiven Erfahrungseffekten *(„practice makes perfect")* und wurden in der Folge für weitere Hochrisiko-Versorgungsbereiche wie Frühgeburten (Mayfield et al., 1990) und Transplantationen (Banta et al., 1992) erstmalig analysiert. Sowohl bei Viszeral-, Transplantations- und onkologischer Chirurgie als auch bei Frühgeburten zeigte eine höhere Fallmenge statistische Assoziationen zu einer verringerten Mortalität (Banta et al., 1992; Begg et al., 1998; Luft et al., 1979; Mayfield et al., 1990). Da Mindestmengen als versorgungssteuerndes Element vor- bzw. nachteilig für die Versorger in den Gesundheitsmarkt und ihre Wettbewerbsfähigkeit eingreifen können, waren Mindestmengen Gegenstand mehrerer Klagen hinsichtlich ihrer wissenschaftlichen Belastbarkeit mit teilweisen Aussetzungen u.a. im Bereich der Knie-Totalendoprothetik (TEP) (Geraedts, 2012).

1.4 Risikoadjustierung: ein Schlüsselelement in Qualitätssicherung und (Fall-)Menge-Outcome-Analysen

Wie in den Kapiteln 1.2 und 1.3 beschrieben, gehören die verpflichtende eQS sowie Mindestmengen zu regulativen Kernelementen der stationären Versorgung in Deutschland. Stationäre Versorger sind gesetzlich verpflichtet, durch Qualitätssicherungsbögen bei der Versorgung diverser Indikationen wie etwa (Früh-)Geburten oder verschiedenen chirurgischen Eingriffen eine hohe Versorgungsqualität nachweislich zu berichten (Gemeinsamer Bundesausschuss, 2021).

Während beispielsweise Appendektomien als unkomplizierte Eingriffe mit geringen Mortalitäts- und Komplikationsraten von einer hohen Zahl an Versorgern behandelt werden (Stöß et al., 2021), werden Frühgeborene mit einem Geburtsgewicht <1.250g in meist neonatalintensivmedizinisch spezialisierten und an eine Mindestfallmenge gebundenen Kliniken behandelt (Gemeinsamer Bundesausschuss, 2020). Mindestmengen gehen wie in Kapitel 1.3 dargestellt von einer auf einem Erfahrungsprinzip basierenden protektiven Fallmengen-Outcome-Beziehung aus (Geraedts, 2012).

Während der direkte Nutzen legislativer Mindestmengen umstritten ist (Geraedts et al., 2008), weisen sowohl jüngere (Levaillant et al., 2021) als auch ältere Studien (Gandjour et al., 2003; Halm et al., 2002; Shahian & Normand, 2003) auf eine mehrheitlich protektive Assoziation zwischen Fallmenge und beispielsweise Mortalität oder Komplikationen insbesondere für Hochrisiko-Versorgungsbereiche wie Frühgeburten oder Transplantationen hin (Lee et al., 2019; Walther et al., 2020; Yoo et al., 2019). Dennoch behindern heterogen definierte Fallmengengruppen, fehlende Daten zu Versorgungsprozessen, Studien mit niedrigem Evidenzgrad (Querschnittstudien) sowie die Methodik der Risikoadjustierung eine durchgehend rechtssichere und valide Definition von Mindestmengen (Christian et al., 2005; Geraedts, 2012; Geraedts et al., 2008; Halm et al., 2002; Levaillant et al., 2021; Luft et al., 1987).

Die Fallmenge fungiert zudem als Surrogatvariable, die unter anderem von (struktureller und personeller) Leistungsfähigkeit des Versorgers, Klinikgröße, Versorgungsauftrag, Reisebereitschaft/ -fähigkeit, Komorbiditäten, Akuität, ländlich/städtischer Lokalisierung oder Trägerschaft beeinflusst wird (Bouche et al., 2008; Chernew et al., 1998; Victoor et al., 2012; Yamamoto & Fushimi, 2009; Yoshii & Fushimi, 2006).

Sowohl für die Analyse bei Komplikationen in der eQS als auch für Untersuchungen der Assoziation zwischen (Mindest-)Fallmengen und Outcome gilt es, medizinische Risiken statistisch zu berücksichtigen, um Selektionseffekten zwischen „großen“/

(überregionalen) und „kleinen“ (regionalen/lokalen) stationären Versorgern/ Krankenhäusern vorzubeugen und somit Fehlinterpretationen zu vermeiden (Luft et al., 1987). In Abhängigkeit des Falls kann das Risiko adverser Ereignisse durch bereits bei Aufnahme vorliegende Komorbiditäten oder durch erhöhte Akuität von beispielsweise Notfällen, Wochenendaufnahmen/ -eingriffen und Zuverlegungen stark ansteigen (Anderson et al., 1992; Chen et al., 2019; Chow et al., 2017; Hernandez-Boussard et al., 2017; Honeyford et al., 2018; Huijts et al., 2018; McCallum et al., 2016; Mueller et al., 2019; Mullen et al., 2017; Pauls et al., 2017; Restrepo et al., 2018; Sharp et al., 2017; Sharp et al., 2018).
Um diese fallindividuellen Risiken zu berücksichtigen, werden *risikoadjustierte* (Qualitäts-)Indikatoren angewendet (Geraedts & de Cruppé, 2022; Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2022). Diese statistische Berücksichtigung erfolgt entweder über die Bildung von Gruppen bei heterogenen Populationen (Stratifizierung), die Berechnung einer (multivariaten) Regressionsanalyse oder die Bildung apriori definierter (Komorbiditäts-)Scores, wie z.B. den Elixhauser- (Elixhauser et al., 1998) oder Charleson-Index (Charlson et al., 1987; Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2022).
Die adjustierbaren Risiken können nach:

- Demografie (u.a. Alter, Geschlecht),
- Zugang zur Versorgung (u.a. Versicherungsstatus, Entfernung zu Versorger),
- Komorbiditäten (individuell, kombiniert bspw. durch Elixhauser, Case-Mix Index etc.),
- Krankheitsschwere,
- Soziale Risiken (u.a. Armut, fester Wohnsitz),
- Psychologische Risiken (u.a. Resilienz, Risikoaversion) und
- Verhalten (u.a. Therapieadhärenz) (Braithwaite, 2018) gruppiert werden.

1.5 Versorgungs- und Versorgersetting in der Risikoadjustierung

Das IQTIG gibt an, für etwa ein Viertel der Qualitätsindikatoren insbesondere im Hinblick auf Alter, Geschlecht und Komorbiditäten zu adjustieren(Vorbeck et al., 2021). Sowohl quantitativ als auch qualitativ steht dieses Vorgehen in der fachlichen Kritik. Insbesondere die Rolle einer risikoadaptierten Versorgung wird nach Geraedts, Kraska und Vorbeck nur unzureichend durch das IQTIG abgebildet (Geraedts & de Cruppé, 2022; Geraedts et al., 2017; Kraska et al., 2017; Vorbeck et al., 2021). Der Terminus „risikoadaptiert“ bedeutet dabei, dass größere Versorger in der Regel komplexere Akut- und Elektivfälle in überregionaler Verantwortung versorgen und die Chancen von

Komplikationen aufgrund der komplexeren/ kritischeren medizinischen Ausgangsbedingungen steigen.

Wird diese Problematik statistisch nicht berücksichtigt, können Verzerrungen zur Fehlinterpretation, sowohl hinsichtlich der Beurteilung der Versorgungsqualität (Kraska et al., 2017; Vorbeck et al., 2021) als auch bezüglich der Rolle von Fallmenge und Ergebnis (Geraedts, 2012) führen. Die versorgerseitigen Einflussfaktoren (u.a. Fallmenge, Trägerschaft etc.) sowie der Akutstatus weisen dabei darauf hin, dass möglichst kombinierte Risikosets - bestehend aus Versorgung (u.a. Aufnahmeanlass), Versorger (u.a. Fallmenge) und Fall - in einer Analyse berücksichtigt werden sollten. Neben den bereits hinlänglich untersuchten und bekannten fallindividuellen Risikofaktoren wie bspw. Alter, Geschlecht oder Komorbiditäten (Hentschker et al., 2018; Morche et al., 2016; Nimptsch & Mansky, 2017; Nimptsch et al., 2017; Trenner et al., 2020; Wirth et al., 2022) bleibt ungeklärt, in welcher Form **Versorgungssetting** und **Versorgersetting** unter Berücksichtigung fallindividueller Risiken als protektive- oder Risikofaktoren mit Patient:innensicherheitsoutcomes assoziiert sind. Für eine adäquate Risikoanalyse der Patient:innensicherheit lassen sich demnach drei Gruppen (Abbildung 2) ableiten:

- Fall: Alter, Geschlecht, Komorbiditäten
- Versorgungssetting: versorgungsbegleitende Kontextfaktoren wie Aufnahmeanlass (u.a. Notfall, Zuverlegung, chirurgische Eingriffe) oder Aufnahmezeitpunkt (Wochenende vs. Werktag)
- Versorgersetting: versorgerseitige Charakteristika wie Fallmenge, Trägerschaft oder der Urbanisierungsgrad/ Lokalisierung.

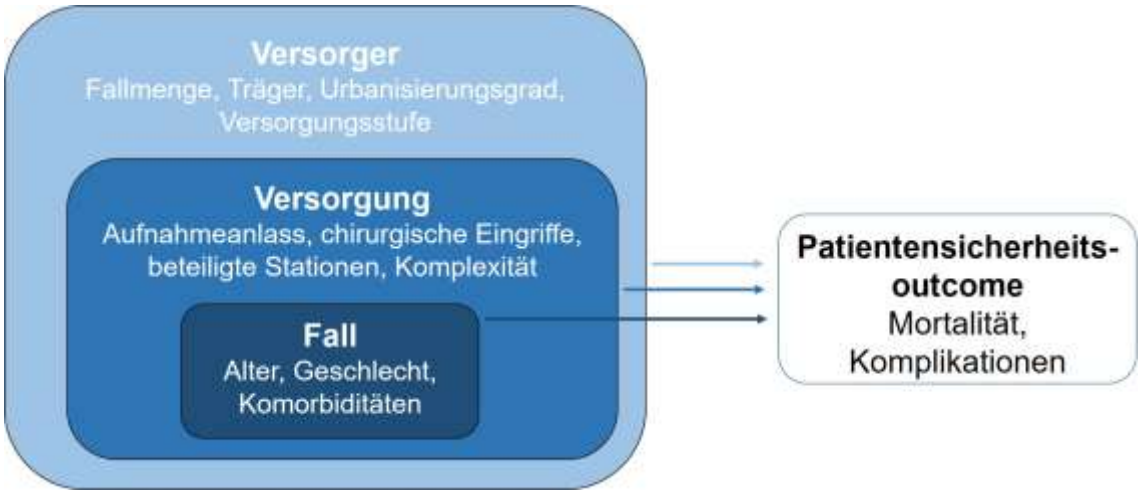

Abbildung 2 - Versorger-, Versorgung- und Falleinfluss auf das Outcome (eigene Darstellung)

2 Forschungsziele und Einzelfragestellungen

Das Ziel dieser kumulativen Dissertation ist es, den **Einfluss von Versorger- und Versorgungssetting auf die Patient:innensicherheit** zu analysieren. Daraus resultieren zunächst zwei Forschungsziele:

I. Forschungsziel 1: Für den Versorgungskontext insbesondere die Rolle des Aufnahmeanlasses als Hinweis für die Akuität und Komplexität des Falls unter Berücksichtigung von Alter, Geschlecht und Komorbiditäten näher untersucht.
II. Forschungsziel 2: Aufgrund der Vielzahl verschiedener Variablen, die aufseiten der stationären Versorger einen Einfluss auf die Patientsensicherheit haben können (bspw. Bettenzahl, Trägerschaft, Versorgungsschwerpunkt), sollte insbesondere die Fallmenge vor dem Hintergrund ihrer versorgungs- und wissenschaftspolitischen Relevanz analysiert.

Für die Analyse des Einflusses des Versorger- (Forschungsziel 1) und des Versorgungssettings (Forschungsziel 2) auf die Patient:innensicherheit wurden unter Nutzung unterschiedlicher Daten und Methoden drei Einzelfragen aus den Versorgungsbereichen *Geburtshilfe, kolorektale Resektionen und Dekubitus* abgeleitet:

1 Sind neonatale oder maternale Mortalität und Komplikationen bei Niedrigrisiko-Geburten mit der Fallmenge des versorgenden Krankenhauses assoziiert?

Die Münchner Perinatalstudie und die daraus folgende Perinatalerhebung bildeten die Grundlage für die heutige eQS. Ausgangspunkt für diese Untersuchung war eine hohe 7-Tage-Mortalität bei Neugeborenen (Perinatalmortalität) im Großraum München zwischen 1970 und 1972 (Conrad, 1977). Die Ziele dieser Erhebung waren die Konzeption einer detaillierten Datenquelle durch die anamnestische Erfassung maternaler und fetaler Risiken für wissenschaftliche Auswertungen und die Förderung ärztlicher Sensibilität auf klinisch zu berücksichtigende Risikofaktoren bei Mutter und Kind. Die Ergebnisse der Erhebung wiesen auf die klinische Relevanz der Mutterschaftsvorsorge als Schlüsselelement angemessener Versorgung, insbesondere bei der vulnerablen Gruppe der Früh- und Risikogeburten hin. Zu Frühgeburten zählen alle Geburten vor Vollendung der 37. Schwangerschaftswoche mit einer Prävalenz von bspw. ca. 10% in den Vereinigten Staaten und ca. 8% in Deutschland (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2017; World Health Organization, 2012). Eine Frühgeburt beinhaltet das Risiko körperlicher Unreife bei Geburt, verbunden mit der Notwendigkeit (neonatal)intensivmedizinischer Versorgung.

Postnatal und langfristig können mit einer Frühgeburt kausal assoziierte gesundheitliche Probleme wie Bewegungsstörungen, Lungenerkrankungen, kognitive Einschränkungen oder der Verlust der Hör- und Sehfähigkeit die Lebensqualität und -erwartung der Säuglinge deutlich reduzieren (World Health Organization, 2012).

Die Versorgung von Früh- und Risikogeburten wird national durch Mindestmengen und international durch Strukturvorgaben im Rahmen perinataler Regionalisierungs- und Zentralisierungsprogramme gesteuert (Kunz et al., 2020). Sowohl Mindestmengen als auch perinatale Regionalisierung führen zu bzw. inkludieren definierte personelle und materielle Infrastrukturen (Kunz et al., 2020; Walther et al., 2020). Der vermutete Erfahrungseffekt und die inhärente Notwendigkeit leistungsfähiger Strukturen zur Bewältigung hoher Fallmengen soll zu einer kontinuierlich hochwertigen Versorgung dieser vulnerablen Gruppe führen. Bei Frühgeburten wird in der Literatur von überwiegend positiven Fallmengen- und Regionalisierungseffekten auf neonatale und maternale Outcomes, wie unter anderem Mortalität und Komplikationen sowohl in älteren (Lasswell et al., 2010) als auch in aktuellen Publikationen ausgegangen (Clapp et al., 2020; Handley et al., 2021; Jensen & Lorch, 2015).

Zusammengefasst ist der Einfluss der Fallmenge auf den Outcome von Früh- und Risikogeburten in der Literatur sowohl auf Primärstudienebene als auch in gepoolter Evidenz bereits breit diskutiert und analysiert. Auf Ebene der Niedrigrisiko-Geburt hingegen gibt es nach Durchführung und Publikation einer Vorarbeit (Walther et al., 2020) bislang ausschließlich **Primärstudien, ohne dass diese systematisch** und nach einer konkreten Fragestellung **zusammengefasst** und hinsichtlich ihrer **Studienqualität bewertet** wurden. Das Ziel war somit, die Untersuchung von **Zusammenhängen zwischen Fallmenge und neonatalen sowie maternalen Outcomes bei Niedrigrisiko-Geburten erstmalig** durch ein **systematisches Review**.

2 *Welche Zusammenhänge bestehen zwischen Versorger- und Versorgungsvariablen bei der Patient:innensicherheit kolorektaler Resektionen?*

Resektionen am Kolon (Dickdarm) und Rektum (Enddarm) sind elektive Eingriffe, die unter anderem zur Entfernung benignen und malignen Gewebes dienen (Reich, 2010). Insbesondere in der Chirurgie wird die Rolle von Fallmengen auf das Patientenoutcome seit mehreren Jahrzehnten für verschiedene Anwendungen diskutiert. Bei kolorektalen Resektionen wurden insbesondere Mortalität und solitäre Outcomes bei Fallmengen-untersuchungen analysiert (Levaillant et al., 2021; Luft et al., 1979; Luft et al., 1987; Morche et al., 2016). Systematische Reviews, teils mit Meta-Analysen legen einen

Überlebensvorteil bei hohen Fallmengen nahe (Chioreso et al., 2018; Huo et al., 2017). Zugleich sollte Patient:innensicherheit in der kolorektalen Chirurgie nicht ausschließlich durch Mortalität beschrieben werden. Umfassende Analysen sollten mehrere Outcomes wie Mortalität und nicht-letale Komplikationen in die Analyse einschließen, um ein umfassendes Bild von der Patient:innensicherheit kolorektaler Resektionen ableiten zu können (Almoudaris et al., 2013; Goodacre et al., 2015; O'Brien et al., 2014).

Die bestehende Literatur lässt darauf schließen, dass Risikofaktoren und/oder Outcomes solitär und in nur geringem Maße in kombinierter Form analysiert wurden. Für kolorektale Resektionen betrifft das fallindividuelle (insb. Alter, Geschlecht, Komorbiditäten), versorgungs- (insb. Aufnahmeanlass, Wochenendeingriff) und versorgerbezogene (insb. Fallmenge, Trägerschaft, Urbanisierungsgrad) Risikofaktoren (Anderson et al., 1992; Chioreso et al., 2018; Chow et al., 2017; Huo et al., 2017; McCallum et al., 2016; Mullen et al., 2017; O'Leary et al., 2019; Sharp et al., 2017; Sharp et al., 2018). Der Mehrwert bestand in der erstmaligen Analyse **mehrerer Risikofaktorensets** in Versorgungs- (u.a. Notfall, Zuverlegung), Versorger- (u.a. Fallmenge, Trägerschaft) und Fallkontext (Alter, Geschlecht, Komorbiditäten) auf **multiple Outcomes der Patient:innensicherheit** (u.a. Mortalität, postoperatives Lungenversagen).

3 Welche Rolle nimmt der Versorgungskontext als Risikofaktor bei der Inzidenz von Dekubitalulcera ein?

Die Ausbildung eines Dekubitus ist eine schwerwiegende Komplikation in der stationären Versorgung. Der konstante Druck auf bestimmte Körperteile/ -regionen aufgrund einer eingeschränkten Mobilität, z.B. im Rahmen von Beatmungen, Anästhesien oder einer langen Liegedauer behindert den Blutfluss der Gefäße und somit die konstante und gleichmäßige Oxygenierung des Körpergewebes und der Nervenzellen des betroffenen Patienten und führt unbehandelt zu Gewebenekrose und starken Schmerzen (Coleman et al., 2013). Aufgrund der Vermeidbarkeit durch vor allem regelmäßige Mobilisierung und Umlagerung des Patienten wird Dekubitus als risikoadjustierter Patient:innensicherheitsindikator in Qualitätssicherungsprogrammen mehrerer Länder, u.a. auch Deutschland geführt (Kottner et al., 2018). Der Aufnahmeanlass als Indikator für die Akuität eines Falls wird hierbei nicht berücksichtigt und wurde im Hinblick auf die Risikoanalyse von Dekubitus bisher noch nicht in andere Analysen einbezogen (Coleman et al., 2013; Kottner et al., 2018). Übliche Risikofaktoren des Versorgungskontexts sind die Verweildauer, intensivmedizinische Behandlung und Beatmung (Afzali Borojeny et al., 2020; Eberlein-Gonska et al., 2013; Shafipour et al., 2016). Zudem bedingen sich die

Komplexität dieses Krankheitsbildes und die verschiedenartigen Risikofaktoren gegenseitig (Coleman et al., 2013), sodass eine Adjustierung bei logistischen Regressionen Interaktionsterme benötigt (Hosmer & Lemeshow, 1992; Rothman, 2012). Die Komplexität von Dekubitalulcera in ihrer Prävention, Entstehung und die komplexe Behandlung (Kottner et al., 2018) dieser patient:innensicherheitsrelevanten Ereignisse führte zusätzlich zu der Frage, ob diese Komplikation auf Grundlage versorgungsnaher Daten prädiktierbar sind. Aus der Dokumentation eines Dekubitus muss hervorgehen, ob dieser bei Aufnahme vorlag (*Present on admission*) oder im Rahmen der stationären Behandlung erstmalig (*inzident*) auftrat (Houchens et al., 2008). Ein fehler- oder lückenhafter Bericht prävalenter Dekubitalulcera wirkt sich in der Folge direkt auf die öffentlichen Benchmarks des Versorgers aus (Glance et al., 2008).
Das seit 2008 vereinheitlichte Dekubitusscreening des Universitätsklinikums Carl Gustav Carus Dresden ermöglicht die Identifikation prävalenter Dekubitalulcera. Das ermöglicht in einem monozentrischen Setting die Generierung eines mehrjährigen Datensatzes inklusive einer Kombination klinischer Daten und Abrechnungsdaten. Wie in Kapitel 1.4 dargestellt, adjustiert das IQTIG für patientenseitige Risiken, wie Alter und Komorbiditäten, jedoch nicht für den Versorgungskontext als möglichen Indikator für die Akuität eines Falls (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, 2020b). Der Mehrwert begründet sich in der **erstmaligen Analyse des Einflusses des Versorgungskontexts** (u.a. Aufnahmeanlass) auf die stationäre Dekubitusinzidenz sowie einer Prädiktionsanalyse dieses patient:innensicherheitsrelevanten Ereignisses.

3 Methoden, Ergebnisse und Publikation

3.1 Methodische Überschneidungen

In der vorliegenden Dissertation kamen mit der Planung, Registrierung und Durchführung eines systematischen Reviews und zweier Querschnittstudien unterschiedliche Methoden und Datenquellen zum Einsatz. *Einzelfragestellung (1)* und *(2)* untersuchten sowohl mit der Fallmenge als auch Mortalität die gleichen Prädiktoren und Outcomes. Für *Einzelfragestellung* (2) und (3) bestehen die verbindenden Elemente unter anderem in der Variable Aufnahmeanlass, dem durchgeführten Querschnittdesign und der Nutzung von Daten nach §21 KHEntgG (Tabelle 1).

Tabelle 1 - Einzelfragestellungen, analysierte Variablen und Designs

Population	**Variablen**		**Outcome**	**Design**	**Datenquelle**
	Versorger	Versorgung			
Einzelfragestellung (1): Ist das Geburtsoutcome bei Niedrigrisiko-Geburten mit der Fallmenge des Krankenhauses assoziiert?					
Unselektierte Geburtskohorten, a priori-definierte Niedrigrisiko-Geburten (bspw. Termingeburt)	Fallmenge	-	Mortalität Kaiserschnitt Wiederaufnahme Komplikationen Entwicklungsverzögerungen	Systematisches Review	Primärstudien
Einzelfragestellung (2): Welche Assoziationen bestehen zwischen Versorger- und Versorgungsvariablen und Patient:innensicherheitsoutcomes bei kolorektalen Resektionen?					
Kolorektale Resektionen	Fallmenge Trägerschaft Urbanisierungsgrad Universitätsklinik	Aufnahmeanlass Wochenendchirurgie	Mortalität postoperatives Lungenversagen Nierenversagen postoperative Wundinfektionen	Querschnitt	Abrechnungsdaten (§21 KhEntgG) von 232 deutschen Krankenhäusern
Einzelfragestellung (3): Welche Rolle nimmt der Versorgungskontext als Risikofaktor bei der Inzidenz von Dekubitalulcera ein?					
Somatisch behandelte Fälle	-	Aufnahmeanlass Anzahl beteiligter Stationen Intensivmed. Behandlung	Dekubitusinzidenz im stationären Aufenthalt	Querschnitt	Abrechnungsdaten (§21 KhEntgG), Dekubitus-dokumentation (intern), Anästhesien (intern)

3.2 Systematisches Review

Der Einfluss der Fallmenge auf den Outcome von Reifgeborenen (Einzelfragestellung 1) wurde in *Publikation (1)* anhand eines systematischen Reviews untersucht. Das Ziel des systematischen Reviews ist es, neben der studienübergreifenden Beantwortung wissenschaftlicher Fragestellungen, den Forschungsstand eines Themas aufzubereiten, qualitativ zu bewerten und praktische Implikationen für die klinische und Versorgungspraxis und weitere Forschung zu formulieren.

Ein systematisches Review ist eine standardisierte, strukturierte und somit systematisch angefertigte Übersichtsarbeit wissenschaftlicher Literatur. Nach Formulierung der Forschungsfrage werden konkretisierte Einschlusskriterien im Hinblick auf Population, Intervention/Exposition, Vergleichsgröße, Outcome und Studientyp (PICOS-Schema) herausgearbeitet und medizinische Literaturdatenbanken (u.a. Medline, Embase) auf Grundlage einer an den Einschlusskriterien abgeleiteten Suchstrategie durchsucht (Gurevitch et al., 2018; Mulrow, 1994). Die eingeschlossenen Studien werden im Hinblick auf die Forschungsfrage charakterisiert und in ihrer Studienqualität bewertet. Die Notwendigkeit dieser strukturierten Vorgehensweise begründet sich in der stark zunehmenden Anzahl wissenschaftlicher Publikationen (Mulrow, 1994). Das vormals angewandte narrative - nicht systematische - Review, birgt trotz hoher Publikationszahlen viele Schwächen (Bastian et al., 2010): aufgrund der fehlenden Strukturierung der Fragestellung anhand klarer Kriterien, kann diese unschärfer formuliert sein. Narrative Reviews beinhalten zudem keine Bewertung der Studienqualität. Diese ist jedoch entscheidend für die inhaltliche und methodische Beurteilung eines Forschungsfelds und die Ableitung von Handlungsempfehlungen (Goldschmidt, 1986). Die stark steigende Anzahl an Primärstudien und insbesondere nicht systematischen Reviews offenbart die Notwendigkeit systematisch durchgeführter Literaturübersichten. Einerseits ermöglicht dies, sogenannten *„research waste“* bei Primärstudien zu identifizieren und andererseits verhindert es bei gründlicher Vorbereitung dessen Erzeugungdurch die redundante Beantwortung gleicher Fragestellungen (Bastian et al., 2010; Chalmers & Glasziou, 2009; Page et al., 2021; Shea et al., 2017). Die Ergebnissynthese als Kern eines systematischen Reviews kann bei ausreichender inhaltlicher wie statistischer Homogenität quantitativ gepoolt (Meta-Analyse) oder qualitativ erfolgen.

3.3 Querschnittstudie

Für die Analysen zu den explorativen Einzelfragestellungen in den *Publikationen (2)* und *(3)* wurden Querschnittdesigns angewendet. Querschnittstudien gehören zum Bereich der Beobachtungsstudien und identifizieren die Prävalenz oder Assoziationen zwischen abhängigen und unabhängigen Variablen zu einem Zeitpunkt. Es gibt kein Follow-Up und sind verglichen zu Längsschnittdesigns kostengünstiger, einfacher zu planen, weniger zeitaufwändig und eignen sich insbesondere zur Analyse explorativer Fragestellungen, beispielsweise bei noch nicht studierten Assoziationen zwischen unabhängigen Variablen und einem oder auch mehrerer Outcomes (Olsen & St George, 2004). Beide Fragestellungen eigneten sich durch die Analyse von vorher noch nicht angewendeten Variablen(-sets) mit einem oder mehreren Outcomes für eine explorative Querschnittanalyse. Querschnittstudien können mit bereits vorhandenen, retrospektiv erhobenen, also nicht prospektiv für den Studienzweck erhobenen Daten durchgeführt werden. Stationäre Abrechnungsdaten nach §21 KHEntgG wurden für die Analysen der Einzelfragestellungen in den *Publikationen (2)* und *(3)* herangezogen.

Verglichen zu Primärdaten besitzen Abrechnungsdaten als Teil von versorgungsnahen Daten durch die schnelle Verfügbarkeit, Vollständigkeit, homogen gestaltete und mehrjährig analysierbare Datensätze den Vorteil, vergleichsweise große Populationen kostengünstig und schnell analysieren zu können. Der Nachteil von Abrechnungsdaten liegt in der mangelnden Zweckbestimmung für wissenschaftliche Analysen. Umfang, Erfassungstiefe, Beschränkung auf professionelles und abrechnungsrelevantes Behandlungsgeschehen sowie die durch die Anonymisierung eingeschränkten Validierungsmöglichkeiten schränken die Aussagekraft und den Detailgrad ein (F. Hoffmann et al., 2008; W. Hoffmann et al., 2008; Swart et al., 2011). Zusätzlich ist insbesondere bei stationären Aufenthalten nicht kodiert, welche Diagnosen bereits bei Aufnahme vorlagen und welche erst im Verlauf der Behandlung auftraten (*present on admission*) (Heller, 2008; Maass et al., 2011). Eine Möglichkeit zur Abmilderung dieser Limitation ist die Verwendung validierter und klinisch konsentierter Definitionssets (*core outcome sets*) für die Ableitung von Populationen, Kovariaten und Outcomes (Clarke, 2007; Clarke & Williamson, 2016). Einheitlich verwendete Definitionen ermöglichen unter anderem in Katalogen des International Classification of Diseases (ICD) und dem Operationen- und Prozedurenschlüssel eine klinisch nachvollziehbare Definition von Krankheitsbildern (u.a. in German Inpatient Quality Indicators) und somit eine transparente und nachvollziehbare Analyse, wie beispielsweise den Elixhauser Komorbiditätenkatalog oder die Verwendung von in versorgungsnahen Daten validierten

Patient Safety Outcomes (Elixhauser et al., 1998; Maass et al., 2015; Mansky, 2008; Mansky et al., 2017). Die Verwendung von core outcome sets und somit einheitlich definierter Outcomes ermöglicht zudem die Vergleichbarkeit mehrerer Studien beispielsweise im Rahmen eines systematischen Reviews (Clarke, 2007; Clarke & Williamson, 2016). Zudem kann, wenn möglich, die Hinzunahme und ein Matching zwischen klinischen und Abrechnungsdaten zur Komplettierung fehlender Informationen erfolgen.

3.4 Einzelfragestellung (1): Ist das Geburtsoutcome bei Niedrigrisiko-Geburten mit der Fallmenge des Krankenhauses assoziiert?

Die Planung und Durchführung von Einzelfragestellung (1) erfolgte nach den Berichts- und Qualitätskriterien der „Preferred Reporting Items for Systematic Reviews and Meta-Analyses“ (PRISMA) (Moher et al., 2009) und der zweiten Version des „A MeaSurement Tool to Assess Systematic Reviews“ (AMSTAR 2) Instruments (Shea et al., 2017). Hierzu gehören unter anderem die apriori Veröffentlichung des Review-Protokolls nach dem PICOS-Schema (Population, Intervention/ Exposition, Comparator, Outcome, Studientyp), der Bericht der Suchstrategie, eine doppelt unabhängige Sichtung, der begründete Ein- und Ausschluss, die Extraktion eingeschlossener Studien und die Bewertung der Studienqualität. Zunächst wurde ein Reviewprotokoll angefertigt und bei dem „International Prospective Register of Systematic Reviews“ (PROSPERO) registriert (Walther et al., 2018).

Einschlusskriterien

Es wurden Studien eingeschlossen, die bei Niedrigrisiko-Geburten *(Population)* die Einflüsse von Fallmenge *(Exposition/ Vergleichsgröße)* auf die Mortalität (primäres *Outcome*) von Mutter und Kind im Rahmen einer analytisch angelegten Primärstudie *(Studientyp)* untersuchten (S. 31, Table 1). Neben Mortalität wurden zusätzlich sekundäre, auf Komplikationen hindeutende Outcomes (u.a. Notkaiserschnitt) ausgewertet. Vor dem Hintergrund einer Vergleichbarkeit unterschiedlich ausgestatteter und leistungsfähiger Gesundheitssysteme wurde als Einschlusskriterium festgelegt, dass die Studie in einem Land mit Neonatalmortalität <5/1000 nach dem United Nations Child Mortality Report (UN) durchgeführt wurde (UN Interagency Group for Child Mortality Estimation, 2017).

Suchstrategie und Studienselektion

Aus den Einschlusskriterien wurde die Suchstrategie für die zwei Datenbanken Medline und EMBASE via OVID Interface abgeleitet. Sowohl Titel-Abstract- als auch Volltext-Screening erfolgten doppelt unabhängig. Zusätzlich wurde eine händische Suche in den Referenzlisten (Rückwärtsrecherche) und Zitationen (Vorwärtsrecherche) der eingeschlossenen Artikel durchgeführt und klinische Experten für die Identifikation etwaig fehlender Literatur eingebunden.

Qualitätsbewertung

Die doppelt unabhängig durchgeführte Qualitätsbewertung erfolgte mit der Checkliste für Kohortenstudien des Scottish Intercollegiate Network (SIGN) auf der Grundlage a priori definierter Kriterien (S.46, Additional file 2) (Scottish Intercollegiate Guidelines Network).

Datenextraktion und Synthese

Die Datenextraktion umfasste die Studiencharakeristika (u.a. Population, Land) und Ergebnisse zu den analysierten Outcomes (u.a. Fallmengen, Ergebnis) und wurde durch eine Person durchgeführt und durch eine weitere auf Korrektheit überprüft. Für die Datensynthese bestand das Ziel darin, geeignete Studien für eine Meta-Analyse zusammenzuführen, sofern eine inhaltliche (Population, Fallmengen/ -schwellen, Outcomes, Risikoadjustierung) und statistische Homogenität gegeben war. Andernfalls erfolgt eine qualitative Synthese und Zusammenfassung der Studienergebnisse.

Ergebnisse

Nach Anwendung der Suchstrategie am (18.04.2018 und 26.02.2020) und Bereinigung von Dubletten wurden 7.955 Ergebnisse im Titel-Abstract-Screening in doppelt unabhängigem Verfahren durchgesehen. Nach dem Volltextscreening von 43 Studien wurden 13 Studien eingeschlossen (S. 30, Figure 1). Alle eingeschlossenen Studien wurden als retrospektive, beobachtende Designs mit Geburtsregistern als primäre Datenquelle angelegt. Die Studienqualität war bei 12 von 13 Studien akzeptabel. Bei einer Studie mit inakzeptabler Studienqualität war aufgrund fehlender Populations-charakteristika die Vergleichbarkeit zwischen den untersuchten Gruppen nicht gegeben (Moster et al., 2001). Eine Meta-Analyse war aufgrund unterschiedlich definierter Populationen, Fallschwellen/ Vergleichsgrößen und Outcomes nicht angemessen. Qualitativ zeigte eine Mehrheit der Studien bei der Perinatal- oder 7-Tages-Mortalität

einen Volume-Outcome-Effekt. Die verbleibenden Outcomes Totgeburt, Neonatalmortalität, maternale und neonatale Komplikationen sowie Kaiserschnitte zeigten insignifikante oder widersprüchliche Effekte über die Studien hinweg.

Publikation

Das systematische Review wurde unter dem Titel „Are birth outcomes in low risk birth cohorts related to hospital birth volumes? A systematic review“ am 08. Februar 2021 bei *BMC Pregnancy & Childbirth* eingereicht und am 27. Juli 2021 publiziert (Walther et al., 2021).

3.5 Einzelfragestellung (2): Welche Assoziationen bestehen zwischen Versorger- und Versorgungsvariablen und Patient:innensicherheitsoutcomes bei kolorektalen Resektionen?

Diese explorative Querschnittanalyse war Teil der durch den Innovationsfonds-geförderten IMPRESS-Studie. IMPRESS war eine cluster-randomisierte kontrollierte Studie zur Effektivität des Peer Reviews, der Initiative Qualitätsmedizin (IQM) zur Mortalität von Beatmungsfällen mit über 24-stündiger Beatmungsdauer bei einer dreijährigen Studienlaufzeit (2016 - 2018). Die Qualität und Patient:innensicherheit kolorektaler Resektionen waren neben Herzinfarkt, Schlaganfall, chronisch obstruktiver Lungenkrankheit (COPD), Pneumonie und Beatmung ein sekundäres Ziel der IMPRESS-Studie (Schmitt et al., 2021). Alle 232 teilnehmenden Krankenhäuser nahmen nach informierter Einwilligung an der Studie teil. Das Studienprotokoll wurde durch die Ethikkommission der Technischen Universität Dresden (TUD) begutachtet und positiv beschieden (IRB00001473 and IORG0001076; Datum: 24/04/2017).

Datenquellen

Die Datenquellen für die Analyse bestehen aus Abrechnungsdaten nach §21 KHEntgG und dem deutschen Krankenhausverzeichnis. Abrechnungsdaten nach §21 KHEntgG erfüllen nach Drösler et al. die übergeordneten Kriterien Relevanz, Qualität und Qualitätsdarlegung klinischer Messgrößen für die Qualitätsmessung der Gesundheitsversorgung, definiert durch das ÄZQ (Drösler et al., 2007). Diesen Daten fehlt die Information, ob eine Diagnose bereits bei Aufnahme vorhanden war (*present on admission*) (Heller, 2008). Dieser limitierende Umstand erfordert eine sorgfältige Definition und Auswahl relevanter Patient:innensicherheitsoutcomes (Drösler et al., 2007).

Population

Für eine korrekte Identifikation kolorektaler Resektion wurden die GIQI herangezogen. Dieser Definitionskatalog beinhaltet neben Berechnungsgrundlagen von Qualitätsindikatoren auf Grundlage von Abrechnungsdaten nach §21 KHEntgG Definitionen verschiedener konservativer und chirurgischer Eingriffe, unter anderem kolorektaler Resektionen (Mansky et al., 2017). Folglich wurden alle Fälle aus den Gruppen „partielle Kolonresektion“, „totale Kolonresektion“ und „Rektumresektion“ eingeschlossen (S. 62-66, Supplemental material S2-S4). Die Eingriffe (partielle/ totale) Kolon- und Rektumresektion wurden stratifiziert, also nach Gruppen getrennt berechnet.

Kovariaten

Die Kovariaten wurden der übergeordneten Fragestellung dieser Dissertation entsprechend in die Gruppen Fall-, Versorgungs- und Versorgervariablen eingeteilt:

1. Fallvariablen umfassten Alter, Geschlecht und Komorbiditäten. Die Komorbiditäten wurden nach den Elixhauser-Gruppen definiert. Dieses auf ICD-10 basierende Komorbiditätenset wurde für die statistische Berücksichtigung chronischer Erkrankungen in Analysen mit Abrechnungsdaten entwickelt (Elixhauser et al., 1998).
2. Versorgungsvariablen umfassten das Aufnahmedatum, den Aufnahmeanlass (Einweisung, Notfall, Zuverlegung) und den Typ der kolorektalen Resektion (totale/ partielle Kolonresektion, Kolon- und Rektumresektion)
3. Versorgervariablen beinhalteten die Trägerschaft, Status Uniklinik ja/nein, Urbanisierungsgrad und die jährliche Fallmenge.

Patient:innensicherheitsoutcomes

Neben der Krankenhausmortalität wurden die a priori validierten, nicht-letalen Patient:innensicherheitsoutcomes postoperatives Lungenversagen, Nierenversagen und postoperative Wundinfektionen definiert für die Analyse ausgewählt (Maass et al., 2015).

Statistische Analyse

Für die Berechnungen von Assoziationen zwischen den drei Kovariatensets und den Patient:innensicherheitsoutcomes wurden Mehrebenen-Regressionsmodelle genutzt. Diese Modelle bieten die Möglichkeit, hierarchisch strukturierte Daten, die mehreren Ebenen zugeordnet sind, zu analysieren. Im Falle dieser Analyse wird die Hierarchie durch die Fälle auf Individualebene und deren Behandlungen auf stationärer Ebene abgebildet. Bei Fällen, die vom selben Versorger behandelt werden, kann man von einer

ähnlichen Versorgungsstrategie und somit einer Korrelation zwischen Versorger und Outcome ausgehen. Eine Mehrebenen-Regression ist in der Lage diesen Umstand statistisch über einen „random intercept“ abzubilden (Snijders & Bosker, 2012). Um die Interpretierbarkeit der geschätzten Effektgrößen zu verbessern, wurden die geschätzten Regressionskoeffizienten in Odds Ratios (OR) umgewandelt. Ein geschätzter Effekt wurde als statistisch signifikant betrachtet, wenn der p-Wert< 0,05 lag. Die statistische Analyse wurde mit Stata V15.1 durchgeführt.

Ergebnisse

In die Analyse wurden 54.168 Kolonresektionen (209 Versorger) und 20.395 Rektumresektionen (200 Versorger) eingeschlossen (S. 53, Figure 1). Kolonresektionen wurden im deskriptiven Vergleich (S. 55, Table 1) zu Rektumresektionen durchgängig häufiger als Notfall (29.7% vs. 18.3%) oder Zuverlegung (3.5% vs. 1.9%) aufgenommen und an Wochenenden operiert (8,6% vs. 3,8%). Zudem wurden häufiger Tod (9.6% vs. 4.2%) und postoperatives Lungenversagen (16.7% vs. 12.2%), Nierenversagen (15.2% vs. 10.3%) und postoperative Wundinfektionen (11.3% vs. 11.2%) dokumentiert. Die Regressionsanalyse des Versorgungskontexts zeigte, dass Aufnahmen als Notfall und Zuverlegungen aus anderen Krankenhäusern durchgängig mit einem erhöhten Risiko negativer Patientenoutcomes assoziiert waren (S. 56-57, Tables 2-3). Das gilt für alle vier Outcomes Tod, postoperatives Lungenversagen, Nierenversagen und postoperative Wundinfektionen bei Kolon- und Rektumresektionen. Wochenendchirurgie war mit Ausnahme postoperativer Wundinfektionen ebenfalls bei Kolon- und Rektumresektionen durchgängig mit einem erhöhten Risiko für Tod, postoperatives Lungenversagen und Nierenversagen assoziiert. Die Regressionsanalyse von Variablen des Versorgerkontexts zeigte entweder inkonsistente oder heterogene Assoziationen. Eine ansteigende Fallmenge war bei Rektumresektionen protektiv mit Tod (OR 0.70 (95% CI, 0.61-0.80)), postoperativem Lungenversagen (OR 0.84 (95% CI, 0.72-0.98)) und Nierenversagen (OR 0.85 (95% CI, 0.76-0.95)) assoziiert. Bei Kolonresektionen verblieben die Assoziationen mit Ausnahme eines erhöhten Risikos postoperativer Wundinfektionen (OR 1.16 (95% CI, 1.03-1.32)) bei steigender Fallmenge insignifikant. Für die verbleibenden Variablen Urbanisierungsgrad, Status als Universitätsklinikum oder Trägerschaft lagen keine konsistenten oder übergreifenden Assoziationen vor.

Zusammenfassend zeigte die Analyse durchgängige und homogene Assoziationen zwischen Patient:innensicherheitsoutcomes zwischen Aufnahmeanlass (vier von vier) und Wochenendchirurgie (drei von vier). Hinsichtlich der Fallmenge konnten für die Rektumresektionen konsistente Assoziationen berichtet werden.

Publikation

Das Manuskript wurde unter dem Titel „Relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: cross-sectional evidence from a nationwide sample of 232 German hospitals" am 18. Oktober 2021 im Fachmagazin *BMJ Open* eingereicht und am 25. Juli 2022 publiziert (Walther, Schmitt, et al., 2022).

3.6 Einzelfragestellung (3): Welche Rolle nimmt der Versorgungskontext als Risikofaktor bei der Inzidenz von Dekubitalulcera ein?

Die Analyse erfolgte mittels einer Querschnittstudie ohne Intervention auf Grundlage der Guten Praxis Sekundärdatenanalyse (Swart et al., 2015) und wurde durch die Ethikkommission der Technischen Universität Dresden (TUD) begutachtet und positiv beschieden (BO-EK-520112021, IRB00001473, IORG0001076).

Population

Die Studienpopulation umfasste somatisch behandelte, erwachsene Patienten und Patientinnen ≥19 Jahre des Universitätsklinikums Carl Gustav Carus Dresden (UKD) mit Aufnahme und Entlassung von 2014 bis 2018 und einer stationären Verweildauer von mindestens 48 Stunden. Der ausschließliche Einschluss einer erwachsenen, somatisch behandelten Population begründet sich darin, dass sowohl Kinder und Jugendliche als auch psychotherapeutisch behandelte Fälle datenschutzrechtlich hochvulnerable Gruppen darstellen und zudem signifikant seltener von Dekubitusulcera betroffen sind (Eberlein-Gonska et al., 2013). Nach Anwendung dieser Einschlusskriterien lag eine auszuwertende Population von 149.006 Fällen für den oben genannten Zeitraum zugrunde.

Patient:innensicherheitsoutcome

Das primäre Outcome war die Dekubitusinzidenz im stationären Aufenthalt. Vor dem Hintergrund, dass die standardisierte Dekubitusdokumentation keinen Zeitstempel enthielt, wurden alle Dekubitusdiagnosen des Aufnahmetags als prävalent gewertet. Alle dokumentierten Dekubitusulcera in Folge- oder Entlassbefunden wurden als inzident gewertet. Als unabhängige Variablen wurden in dieser Untersuchung der Aufnahmeanlass als Notfall oder Zuverlegung, die Summe behandlungsbeteiligter Stationen, (die Dauer) chirurgische(r) Anästhesien, intensivmedizinische Behandlung mit und ohne Beatmung adjustiert für Alter, Geschlecht und Komorbiditäten untersucht.

Datenquellen

Ein relevantes Problem bei der Auswertung von Dekubitalulcera ist die Identifikation prävalenter, also bereits bei Aufnahme vorliegender (*present on admission*) Dekubitalulcera (Houchens et al., 2008). Daher wurden auf Grundlage der Fallnummer Abrechnungsdaten nach §21 KHEntgG mit flächendeckend erhobenen Datensätzen des Krankenhausinformationssystems ORBIS zusammengeführt. Die „Mitternachtsstatistik", eine Belegungsdokumentation je Station, wurde für die Berechnung der beteiligten Stationen im Rahmen der Behandlung, die „Dekubitusdokumentation" für die zweifelsfreie Bestimmung inzidenter Dekubitalulcera und die „Anästhesiezeiten" für die Analyse chirurgischer Anästhesien als Risikofaktoren herangezogen. Die Abrechnungsdaten nach §21 KHEntgG dienten zur Identifikation des Alters, des Geschlechts und der Komorbiditäten.

Statistische Analyse

Für die Prädiktions- und Regressionsberechnungen kamen sog. „Bayesian Additive Regression Trees" (BART) zum Einsatz. Hierbei handelt es sich um ein nicht-parametrisches Verfahren maschinellen Lernens, das sich mit der Bildung multipler Regressionsbäume sowie fortgeschrittenen Prädiktionsmöglichkeiten für verschiedene Fragestellungen eignet. Dekubitalulcera stellen ein multifaktorielles Erkrankungsbild dar. Die heterogenen Interaktionen zwischen der Dekubitusinzidenz sowie den zugrundeliegenden Risikofaktoren lassen sich nur limitiert mit parametrischen Verfahren wie einer logistischen Regression über a priori definierte Interaktionen darstellen. BART als nichtlineares Verfahren benötigt hingegen keine a priori Definition von möglichen Interaktionen und ermöglicht die Identifikation und Analyse vielschichtiger und nichtlinearer Interaktionen durch die Bildung multipler Regressionsbäume. Zudem kann BART metrische Variablen wie bspw. Alter oder die Dauer einer Anästhesie in einer funktionalen Form abbilden. Das ermöglicht eine detailliertere Betrachtung metrischer Variablen, wie beispielsweise der Anästhesiezeit oder dem Alter und erspart die Bildung von (arbiträren) Gruppen (Chipman et al., 2010). In das Risikomodell wurden neben Alter, Geschlecht und Komorbiditäten unterschiedliche Aspekte des Versorgungskontextes, wie Zuverlegungen, Notfälle und die Länge der Anästhesie bei operativen Eingriffen als Surrogatvariable eingeschränkter Lagerungsfähigkeit aufgenommen. Für Sensitivitätsanalysen, insbesondere des Prädiktionsmodells, kamen Receiver Operating Curve - Analysen (ROC) und Konfusionsmatrizen zum Einsatz (Metz, 1978). Für einen Vergleich der Prädiktionsgüte wurden BART- und random forest-Regressionen,

Logistische Regression sowie least absolute shrinkage and selection operator (LASSO) Regressionen miteinander verglichen.

Ergebnisse

In den 149.006 analysierten Fällen gab es eine annähernd geschlechtliche Gleichverteilung (51,5% männlich, 48,5% weiblich) mit einem medianen Alter von 64 Jahren. 35,5% der Fälle wurden als Notfall und 3,5% als Zuverlegung stationär aufgenommen. Etwa die Hälfte der Fälle beinhaltete Vollanästhesien und 19,6% der Fälle wurde intensivmedizinisch behandelt. Bei 3,1% (n=4.663) der Fälle wurde ein inzidenter Dekubitus dokumentiert.

Die Regressionsanalyse zeigte, dass die Aufnahme als Notfall oder Zuverlegung (S. 97, Figure 5), die steigende Zahl behandlungsbeteiligter Stationen (S. 96, Figure 4) sowie eine steigende Dauer chirurgischer Anästhesien (S. 96, Figure 3) mit dem Auftreten inzidenter Dekubitalulcera assoziiert waren.

Die Prädiktionsanalyse zeigte, dass intensivmedizinische Beatmung, Alter, Dauer chirurgischer Anästhesien sowie die Zahl behandlungsbeteiligter Stationen den höchsten Einfluss für die Prädiktion von Dekubitalulcera ausüben (S. 95, Figure 1). Das bedeutet, dass bei einem Vorliegen dieser Variablen im Vergleich zu den anderen potenziellen Risikofaktoren ein erhöhtes Dekubitusrisikos prädiktiert wird. Hinsichtlich der Prädiktionsgüte zeigte die ROC-Analyse ein area under the curve (AUC) zwischen 0,89 bis 0,90 bei den vier miteinander verglichenen Verfahren (BART, LASSO, logistische Regression, random forest.) Wird die AUC alleinig betrachtet, spräche das für eine starke Prädiktionsgüte aller vier Modelle (Metz, 1978). Die Analyse der Konfusionsmatrizen, also der Gegenüberstellung zwischen prädiktiertem und realem Ergebnis zeigte, dass 90-96% aller inzidenten Dekubitusfälle durch die vier Modelle nicht, also „falsch negativ“, prädiktiert wurden. Das führte zu niedrigen Sensitivitätswerten in der Gesamtpopulation (0,04-0,10). Die „falsch-negativen“ Prädiktionen waren in den Risikogruppen intensivmedizinische Behandlung (84%-93%), Beatmung (76%-87%) und durchgeführte Anästhesie (87%-94%) niedriger. Die Sensitivität war in den Subgruppen entsprechend höher (0,10-0,24).

Publikation

Das dieser Dissertation zugrundeliegende Manuskript zu Vorhersagemöglichkeiten und der Relevanz des Versorgungskontexts von Dekubitalulcera wurden unter dem Titel „Prediction of inpatient pressure ulcers based on routine healthcare data using machine

learning methodology“ am 15.11.2021 bei *Scientific Reports* eingereicht und am 23.März 2022 publiziert (Walther, Heinrich, et al., 2022).

3.7 Übergreifende Einordnung

Die in den drei Publikationen beschriebenen Ergebnisse zeigten mit Geburtsmortalität und -komplikationen (Walther et al., 2021), postoperativer Mortalität, Lungenversagen, Nierenversagen, Wundinfektionen (Walther, Schmitt, et al., 2022) und Dekubitus (Walther, Heinrich, et al., 2022) relevante und etablierte Patient:innensicherheits-indikatoren der deutschen und internationalen Qualitäts- und Patient:innensicherheits-forschung (Drösler et al., 2009).

Publikation (1) untersuchte mit einem international ausgerichteten systematischen Review die Frage des Einflusses von Fallmengen in der Niedrigrisiko-Geburtshilfe national und (gesundheits-)systemisch übergreifend auf Mortalitäts- und Komplikations-outcomes. Die eingeschlossenen Studien waren durchgängig retrospektive Querschnitt-studien mit versorgungsnahen und insbesondere Registerdaten (Walther et al., 2021).

Publikation (2) folgte mit der Querschnittanalyse von Abrechnungsdaten aus 232 deutschen Krankenhäusern einem nationalen Ansatz und beinhaltete u.a. mit Fallmenge und Aufnahmeanlass Versorgungs- und Versorgerkontext im Rahmen einer über-greifenden Analyse von Mortalitäts- und Komplikationsoutcomes (Walther, Schmitt, et al., 2022).

Publikation (3) folgte mit der Untersuchung der Prädiktierbarkeit und dem Einfluss des Versorgungskontexts inzidenter Dekubitalulcera in einem monozentrischen Setting. Durch die Verbindung von klinischen Daten und Abrechnungsdaten konnte das present on admission-Problem Versorgungsnaher Daten bei Dekubitus aufgelöst werden und mit Aufnahmeanlass, Anzahl beteiligter Stationen, intensivmedizinischer Behandlung inkl. Beatmung sowie der Dauer chirurgischer Anästhesien die Rolle des Versorgungs-kontextes untersucht werden (Walther, Heinrich, et al., 2022).

Alle Publikationen haben gemein, dass in Bezug auf Fallmenge und Aufnahmeanlass beobachtende Designs vorliegen. Das Review zum Einfluss von Fallmengen auf die Reifgeborenenversorgung beinhaltete ausschließlich beobachtende Registerstudien. Die nationale Untersuchung kolorektaler Resektionen und die monozentrische Dekubitusanalyse wurden mit bereits vorhandenen versorgungsnahen Daten durch-geführt.

4 Publikationen und Impact-Faktoren nach Journal Citation Report

1 **Walther, F.**, Kuester, D., Bieber, A., Malzahn, J., Rüdiger, M., & Schmitt, J. (2021). Are birth outcomes in low risk birth cohorts related to hospital birth volumes? A systematic review. *BMC Pregnancy and Childbirth*, 21(1), 531. https://doi.org/10.1186/s12884-021-03988-y

2 **Walther, F.,** Schmitt, J., Eberlein-Gonska, M., Kuhlen, R., Scriba, P., Schoffer, O., & Roessler, M. (2022). Relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: cross-sectional evidence from a nationwide sample of 232 German hospitals. *BMJ Open*, 12(7), e058481. https://doi.org/10.1136/bmjopen-2021-058481

3 **Walther, F.**, Heinrich, L., Schmitt, J., Eberlein-Gonska, M., & Roessler, M. (2022). Prediction of inpatient pressure ulcers based on routine healthcare data using machine learning methodology. *Scientific Reports*, 12(1), 5044. https://doi.org/10.1038/s41598-022-09050-x

Tabelle 2 - Übersicht der Publikationen und Impact-Faktoren nach Journal Citation Report 2021 (JCR)

#	Journal	Impact-Factor Journal Citation Report	Themenkategorie (Science Edition)	Median des Impact-Factors in Themen-kategorie	Rang in Themen-kategorie
(1)	BMC Pregnancy & Childbirth	3,105	Obstetrics & Gynecology	3,015	36/85
(2)	BMJ Open	3,007	Medicine, General & Internal	2,982	86/172
(3)	Scientific Reports	4,997	Multidisciplinary Sciences	2,604	19/74

4.1 Publikation (1): Are birth outcomes in low risk birth cohorts related to hospital birth volumes?

Publiziert in:
BMC Pregnancy Childbirth

2021 Impact-Factor nach dem Journal Citation Report:
Journal Impact Factor: 3,105

Gelistet unter anderem in der folgenden Themenkategorie:
Obstetrics & Gynecology
Median des Impact Factors der Themenkategorie: 3,015
Rang in der Themenkategorie: 36 von 85

Referenz:
Walther, F., Kuester, D., Bieber, A., Malzahn, J., Rüdiger, M., & Schmitt, J. (2021). Are birth outcomes in low risk birth cohorts related to hospital birth volumes? A systematic review. *BMC Pregnancy and Childbirth*, 21(1), 531. https://doi.org/10.1186/s12884-021-03988-y

Walther et al. BMC Pregnancy Childbirth (2021) 21:531
https://doi.org/10.1186/s12884-021-03988-y

BMC Pregnancy and Childbirth

RESEARCH Open Access

Are birth outcomes in low risk birth cohorts related to hospital birth volumes? A systematic review

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Abstract

Background: There is convincing evidence that birth in hospitals with high birth volumes increases the chance of healthy survival in high-risk infants. However, it is unclear whether this is true also for low risk infants. The aim of this systematic review was to analyze effects of hospital's birth volume on mortality, mode of delivery, readmissions, complications and subsequent developmental delays in all births or predefined low risk birth cohorts. The search strategy included EMBASE and Medline supplemented by citing and cited literature of included studies and expert panel highlighting additional literature, published between January/2000 and February/2020. We included studies which were published in English or German language reporting effects of birth volumes on mortality in term or all births in countries with neonatal mortality < 5/1000. We undertook a double-independent title-abstract- and full-text screening and extraction of study characteristics, critical appraisal and outcomes in a qualitative evidence synthesis.

Results: 13 retrospective studies with mostly acceptable quality were included. Heterogeneous volume-thresholds, risk adjustments, outcomes and populations hindered a meta-analysis. Qualitatively, four of six studies reported significantly higher perinatal mortality in lower birth volume hospitals. Volume-outcome effects on neonatal mortality ($n = 7$), stillbirths ($n = 3$), maternal mortality ($n = 1$), caesarean sections ($n = 2$), maternal ($n = 1$) and neonatal complications ($n = 1$) were inconclusive.

Conclusion: Analyzed studies indicate higher rates of perinatal mortality for low risk birth in hospitals with low birth volumes. Due to heterogeneity of studies, data synthesis was complicated and a meta-analysis was not possible. Therefore international core outcome sets should be defined and implemented in perinatal registries.

Systematic review registration: PROSPERO: CRD42018095289

Keywords: Mortality, Infant, Low risk birth, Perinatal regionalization, Volume-outcome

Background

Several studies have shown mortality of high-risk-infants can be reduced if these infants are treated in highly equipped neonatal intensive or intermediate care units [1]. Therefore, different levels of care have been introduced for treatment of pregnant women and their newborns in relation to the medical condition. For each level certain requirements in terms of infrastructure, staffing, equipment and qualifications are defined. If a centre does not fulfill these requirements, a specialized care is usually not allowed [2, 3]. Since experience of the care team is likely to be also of advantage, it could be assumed that infants will benefit from hospitals with high annual birth volume. That assumption is supported by our recent systematic review, showing for very low birth

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weight infants an improved maternal and neonatal outcome in centers with higher birth volumes in high-risk births [4].

Important other risk factors for pregnancy and birth complications are higher maternal age, comorbidities (e.g. placenta praevia, pre-existing or gestational diabetes) or smoking. These factors are likely to increase the risks for maternal or neonatal adverse events [5–10]. Currently, appropriate management of these risks is still being discussed [11–15]. In order to better study the impact of different interventionson on subsequent outcome, a homogenous definition of birth outcomes is needed and core outcome sets (COS) are currently developed [5, 6]. COS are multilaterally consented and standardized sets of outcomes which should be reported in clinical trials to guarantee comparabilityIn recent years, COS have been increasingly developed and registered for perinatal and maternal care [16], like gestational diabetes [17], preterm birth [18], maternity care [19], neonatal medicine [20] or pregnancy and childbirth [21]. However, currently there are no COS available to study the impact of birth volume on outcome of low risk pregnancies. For both this reason and since birth complications are difficult to predict in low risk pregnancies, it remains unknown whether women with a low risk pregnancy could also benefit from care in hospitals with higher birth volumes.

The aim of this systematic review was to summarize and critically appraise the impact of hospital case volume on mortality and morbidity in low risk birth cohorts.

Methods

We conducted this systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist [22] and registered the review protocol (CRD42018095289) in the International Prospective Register of Systematic Reviews [23]. The original search strategy (Additional file 1) and review was designed to identify studies on the effects of either perinatal regionalization or hospital birth volume on infant and maternal outcomes. Here we report on the results of volume-outcome-relationships.

Eligibility criteria, information sources, search strategy

Inclusion and exclusion criteria (Table 1) addressed population, intervention, comparison, outcome and study type (PICOS). *Interventions/ expositions* included volume effect estimates on mortality as primary outcome and secondarily on caesarean sections, readmissions, birth complications, developmental delays *(outcome)* in all births or a pre-defined low risk birth cohort *(population)*. In order to ensure comparability and current status of obstetric care, observational or interventional studies *(study type)* from countries with neonatal mortality rates below 5 per 1000 births (UN Child mortality report) that were published in English or German language after 01/01/2000 were included [24].

Study selection

We systematically searched Medline and EMBASE on 18/04/2018 and on 26/02/2020. The search strategy included a combination of free text words and database-specific subject-headings (Additional file 1) using Ovid interface. We used Endnote X7 for the creation of the literature database and the removal of duplicates. Two authors (FW, AB) independently screened titles/abstracts and full texts for eligibility. Additionally, an expert panel (MR, JM, Rainer Rossi) highlighted missing relevant papers. After full-text-screening, we conducted a hand search including forward (citing literature) and backward (cited literature) screening of included studies. Discrepancies during screening, extraction or quality assessment were solved by consulting of another reviewer (JS). For interpretation of reliability, we applied the prevalence-adjusted bias-adjusted kappa (PABAK). The advantage of PABAK in contrast to Kappa value is the consideration of the high class imbalance [25].

Table 1 PICO-Scheme

	Inclusion criteria	Exclusion criteria
POPULATION	all births, term/ normal birth weight birth or low risk birth in a nationwide setting with < 5/1000 neonatal deaths	Preterm birth, low birth weight birth, other risk-selections (e.g. gestational diabetes, multiple births)
EXPOSITION	comparison of different hospital birth volumes or -sizes	No comparison of different hospital birth volumes or -sizes
COMPARISON	other birth volumes	No comparator provided
OUTCOME	Primary Outcome: Maternal or infant mortality Secondary Outcomes: Caesarean sections, readmissions, birth complications, developmental delays	No measurement of maternal or infant mortality
STUDY TYPE	Observational and interventional studies	Descriptive studies, systematic reviews

Data extraction and data synthesis

We predefined a data extraction form in MS Excel including study charateristics (e.g. population, period, country) and outcomes (e.g. definition, exposing/ referencing annual volume, result, estimator) was used. One reviewer extracted (FW) and a second (DK) verified the results resolving discrepancies by consensus or consulting a third reviewer (JS). To decide whether individual studies can be pooled in a meta-analysis, we reviewed methodological quality, comparability of the study contexts (population, outcomes, volume-thresholds and risk adjustment) and statistical heterogeneity. If studies were considered as not comparable, a qualitative synthesis followed.

Critical appraisal process

Two independent reviewers (FW, DK) performed the quality assessment using the Methodology Checklist for Cohort studies of the Scottish Intercollegiate Guidelines Network (SIGN). This checklist contains 14 items with a final quality rating of the studies in "high quality", "acceptable" and "inacceptable" [26]. Methodological explanations and definitions in the context of the application of the checklist are presented in Additional file 2.

Patient and public involvement

No patient involved.

Results

Study selection

After screening of 7955 records 13 studies met our predefinded eligibility criteria were included in the systematic review (Fig. 1) [27–39]. Additional file 3 contains the reasons for exclusion of the remaining 30 full texts [40–69]. The high prevalence and bias adjusted Kappa (PABAK) (Fig. 1) in both title-abstract and full-text-screnning suggests no systematic differences between the raters.

Study characteristics

Table 2 shows the characteristics of included studies. The observation period varied between 29 years (1967–1996) [33] and one year [35, 39]. The earliest observation started in 1967 [33] and the latest ended 2012 [39]. All of the included studies used cross-sectional designs to analyse retrospective cohorts in perinatal registers (Additional file 4). The studies were conducted in Finland [30, 32, 34], the United States [28, 35, 39], Sweden [27], Norway [33], Germany, [29] the United Kingdom, [31] Australia, [36] the Netherlands [70] and Canada [37]. The analyzed populations consist of either all births [27, 28, 30, 31, 33–35, 37, 39] and/ or a predefined low risk

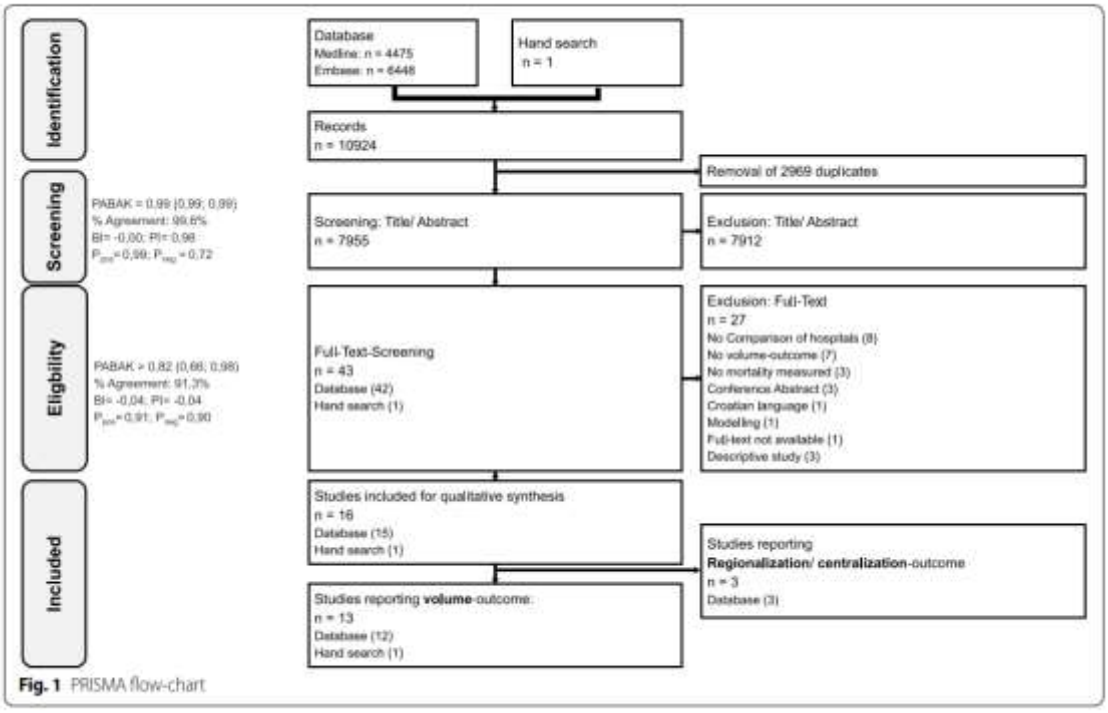

Fig. 1 PRISMA flow-chart

Table 2 Characteristics of included studies

Study	Period	Country	Birth population	Grouped annual hospital volume	Outcomes	Outcome definition
Finnstrom et al. 2006[27]	1985–1999	SWE	births: all singletons (n = 1.538.814)	< 500, 500–999, 1000–2499 (ref.), ≥ 2500	1) neonatal mortality	1) ≤ 27d
Friedman et al. 2016[28]	1998–2010	US	women: all hospital (n = 50.433.539)	50, 1000 (ref.), 1500, 2250	1) maternal mortality 2) maternal complications	1) failure to rescue 2) severe morbidity[1]
Heller et al. 2002[29]	1990–1999	GER	births: BW > 2500 g (n = 582.655);	≤ 500, 501–1000, 1001–1500, > 1500 (ref.)	1) Early-neonatal death	1) ≤ 7d
Heinminki et al. 2011[30]	1991–2008	FIN	births: all (n = 474.419) + BW > 2499 g in non-UH	< 750, 750–1499, ≥ 1500, UH (ref.)	1) perinatal mortality 2) CS	1) ≤ 7d
Joyce et al. 2004[31]	1994–1996	UK	births: all (n = 540.834)	N/A: Volume entered the analysis as continuous variable	1) stand. stillbirth rates 2) stand. neonatal mortality	1) > 24 wk GA 2) ≤ 28d
Karalis et al. 2016[32]	2005–2009	FIN	births: low risk[2] (n = 276.066)	births: ≤ 999, 1000–1999, ≥ 2000, UH (ref.)	1) stillbirths 2) early neonatal death	1) Intrapartum: undefined 2) undefined
Moster et al. 2001[33]	1967–1996	NO	births: all (n = 1.650.852)	≤ 100, 101–500, 501–1000, 1001–2000, 2001–3000, > 3000 (ref.)	1) neonatal mortality	1) ≤ 28d
Pyykonen et al. 2014[34]	2006–2010	FIN	women: all[3] (n = 290.288) + low risk[4] (n = 276.287)	< 1000, 1000–2999 (ref.), < 3000	1) perinatal mortality 2) neonatal mortality 3) early neonatal mortality 4) stillbirths	1) stillbirth + death ≤ 7d 2) ≤ 28d 3) ≤ 7d 4) ≥ 22wk GA
Snowden et al. 2012[35]	2006	US	women: all (n = 527.617), low risk[5]	Urban: ≤ 50–1199 (ref.), 1200–2399, 2400–3599, ≥ 3600 Rural: 50–599 (ref.) 600–1699, ≥ 1700	1) neonatal mortality	1) undefined
Tracy et al. 2006[36]	1999–2001	AUS	births: low risk/ term[6] (n = 331.147)	< 100, 100–500, 501–1000, 1001–2000, > 2001 (ref.)	1) neonatal mortality 2) CS (labour) 3) Overall CS	1) ≤ 28d
de Graaf et al. 2010[38]	2000–2006	NEL	women: singleton (n = 655.961)	< 750, 750–999, 1000–1249, 1250–1499, 1500–1749, ≥ 1750 (ref.)	1) perinatal mortality 2) neonatal complications	1) ≤ 7d 2) Perinatal adverse outcome[7]
Restrepo et al. 2018[39]	2012	US	births: live 20–44 wk GA (n = 32.140)	N/A: Volume entered the analysis as continuous variable	1) neonatal mortality	1) ≤ 28d
Aubrey-Brassler et al. 2019[37]	2006–2009	CA	women: all (n = 820.761)/ births: all (n = 827.504)	No services usually: 1–49; 50–99; 100–199; 200–499; 500–999; 1000–2499, > 2500 (ref.)	1) perinatal mortality 2) maternal complications	1) Death [...][8] 2) Maternal Morbidity & Mortality[9]

Notes:

1: heart/ renal/ respiratory failure, acute myocardial infarction, liver disease, disseminated intravascular coagulation, coma, delirium, puerperal cerebrovascular disorders, pulmonary edema or embolism, sepsis, shock, status asthmaticus, status epilepticus

2: Exclusion: Low BW, multiple pregnancy, antepartum stillbirth, out-of-hospital birth, major congenital anomalies, birth defects

3: Exclusion: birth in university hospital, length of stay > 7d

4: Exclusion: birth in university hospital, length of stay > 7d, multiple pregnancy, pre-/postterm birth

5: Exclusion: preterm birth, low BW

6: Exclusion: Low BW, multiple pregnancy, preterm, age, complications

7: intrapartum death, death ≤ 7d, 5-min Apgar < 7, NICU transfer

8: sudden infant death syndrome, sudden cardiac death, stillbirth (GA ≤ 20 wk), in-hospital death liveborn neonate

9: Eclampsia, Previa with hemorrhage abruption, Intrapartum + postpartum hemorrhage + transfusion or hysterectomy, Rupture of uterus before or during labor, Obstetric shock, Sepsis, Other complications of obstetric procedures, Obstetric embolism, Cardiovascular disease, Acute renal failure, Death, obstetric or unspecified, Neurologic disease, Hematologic disease, Respiratory disease, Diabetic ketoacidosis, Peritonitis or parametritis, Toxic liver disease or hepatic failure, Canadian Classification of Health Interventions, Assisted ventilation or resuscitation, Dialysis, Hysterectomy, Evacuation of incisional hemato-ma, Repair of bladder, urethra or intestine, Embolization or ligation of pelvic vessels or suturing of uterus, Blood transfusion

population [29, 32, 34, 36, 38] excluding e.g. low birth weight or multiple births. Annual volumes and its comparators were set differently in terms of group sizes and defining births [27, 29–33, 36, 39] or deliveries/ pregnancies respectively women giving birth [28, 34, 35, 37, 38] as basis for the calculation. While "birth" refer to the neonate, "delivery" describes the mother who is giving birth. Due to multiple pregnancies, number of deliveries is usually lower than the number of births. Unfortunately, not all studies reported both numbers, but Table 2 shows the different annual volumes in the included studies. In addition to the different annual volumes, maximum, [29, 33, 36–39] minimum [35] and mean quantities [27, 28, 34] as well as university clinics (UH) [30, 32] were used as reference volumes. The analyzed outcomes included stillbirths, [31, 32, 34] perinatal/ early [29, 30, 32, 34, 37, 38] and neonatal mortality, [27, 31, 33–36, 39] birth by caesarean section [30, 36] and composite outcomes like perinatal adverse outcome [38] or maternal morbidity/ mortality [37]. Six out of thirtheen studies did not solely focus on volume-outcome relationship, but analyzed influence of geographic accessibility [37], birth at night hours [38], staffing [31], availability of facilities [31], on call arrangements [32], or birth at weekday/ weekend [39].

Results of the critical appraisal

Table 3 shows in detail that most of the included studies (12 out of 13 studies) fulfilled the majority of the queried items leading to an "acceptable" quality [27–32, 34–39]. Quality of one study was rated as "unacceptable" due to lack of comparability (missing baseline-tables, item 1.2) of the investigated groups [33].

Due to the retrospective design and other methodological reasons, some items were not applicable:

- number of participants (item 1.3)
- outcome already present before start of study (item 1.4)
- drop-out (item 1.5)
- comparison between full and lost to follow-up (item 1.6) and
- multiple measured exposure levels (item 1.12).

None of the studies fulfilled the criteria for blinding (item 1.8) and critical recognition of limited possibilities of blinding (item 1.9) in cohort studies. An externally demonstrated validity (item 1.11) and reliability (item 1.10) of the assessed outcomes was not applicable due mortality, caesarean sections or other clinical outcomes are not subjective measures.

We originally planned to perform a meta-analysis but were unable to conduct it due to definitional heterogeneities in the included studies. Additional file 5 provides a tabular overview of heterogeneities identified between the outcomes analyzed. Five studies were excluded from a pooled estimate due to singular report of the outcome maternal mortality, [28] maternal morbidity/ mortality, [37] neonatal complications, [38] missing adjustments [34, 35] and the singular use of risk ratios as estimator, [31] 99% confidence intervals [36] or pearson correlation coefficients [39]. The remaining results for the outcomes stillbirth, [32, 34] perinatal/ early neonatal mortality, [29, 30, 32, 37, 38] neonatal mortality [27, 33, 39] and caesarean sections [30] were not comparable due to heterogeneously defined adjustment variables, populations (all births vs. predefined low risks), outcomes (e.g. undefined vs. defined) and volume-thresholds. Consequently, we summarized the results qualitatively.

Effects of annual volume on neonatal outcomes

Stillbirth was evaluated in three studies [31, 32, 34] and defined as fetal death prior to 22 [34] or 24 [31] weeks of gestation or remained undefined [32]. For hospitals with medium-sized birth volumes (1000–1999 p.a.) stillbirth odds ratio was significantly higher when compared with university hospitals [32]. Similar effects were found for hospitals with birth volumes between 1000–2999, when compared with high birth volumes ($\geq$3000 p.a.) [34]. However, taking all data together there was no clear volume effect on the rate of stilbirths (Fig. 2).

Perinatal or early neonatal mortality has been defined as death within the first 7 days of life [29, 30, 34, 38] or as a combined outcome [34, 37]. One study did not provide a specific definitio [32]. Results were always adjusted, except for one study [34]. Whereas two studies did not report a significant volume-effect, [32, 38] four studies showed significantly higher rates of perinatal/ early neonatal mortality in hospitals with low ($\leq$1000) [29, 30, 34, 37] or very low ($\leq$500) [29, 37] birth volumes (Fig. 2) for either low risk (term infants with birthweight > 2499 g) [29, 34] or all births [30, 37].

Neonatal mortality was defined as 28-day-, [31, 33–36, 39] or 27-day-mortality [27] in order to analyze all [31, 33–36, 39] and/or low risk births [27, 34–36]. The majority of the studies undertook adjustments [27, 31, 33, 36]. As illustrated in Fig. 3 five [27, 33, 35, 36, 39] out of seven studies reported significant volume effect estimates with neonatal mortality being higher in hospitals with lower [33] or higher annual birth volumes [27, 35, 36, 39]. The remaining two studies reported non-significant volume-outcome effects [31, 34].

The study from Moster et al. reported higher neonatal mortality rates in hospitals with low birth volumes however, was lacking comparability between groups due to missing baseline-table and thus, quality was rated

Table 3 Detailed results of sign—quality assessment for cohort studies

Item	Description	Finnstrom et al. 2006 [27]	Friedman et al. 2016 [28]	Heller et al. 2002 [29]	Hemminki et al. 2011 [30]	Joyce et al. 2004 [31]	Karalis et al. 2017 [32]	Moster et al. 2001 [33]	Pyykonen et al. 2014 [34]	Snowden et al. 2012 [35]	Tracy et al. 2006 [36]	de Graaf et al. 2010 [38]	Restrepo et al. 2018 [39]	Aubrey-brassler et al. 2019[37]
1.1	appropriate and clearly focused question	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.2	illustrated comparability between studied groups	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
1.3	number of asked people *(prospective studies)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
1.4	Likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
1.5	Drop-Out rate *(prospective studies)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
1.6	Comparison between full and lost-to-follow-up participants *(prospective studies)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 3 (continued)

Item	Description	Finnstrom et al. 2006 [27]	Friedman et al. 2016 [28]	Heller et al. 2002 [29]	Hemminki et al. 2011 [30]	Joyce et al. 2004 [31]	Karalis et al. 2017 [32]	Moster et al. 2001 [33]	Pyykonen et al. 2014 [34]	Snowden et al. 2012 [35]	Tracy et al. 2006 [36]	de Graaf et al. 2010 [38]	Restrepo et al. 2018 [39]	Aubrey-brassler et al. 2019[37]
1.7	Clearly defined outcomes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.8	Assessment of outcome blinded to exposure status	No	No	No	No	No	No	No	No	No	No	No	No	No
1.9	When blinding impossible, recognition that knowledge of exposure status could have influenced assessment	No	No	No	No	No	No	No	No	No	No	No	No	No
1.10	reliable measurement of exposure	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.11	from other sources is used to demonstrate that the method of outcome assessment is valid and reliable (clearly defined primary outcomes)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 3 (continued)

Item	Description	Finnstrom et al. 2006 [27]	Friedman et al. 2016 [28]	Heller et al. 2002 [29]	Hemminki et al. 2011 [30]	Joyce et al. 2004 [31]	Karalis et al. 2017 [32]	Moster et al. 2001 [33]	Pyykonen et al. 2014 [34]	Snowden et al. 2012 [35]	Tracy et al. 2006 [36]	de Graaf et al. 2010 [38]	Restrepo et al. 2018 [39]	Aubrey-brassler et al. 2019[37]
1.12	Exposure level or prognostic factor is assessed more than once *(prospective studies)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
1.13	confounders identifed and adequately taken into account for analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
1.14	confidence intervals provided	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes
2.1	Overall rating	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Unacceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable

"unacceptable" [33]. In conclusion, methodically limitations hinder conclusive statements regarding the effect of birth volume on neonatal mortality.

Neonatal complications were reported in one study as a combined outcome ("perinatal adverse outcome") including stillbirths, death ≤ 7 days, 5-min Apgar < 7 and a transfer to a neonatal intensive care unit in singleton births. Non-monotonous, significantly higher odds ratios of neonatal complications were reported for units with 750–999 and 1500–1749 births (Fig. 3) compared to at least 1750 births per anno [38].

Effects of annual birth volume on maternal outcomes

Adjusted maternal mortality was reported as failing attempts to resuscitate women with severe complications during birth [28]. The volume-outcome relationships were reported to be non-monotonous in general with lower and higher relative risks of maternal mortality in lower (50) and higher annual birth volumes (≥ 2250–7500) [28].

Adjusted maternal complications were reported in two studies as a combined outcome consisting of maternal mortality and different morbidy outcomes in all births [28, 37]. In a Canadian study the odds ratio were reported to be significantly higher in hospitals with ≤ 1000 births p.a [37]. However, a study from the US reported non-monotonous results with higher risk ratios in hospitals with high (2500) and low (50) annual birth volumes. Without providing results, the relative risks of maternal complications remained higher with a further increase in birth volume [28]. In conclusion, no conclusive statement regarding the impact of birth volume on maternal complication is possible due to contradicting study results as shown in Fig. 4.

An adjusted rate of delivery via caesarean section was reported in two studies [30, 36]. Hemminki et al. reported a significantly higher rate of caesarean sections in "small-hospital-areas" with less than 750 births per year compared to "capital areas" [30]. In contrast, Tracy et al. reported a significantly lower rate of caesarean sections in hospitals with ≤ 500 births [36]. Thus, contradicting study results do not allow conclusions regarding volume-effects on mode of delivery (Fig. 4).

In summary, most studies suggested a volume-outcome relationship on perinatal / early neonatal mortality and however reported either insignificant, non-monotonous or conflicting results regarding volume effects on the remaining outcomes.

Discussion

This systematic review on the effects of hospital case volume on the safety and outcomes of infants classified as being on low risk births has tremendous public health impact, as births of children are so frequent and such an important life event. There is evidence already for high risk births and many other conditions such as preterm birth [1, 23], pediatric intensive care [71] or pediatric heart surgery [72] that hospitals with more experience and higher case numbers provide better healthcare indicated by better health outcomes of patients being treated there. We therefore speculated that higher birth volumes of hospitals were also related to better outcomes in births of low risk or all infants. These studies reported on mortality (stillbirths, perinatal, neonatal, maternal), morbidity (neonatal, maternal) and mode of delivery. Readmissions and developmental delays were not reported. Initially, a pooled estimate was intended. Heterogenities within the definitions and presentations of characteristics led to the decision not to perform a pooled estimate. Therefore, the results were synthesized qualitatively focusing on volume-outcome in general and especially in terms of lower annual birth volumes (≤ 1000). The heterogeneous results reported by two studies in different groups were not discussed by the study authors [30, 34] but might be caused by effect modifications.

While a possible effect of volume on early neonatal mortality was found to be consistent when statistical significance was reached, the influence of birth volume on other outcomes was less consistent. The reason for these inconsistencies has to be discussed. It could be assumed, that inconsistencies can be explained at a systemic level reflecting differences between national health care systems with variations in budgeting, access, geographical and historical conditions. One study included in this review showed differences of caesarean sections in dependence to hospital birth volume [36]. Several explanations could be discussed. It is possible that this could be an effect of perinatal regionalization treating high risk pregnancies in high birth volume hospitals leading into the need of surgical birth interventions. On the other hand, the appropriateness and need for the indication of e.g. epidural anesthesia was also discussed with reference to hospital ownership [15]. However, to further analyze the sensitive topic of appropriateness, qualitative research with primary data is needed. Due to the lack of detail information and

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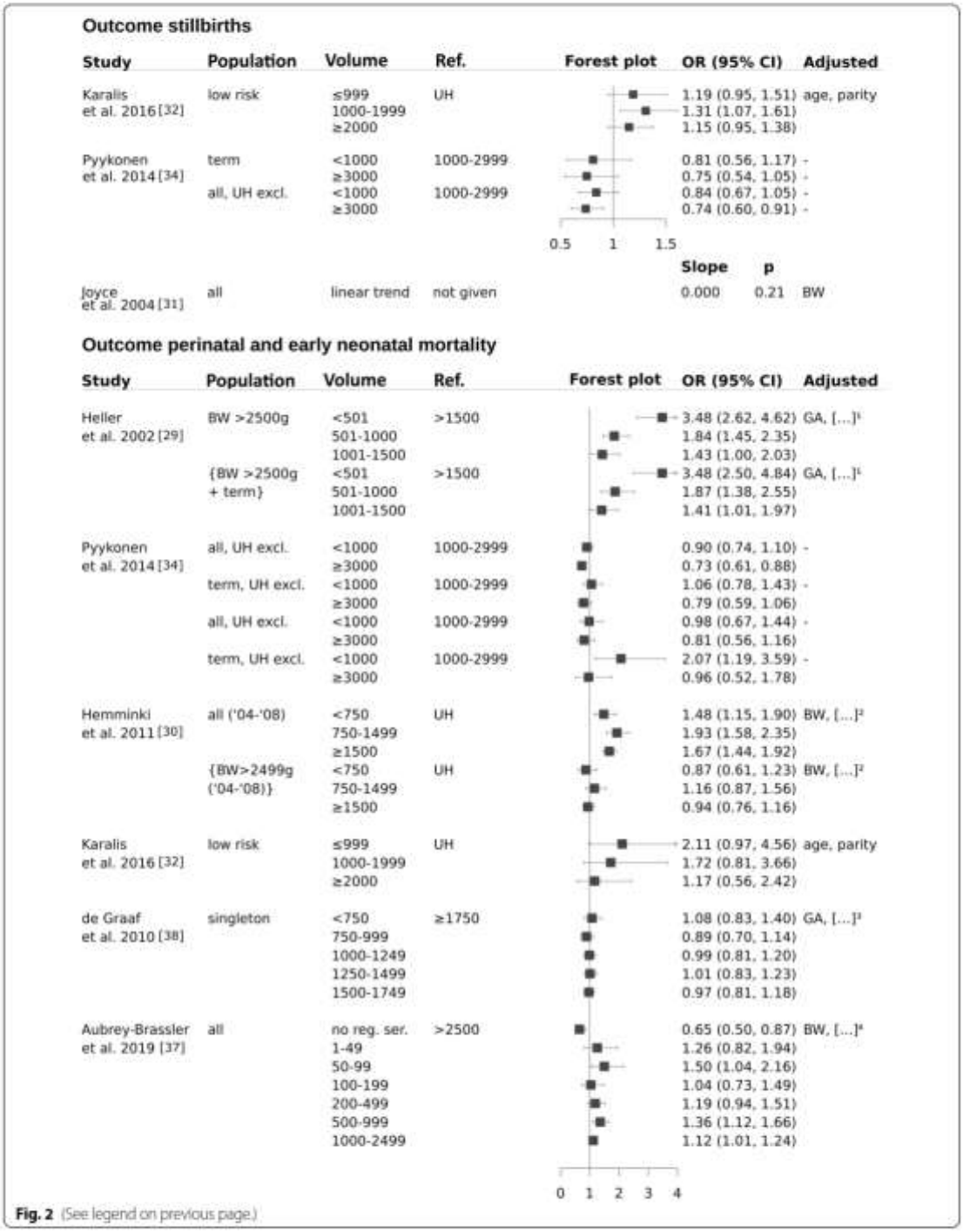
Fig. 2 Stillbirths and early/ perinatal mortality. Legend: [...][1] BW, age, parity, born outside clinic, birth planned and documented clinic, mode of delivery, born before arrival at clinic, time of birth, congenital anomaly/ malformation. [...][2] age, parity, socio-economic position. [...][3] age, parity, mode of delivery, ethnicity, calendar year trend. [...][4] gender, Eclampsia, Premature rupture of membranes, Oligohydramnios, Abruptio placentae, Prolapsed umbilical cord, Noxious influences transmitted via placenta/ breast milk, Congenital anomalies, Hydrops fetalis, Other maternal conditions



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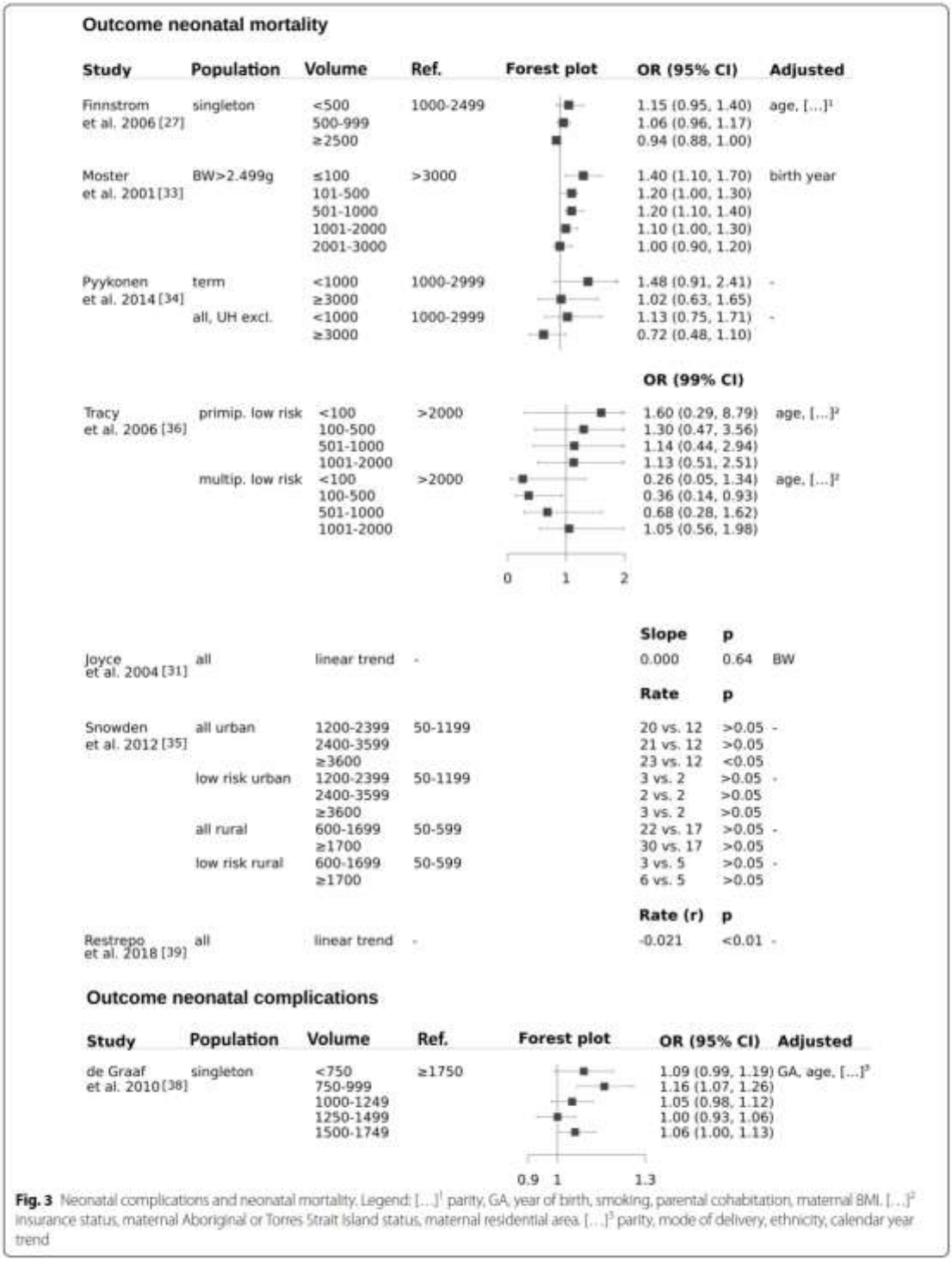

Fig. 3 Neonatal complications and neonatal mortality. Legend: [...]¹ parity, GA, year of birth, smoking, parental cohabitation, maternal BMI. [...]² insurance status, maternal Aboriginal or Torres Strait Island status, maternal residential area. [...]³ parity, mode of delivery, ethnicity, calendar year trend

data quality, routine data must be used with caution in order to avoid over- or misinterpretation [73].

With respect to a risk appropriate care, perinatal regionalization policies vary in terms of general organization, obligation and practice [2, 3]. At the provider level birth/delivery volumes may be only one covariate between several others such as time of birth, [38, 39, 70] personnel and material resources, [31, 32, 74] work environment [75] or qualifications [76] influencing the outcome of newborns indicated by studies included in this review.

Despite of lower early neonatal mortality in hospitals with high annual birth volume, closure of low volume institutions has to be considered very carefully, since reults have been discussed controversially. Some studies suggest a higher rate of unplanned out-of-hospital births [77] and an increased rate of neonatal mortality and stillbirths immediately after closures [58]. Furthermore, an increased rate of adverse birth outcomes [78] and higher stress/ anxiety levels of pregnant women were reported in large rural landscapes with long distances to access perinatal care [79]. Other studies report significantly lower rates of stillbirths and neonatal mortality in both rural and urban regions after closing maternity units [41].

The heterogeneous definitions identified in this and other systematic reviews [80] support the need for a standardized terminology of outcomes, populations and volume-thresholds. The definition of core-outcome sets (COS) would help to overcome that issue. The uniform terminology enables the design of comparable studies and forms the basis for the development of an international perinatal register. A homogeneously created perinatal register would allow individual patient data meta-analyses providing promising results as it has been shown for other indications [81, 82].

Overall most (12/13) of the included studies showed an "acceptable" quality as it is the highest rating for retrospective studies [26]. One study lacked an illustrated comparability of the study groups that led to "unacceptable" quality as it strongly limits transparency. None of the studies blinded the assesors nor was a report of non-blinding included. Nevertheless, we considered the studies as meaningful for interpretation because the assessed outcomes are difficult to manipulate and therefore the lack of blinding seems to be a minor weakness.

Strengths and Limitations

This is the first systematic review explicitly assessing birth volume effects on neonatal outcome in low risk births. The review used transparent methods (independent screening, search strategy), was officially registered, is based on two major databases (combined with extensive hand search and expert panel for highlighting relevant literature) and followed common critical appraisal requirements of systematic reviews determined by AMSTAR 2 [83]. The high inter-rater-reliability ensures comprehensibility. The time and national restriction in the inclusion criteria could be interpreted as a limitation. However, it is well known that international comparisons must take into account the efficacy of health care systems [84, 85]. Thus, we used neonatal mortality rates as an indicator of this efficacy. With respect to the time restriction starting with publication in 2000, this review considered the decline of neonatal mortality and the development of perinatal care in since 1990 [86]. On the other hand, some of the studies have long past study periods (1967–2012) and intervals (1 to 29 years), indicating that the publication date did not work perfectly well as a delimiter to represent only current perinatal care. Almost every study showed an "acceptable" quality with retrospectively collected routine or register data.

Conclusion

The aim of that review was originally to investigate volume-outcome associations in a comparatively low-risk birth cohort. With the exception of 7-day mortality, the review revealed heterogeneous results and major differences in the conception and definitions of the included studies.The qualitative synthesis of the studies indicated increased rates of early neonatal mortality (< 7d) in hospitals with birth volumes below 1000 or 500 births per anno when statistical significance was given. With respect to stillbirths, neonatal mortality, maternal mortality, caesarean section and neonatal and maternal complications the studies included reported inconclusive or insignificant results. Referring to the heterogeneously conducted study concepts in terms of assessed populations, volume-thresholds and outcomes, we recommend the development and use of internationally consented core-outcome sets to provide a homogenous definitional basis in future studies. A uniform

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Fig. 4 Maternal mortality, maternal complications and caesarean sections. Legend: […]1: race, hospital, year, comorbidity index, insurance status, household income, hospital teaching, hospital bed size, hospital region, hospital ownership, hospital location. […]2: GA, CS, Median income, Education rate, Aboriginal population, Unemployment rate, Minority, Statistical area classification, Travel Distance, Delivery hospital volume, Hospital level, HIV, Type 1/2 DM, Gestational/ other/ unspecified DM, Cystic fibrosis, Rheumatic heart disease, Hypertension, ischemic heart disease, Pulmonary hypertension, SLE, Chronic renal disease, Twins/ multiple gestation, Previous CS. […]3: race, hospital, year, comorbidity index, insurance status, household income, hospital teaching, hospital bed size, hospital region, hospital ownership, hospital location. […]4: insurance status, maternal Aboriginal or Torres Strait Island status, maternal residential area. […]5: parity, smoking, socio-economic position

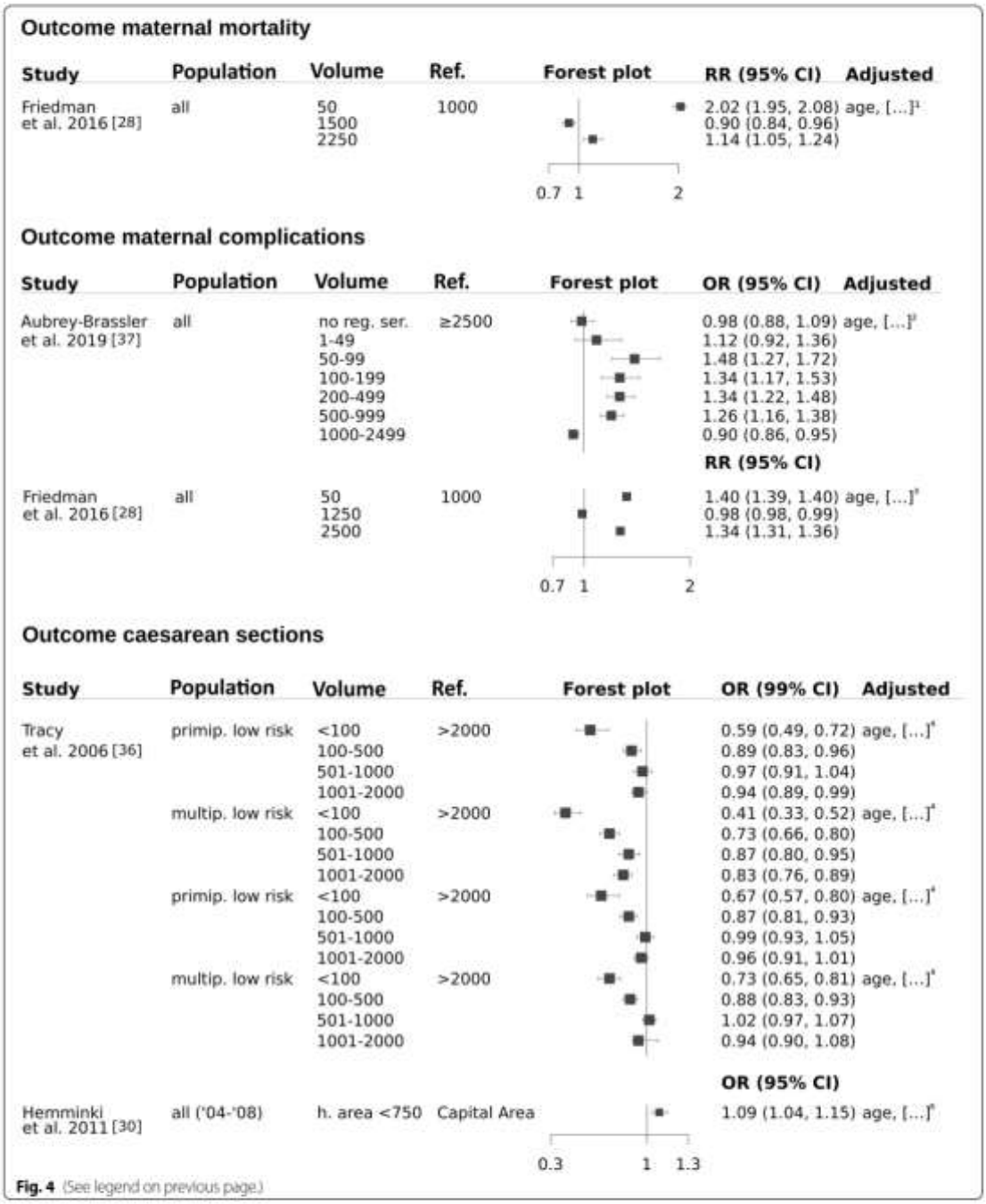

Fig. 4 (See legend on previous page.)

terminology would enable a homogenously conceived internationally birth register for individual patient data meta analyses. Based on these data, strengths and weaknesses of different perinatal settings could be investigated using a common terminology of population, volume and outcome.

Abbreviations
AUS: Australia; B-A: Before-After-Design; BMI: Body mass index; BW: Birth weight; CA: Canada; CI: Confidence interval; CS: Caesarean sections; d: Days; DM: Diabetes mellitus; FIN: Finland; GER: Germany; GA: Gestational age; h: Hospital; HIV: Humane immunodeficiency virus; NICU: Neonatal intensive care unit; NO: Norway; OR: Odds ratio; sv. morb: Severe morbidity; RR: Relative risk; p.a: Per anno; POR: Portugal; SCD: Sudden cardiac death; SIDS: Sudden infant death syndrome; SWE: Sweden; SLE: Systemic lupus erythematosus; UH: University hospital; wk: Week; UK: United Kingdom; US: United States.

Supplementary Information

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Additional file 1.
Additional file 2.
Additional file 3.
Additional file 4.
Additional file 5.

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Authors' contributions
JS, JM and FW conceptualised the review. FW developed the search strategy. FW, DK and AB performed the literature search, data collection and analysis. FW drafted the manuscript. MR and JS contributed to the data synthesis and interpretation. All authors contributed substantially to the production and editing of the final manuscript. The author(s) read and approved the final manuscript.

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Declarations

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N/A

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Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

Additional file 1 - Search strategy per database

	Medline: 4475 Records	**Embase: 6448 Records**
1	Meta-Analysis as Topic/ or meta analy$.tw. or metaanaly$.tw. or Meta-Analysis/ or (systematic adj (review$1 or overview$1)).tw. or exp Review Literature as Topic/	exp Meta Analysis/ or ((meta adj analy$) or metaanalys$).tw. or (systematic adj (review$1 or overview$1)).tw.
2	(cochrane or embase or (psychlit or psyclit) or (psychinfo or psycinfo) or (cinahl or cinhal) or science citation index or bids or cancerlit).ab.	cancerlit.ab. or cochrane.ab. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (psychinfo or psycinfo).ab. or (cinahl or cinhal).ab. or science citation index.ab. or bids.ab
3	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	reference lists.ab.or bibliograph$.ab. or hand-search$.ab. or manual search$.ab. or relevant journals.ab. or relevant articles.ab. or relevant studies.ab.
4	(selection criteria or data extraction).ab. and Review/	(data extraction.ab. or selection criteria.ab. or inclusion criteria.ab.) and review.pt.
5	(comment/ or letter/ or Editorial/ or animal/) not (animal/ and human/)	letter.pt.or editorial.pt. or animal/ not (animal/ and human/)
6	1 or 2 or 3 or 4	1 or 2 or 3 or 4
7	6 not 5	6 not 5
8	infant/ or infant, newborn/ or parturition/ or natural childbirth/ or term birth/ or Birth Weight/ or (term birth or normal birth or normal birth weight or normal birthweight or low risk birth).ti. or (term birth or normal birth or normal birth weight or normal birthweight or low risk birth).ab.	infant/ or newborn/ or birth weight/ or high birth weight/ or term birth/ or childbirth/ or natural childbirth/ or (term birth or normal birth or normal birth weight or normal birthweight or low risk birth).ti. or (term birth or normal birth or normal birth weight or normal birthweight or low risk birth).ab.
9	((perinatal* or matern* or obstetric* or newborn* or neonatal*) AND (care or hospital$ or unit or facility)).ti. or ((perinatal* or matern* or obstetric* or newborn* or neonatal*) and (care or hospital$ or unit or facility)).ab. or nicu.ti. or nicu.ab. or (neonatal and icu).ti. or (neonatal and icu).ab. or perinatal care/ or neonatal intensive care unit/	((perinatal* or matern* or obstetric* or newborn* or neonatal*) AND (care or hospital$ or unit or facility)).ti. or ((perinatal* or matern* or obstetric* or newborn* or neonatal*) and (care or hospital$ or unit or facility)).ab. or nicu.ti. or nicu.ab. or (neonatal and icu).ti. or (neonatal and icu).ab. or perinatal care/ or postnatal care/ or prenatal care/ or neonatal intensive care unit/ or pediatrics/ or neonatology/ or obstetrics/ or perinatology/
10	(region$ or central$ or urban or rural or Volume$ or size or level or type or caseload or case load).ti. or (region$ or central$ or urban or rural or Volume$ or size or level or type or caseload or case load).ab. or health facility size/ or hospitals, high-volume/ or hospitals, low-volume/ or hospitals, public/ or hospitals, rural/ or hospitals, maternity/ or hospitals, pediatric/	(region$ or central$ or urban or rural Volume$ or size or level or type or caseload or case load).ti. or (region$ or central$ or urban or rural Volume$ or size or level or type or caseload or case load).ab. or regionalization/ or high volume hospital/ or low volume hospital/
11	hospital mortality/ or infant mortality/ or mortality/ or newborn mortality/ or prenatal mortality/ or perinatal mortality/ or fetus mortality/ or maternal mortality/ or ((neonatal* or perinatal* or matern*) and (death or mortality)).ti. or ((neonatal* or perinatal* or matern*) and (death or mortality)).ab.	hospital mortality/ or mortality/ or perinatal mortality/ or newborn mortality/ or fetus mortality/ or premature mortality/ or prenatal mortality/ or maternal mortality/ or ((neonatal* or perinatal* or matern*) and (death or mortality)).ti. or ((neonatal* or perinatal* or matern*) and (death or mortality)).ab.
12	8 AND 9 AND 10 not 7 or (case reports/ or clinical conference/ or consensus development conference/ or consensus development conference, nih/ or validation studies/) (Filter 2000, english/ german)	(8 and 9 and 10 and 11) not (7 or case report/ or consensus development/ or practice guideline/ or in vitro study/ or preclinical study/ or in vivo study/ or validation study/ or case study/ (Filter 2000, english/ german)

Additional file 2 - Methods and definitions using CASP checklist for cohort studies

Item 1.1 adresses the presence of a suitable and clearly focused reseach question as it is necessary to assess the relevance and value of the reported results.

Due to a possible selection bias, the study groups should have as similar characteristics as possible to guarantee a comparability (1.2) and the study needs to report the proportion of invited and participating participants for the entire study and study arm (1.3).

Item 1.4 queries the probability or the performing of sensitivity analyses that a participant already has the result at the beginning of the study to identify performance bias.

To address a possible attrition bias item 1.5 and 1.6 query the drop-out and lost to follow-up-rates to detect a possible violation of a representative study sample.

The items 1.7 to 1.12 deal with a transparent and consistent execution of the study with regard to a possible detection bias. This includes clearly defined and consequently measured outcomes (1.7), blinding (1.8) and the reported influence of non-blinding (1.9). To detect the influence of non-blinding a study process analysis (e.g. number of observations, observators) is recommended. In terms of measurement of exposure level, the measurement method should be comprehensibly reported (1.10.) and the measurement itself should be carried out multpiple times (1.12). With regard to the study results, a valid presentation must include a traceable/referenced measurement (1.11), identify and statistically consider possible confounders (1.13) and report confidence intervals (1.14). These items are crucial for the validity, bias and reliability of the outcomes presented.

It should be taken into account that the items 1.3, 1.5, 1.6 and 1.12 are only queried for prospective studies. Consequently, only prospective studies can receive a "high quality" rating, since all criteria must be fulfilled for this rating.[26] An “acceptable” quality was given if at least item 1.1 and 1.2 were fulfilled with regards to a minimum standard of replicability and transparency. Otherwise the study was rated with “unacceptable” quality.

Additional file 3 - Excluded studies with reasons

Reference	Reason f. Exclusion
Adams N, Tudehope D, Gibbons KS, Flenady V: Perinatal mortality disparities between public care and private obstetrician-led care: a propensity score analysis. BJOG : an international journal of obstetrics and gynaecology 2018, 125(2):149-158.	No volume-outcome
Allen VM, Jilwah N, Joseph KS, Dodds L, O'Connell CM, Luther ER, Fahey TJ, Attenborough R, Allen AC: The influence of hospital closures in Nova Scotia on perinatal outcomes. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 2004, 26(12):1077-1085.	No volume-outcome
Badheka A, Rampa S, Wang T, Nalliah R, Caplin J, Allareddy V: Neonatal infections in Hospitals: Nationwide prevalence and outcomes. Critical Care Medicine 2019, 47(1 Supplement 1).	No mortality measured
Clapp MA, James KE, Bates SV, Kaimal AJ: Patient and Hospital Factors Associated With Unexpected Newborn Complications Among Term Neonates in US Hospitals. JAMA network open 2020, 3(2):e1919498.	No mortality measured
Engjom H, Morken NH, Hoydal E, Norheim OF, Klungsoyr K: Obstetric health system structure and perinatal outcomes in Norway. International Journal of Gynecology and Obstetrics 2015, 131(SUPPL. 5):E487-E488.	Conference Abstract
Engjom H, Moster D, Morken NH, Hoydahl E, Norheim OF, Klungsoyr K: Perinatal mortality and health system structure in Norway-a population-based registry study. BJOG: An International Journal of Obstetrics and Gynaecology 2016, 123(Supplement 2):11.	Conference Abstract
Filipovic-Grcic B, Kniewald H, Rodin U, Grizelj R, Stipanovic-Kastelic J, Ninkovic D, Gveric-Ahmetasevic S, Stanojevic M, Furlan IA, Peter B et al: Patterns of newborns' deaths to discharge from hospital in Croatia in the year 2011. Gynaecologia et Perinatologia 2012, 21(SUUPL.1):150-156.	Croatian language
Grytten J, Monkerud L, Skau I, Sorensen R: Regionalization and local hospital closure in Norwegian maternity care--the effect on neonatal and infant mortality. Health services research 2014, 49(4):1184-1204.	No volume-outcome
Heller G, Schnell R, Richardson DK, Misselwitz B, Schmidt S: [Assessing the impact of delivery unit size on neonatal survival: estimation of potentially avoidable deaths in Hessen, Germany, 1990-2000]. Hat die Grosse der Geburtsklinik Einfluss auf das neonatale Uberleben? Schatzung von "vermeidbaren" Todesfallen in Hessen 1990-2000 2003, 128(13):657-662.	Descriptive study
Homer CSE, Thornton C, Scarf VL, Ellwood DA, Oats JJN, Foureur MJ, Sibbritt D, McLachlan HL, Forster DA, Dahlen HG: Birthplace in New South Wales, Australia: an analysis of perinatal outcomes using routinely collected data. BMC pregnancy and childbirth 2014, 14:206.	No Comparison of hospitals
Hughes S, Zweifler JA, Garza A, Stanich MA: Trends in rural and urban deliveries and vaginal births: California 1998-2002. The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association 2008, 24(4):416-422.	No Comparison of hospitals
Hurtado Suazo JA, Demestre Guasch X, Garcia Reymundo M, Ginovart Galiana G, Gimenez A, Calvo Aguilar MJ, Trincado Aguinagalde MJ, Fernandez Colomer B: Comparison of perinatal data between a cohort of Spanish late preterm babies and another of term newborns. Journal of Perinatal Medicine 2015, 43(SUPPL. 1).	Conference Abstract
Iglesias S, Bott N, Ellehoj E, Yee J, Jennissen B, Bunnah T, Schopflocher D: Outcomes of maternity care services in Alberta, 1999 and 2000: a population-based analysis. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 2005, 27(9):855-863.	No Comparison of hospitals
Karalis E, Gissler M, Tapper AM, Ulander VM: Influence of time of delivery on risk of adverse neonatal outcome in different size of delivery units: a retrospective cohort study in Finland. Journal of Maternal-Fetal and Neonatal Medicine 2019, 32(10):1696-1702.	Full-text not available
Koch R, Gmyrek D, Vogtmann C: [Risk adjusted assessment of quality of perinatal centers - results of perinatal/neonatal quality surveillance in Saxonia]. Risikoadjustierte Qualitatsbeurteilung in Perinatalzentren ausgehend von der Perinatal- und Neonatalerhebung in Sachsen 2005, 209(6):210-218.	No Comparison of hospitals
Kozhimannil KB, Interrante JD, Henning-Smith C, Admon LK: Rural-Urban Differences In Severe Maternal Morbidity And Mortality In The US, 2007-15. Health affairs (Project Hope) 2019, 38(12):2077-2085.	No volume-outcome
Krzyzak M, Maslach D, Piotrowska K, Charkiweicz AE, Szpak A, Karczewski J: Perinatal mortality in urban and rural areas in Poland in 2002-2012. Przeglad epidemiologiczny 2014, 68(4):675-679.	No Comparison of hospitals
Lesniczak B, Krasomski G, Rudnicka B, Piekarska E, Oszukowski P, Wozniak P: The perinatal mortality of fetuses and neonates in Poland in the years 1960-2010. Ginekologia i Poloznictwo 2015, 36(2):40-45.	No Comparison of hospitals
Lorch SA, Srinivas SK, Ahlberg C, Small DS: The impact of obstetric unit closures on maternal and infant pregnancy outcomes. Health services research 2013, 48(2 Pt 1):455-475.	No volume-outcome

Neto MT: Perinatal care in Portugal: effects of 15 years of a regionalized system. Acta paediatrica (Oslo, Norway : 1992) 2006, 95(11):1349-1352.	Descriptive study
Parazzini F, Cipriani S, Bulfoni G, Bulfoni C, Bellu R, Zanini R, Mosca F: Mode of delivery and level of neonatal care in Lombardy: a descriptive analysis according to volume of care. Italian journal of pediatrics 2015, 41:24.	No mortality measured
Payne JC, Campbell MK, DaSilva O, Koval J: Perinatal mortality in term and preterm twin and singleton births. Twin research : the official journal of the International Society for Twin Studies 2002, 5(4):260-264.	No volume-outcome
Poeran J, Borsboom GJJM, de Graaf JP, Birnie E, Steegers EAP, Mackenbach JP, Bonsel GJ: Does centralisation of acute obstetric care reduce intrapartum and first-week mortality? An empirical study of over 1 million births in the Netherlands. Health policy (Amsterdam, Netherlands) 2014, 117(1):28-38.	Modelling
Ravelli ACJ, Tromp M, van Huis M, Steegers EAP, Tamminga P, Eskes M, Bonsel GJ: Decreasing perinatal mortality in The Netherlands, 2000-2006: a record linkage study. Journal of epidemiology and community health 2009, 63(9):761-765.	No Comparison of hospitals
Reid LD, Creanga AA: Severe maternal morbidity and related hospital quality measures in Maryland. Journal of Perinatology 2018, 38(8):997-1008.	No mortality measured
Shuvalova MP, Yarotskaya EL, Pismenskaya TV, Dolgushina NV, Baibarina EN, Sukhikh GT: Maternity Care in Russia: Issues, Achievements, and Potential. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 2015, 37(10):865-871.	Descriptive study
Treurniet HF, Looman CW, van der Maas PJ, Mackenbach JP: Regional trend variations in infant mortality due to perinatal conditions in the Netherlands. European journal of obstetrics, gynecology, and reproductive biology 2000, 91(1):43-49.	No Comparison of hospitals
Harvey SM, Oakley LP, Yoon J, Luck J: Coordinated Care Organizations: Neonatal and Infant Outcomes in Oregon. Medical Care Research and Review 2019, 76(5):627-642.	Perinatal Regionalization
Merlo J, Gerdtham U-G, Eckerlund I, Hakansson S, Otterblad-Olausson P, Pakkanen M, Lindqvist P-G: Hospital level of care and neonatal mortality in low- and high-risk deliveries: reassessing the question in Sweden by multilevel analysis. Medical care 2005, 43(11):1092-1100.	Perinatal Regionalization
Serenius F, Winbo I, Dahlquist G, Kallen B: Cause-specific stillbirth and neonatal death in Sweden: a catchment area-based analysis. Acta paediatrica (Oslo, Norway : 1992) 2001, 90(9):1054-1061.	Perinatal Regionalization

Additional file 4 - Information on funding, conflict of interest and datasources within the included studies

Ref.	Funding	CoI	Datasources
Finnstrom et al. 2006[27]	N/A	N/A	Swedish Medical Birth Registry and the Hospital Discharge Registry
Friedman et al. 2016[28]	public	n	Nationwide Inpatient Sample (NIS)
Heller et al. 2002[29]	N/A	N/A	perinatal birth register
Hemminki et al. 2011[30]	no grant received	n	medical birth register data
Joyce et al. 2004[31]	N/A	N/A	Office for National Statistics (ONS) birth and death registrations, the 1991 Census, Royal College of Obstetricians and Gynaecologists (RCOG) hospital recognition returns, Department of Health (DOH) data on hospital staffing levels, survey of risk management practices in Thames maternity units
Karalis et al. 2016[32]	no grant received	n	National Medical Birth Register
Moster et al. 2001[33]	public	N/A	The Norwegian Medical Birth Registry
Pyykonen et al. 2014[34]	no grant received	n	Medical Birth Register data
Snowden et al. 2012[35]	N/A	n	linked birth/infant death certificates with hospital discharge diagnoses for births
Tracy et al. 2006[36]	public	n	National Perinatal Data Collection (NPDC)
de Graaf et al. 2010[38]	no grant received	none	Netherlands Perinatal Registry, a linked professional database of all pregnancies, of 20 weeks and above, in the Netherlands, collected from (referring) midwives, obstetricians and paediatricians.
Restrepo et al. 2018 [39]	public	none	electronic birth certificate records matched with 92 death certificate records from the Texas Department of State Health Services
Aubrey-brassler et al. 2019[37]	public	none	maternal and neonatal delivery hospitalization records were accessed from the Canadian Institute for Health Information (CIHI)

Notes: BMI: body mass index d: days

Additional file 5 Methods and definitions of the outcomes assessed

REFERENCE	OUTCOME DEFINITION	POPULATION	GROUPED HOSPITAL VOLUME	ESTIMATOR	ADJUSTED
STILLBIRTHS					
Karalis et al. 2016[32]	-	low risk	births: ≤999, 1000-1999, ≥2000, UH (ref.)	OR (95% CI)	age, parity
Pyykonen et al. 2014[34]	>22wk GA	term + all (UH excl.)	women: <1000, 1000-2999 (ref.), <3000	OR (95% CI)	-
Joyce et al. 2004[31]	>24wk GA	all	births: Mean/ year (no reference volume)	Slope	BW
PERINATAL/ EARLY NEONATAL MORTALITY					
Heller et al. 2002[29]	≤7d	BW >2500g, BW >2500g + term	births: ≤500, 501-1000, 1001-1500, >1500 (ref.)	OR (95% CI)	GA, BW, age, parity, born outside clinic, birth planned and documented clinic, mode of delivery, born before arrival at clinic, time of birth, congenital anomaly/ malformation
Pyykonen et al. 2014[34]	Stillbirth/death≤7d, death≤7d	All + term, UH excl.	women: <1000, 1000-2999 (ref.), <3000	OR (95% CI)	-
Hemminki et al. 2011[30]	≤7d	all, BW>2499g	births: <750, 750-1499, ≥1500, UH (ref.)	OR (95% CI)	BW, age, parity, socio-economic position
Karalis et al. 2016[32]	-	low risk	births: ≤999, 1000-1999, ≥2000, UH (ref.)	OR (95% CI)	age, parity
de Graaf et al. 2010[38]	≤7d	Singleton	women: <750, 750-999, 1000-1249, 1250-1499, 1500-1749, ≥1750 (ref.)	OR (95% CI)	GA, age, parity, mode of delivery, ethnicity, calendar year trend
Aubrey-Brassler et al. 2019[37]	in-hospital, stillbirth (GA≤20wk), SIDS, SCD	All	women: No services usually; 1-49; 50-99; 100-199; 200-499; 500-999; 1000-2499, >2500 (ref.)	OR (95% CI)	BW, gender, Eclampsia, Premature rupture of membranes, Oligohydramnios, Abruptio placentae, Prolapsed umbilical cord, Noxious influences transmitted via placenta/ breast milk, Congenital anomalies, Hydrops fetalis, Other maternal conditions,
NEONATAL MORTALITY					
Finnstrom et al. 2006[27]	≤27d	Singleton	births: <500, 500-999, 1000-2499 (ref.), ≥2500	OR (95% CI)	age, parity, GA, year of birth, smoking, parental cohabitation, maternal BMI
Moster et al. 2001[33]	≤28d	BW>2.499g	births: ≤100, 101-500, 501-1000, 1001-2000, 2001-3000, >3000 (ref.)	OR (95% CI)	birth year
Pyykonen et al. 2014[34]	≤28d	term, all, UH excl.	women: <1000, 1000-2999 (ref.), <3000	OR (95% CI)	-
Tracy et al. 2006[36]	≤28d	Primip. low risk, multip. low risk	births: <100, 100-500, 501-1000, 1001-2000 >2001 (ref.)	OR (99% CI)	age, insurance status, maternal Aboriginal or Torres Strait Island status, maternal residential area
Joyce et al. 2004[31]	≤28d	All	births: Mean/ year (no reference volume)	Slope	BW
Snowden et al. 2012[35]	-	Urban: all, low risk rural: all, low risk	women: Urban: ≤50-1199 (ref.), 1200-2399, 2400-3599; ≥3600 Rural: 50-599 (ref.) 600-1699; ≥1700	Rate	-
Restrepo et al. 2018[39]	≤28d	All	births: linear trend (no reference volume)	Pearson test	-
NEONATAL COMPLICATIONS					
de Graaf et al. 2010[38]	Stillbirth/ death≤7d, 5-min. Apgar<7, NICU transfer	Singleton	women: <750, 750-999, 1000-1249, 1250-1499, 1500-1749, ≥1750 (ref.)	OR (95% CI)	GA, age, parity, mode of delivery, ethnicity, calendar year trend

MATERNAL MORTALITY					
Friedman et al. 2016[28]	failed rescue	all	women: 50, 1000 (ref.), 1500, 2250	RR (95 % CI)	age, race, hospital, year, comorbidity index, insurance status, household income, hospital teaching, hospital bed size, hospital region, hospital ownership, hospital location
MATERNAL COMPLICATIONS					
Aubrey-Brassler et al. 2019[37]	Eclampsia, Previa with hemorrhage abruption, Intrapartum + postpartum hemorrhage + transfusion or hysterectomy, Rupture of uterus before or during labor, Obstetric shock, Sepsis, Other complications of obstetric procedures, Obstetric embolism, Cardiovascular disease, Acute renal failure, Death, obstetric or unspecified, Neurologic disease, Hematologic disease, Respiratory disease, Diabetic ketoaci-dosis, Peritonitis or parametritis, Toxic liver disease or hepatic failure, Canadian Classification of Health Interventions, Assisted ventilation or resuscitation, Dialysis, Hysterectomy, Evacuation of incisional hemato-ma, Repair of bladder, urethra or intestine, Embolization or ligation of pelvic vessels or suturing of uterus, Blood transfusion	all	women: No services usually; 1-49; 50-99; 100-199; 200-499; 500-999; 1000-2499, >2500 (ref.)	OR (95% CI)	age, GA, CS, Median income, Education rate, Aboriginal population, Unemployment rate, Minority, Statistical area classification, Travel Distance, Delivery hospital volume, Hospital level, HIV, Type 1/2 DM, Gestational/ other/ unspecified DM, Cystic fibrosis, Rheumatic heart disease, Hypertension, Ischemic heart disease, Pulmonary hypertension, SLE, Chronic renal disease, Twins/ multiple gestation, Previous CS
Friedman et al. 2016[28]	heart/ renal/ respiratory failure, acute myocardial infarction, liver disease, disseminated intravascular coagulation, coma, delirium, puerperal cerebrovascular disorders, pulmonary edema or embolism, sepsis, shock, status asthmaticus, status epilepticus.	all	women 50, 1250 2500	RR (95 % CI)	age, race, hospital, year, comorbidity index, insurance status, household income, hospital teaching, hospital bed size, hospital region, hospital ownership, hospital location
CAESAREAN SECTIONS					
Tracy et al. 2006[36]	labour, all	Primip. low risk, multip. low risk	births: <100, 100-500, 501-1000, 1001-2000 >2001 (ref.)	OR (99% CI)	age, insurance status, maternal Aboriginal or Torres Strait Island status, maternal residential area
Hemminki et al. 2011[30]	-	all	h. area <750 births p.a., capital area (ref.)	OR (95% CI)	age, parity, smoking, socio-economic position

4.2 Publikation (2): The relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: Cross-sectional evidence from a nationwide sample of 232 German hospitals

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Relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: cross-sectional evidence from a nationwide sample of 232 German hospitals

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ABSTRACT

Objectives Studies analysing colorectal resections usually focus on a specific outcome (eg, mortality) and/or specific risk factors at the individual (eg, comorbidities) or hospital (eg, volume) level. Comprehensive evidence across different patient safety outcomes, risk factors and patient groups is still scarce. Therefore the aim of this analysis was to investigate consistent relationships between multiple patient safety outcomes, healthcare and hospital risk factors in colorectal resection cases.

Design Cross-sectional study.

Setting German inpatient routine care data of colorectal resections between 2016 and 2018.

Participants We analysed 54 168 colon resection and 20 395 rectum resection cases treated in German hospitals. The German Inpatient Quality Indicators were used to define colon resections and rectum resections transparently.

Primary outcome measures Additionally to in-hospital death, postoperative respiratory failure, renal failure and postoperative wound infections we included multiple patient safety outcomes as primary outcomes/dependent variables for our analysis. Healthcare (eg, weekend surgery), hospital (eg, volume) and case (eg, age) characteristics served as independent covariates in a multilevel logistic regression model. The estimated regression coefficients were transferred into ORs.

Results Weekend surgery, emergency admissions and transfers from other hospitals were significantly associated (ORs ranged from 1.1 to 2.6) with poor patient safety outcome (ie, death, renal failure, postoperative respiratory failure) in colon resections and rectum resections. Hospital characteristics showed heterogeneous effects. In colon resections hospital volume was associated with insignificant or adverse associations (postoperative wound infections: OR 1.168 (95% CI 1.030 to 1.325)) to multiple patient safety outcomes. In rectum resections hospital volume was protectively associated with death, renal failure and postoperative respiratory failure (ORs ranged from 0.7 to 0.8).

Conclusions Transfer from other hospital and emergency admission are constantly associated with poor patient safety outcome. Hospital variables like volume, ownership or localisation did not show consistent relationships to patient safety outcomes.

Trial registration number ISRCTN10188560.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Large and current sample providing a broad span of cases, hospital types, ownerships and locations.
⇒ Comprehensive analysis of multiple patient safety outcomes and multiple sets (case, healthcare, hospital) of risk factors.
⇒ Use of previously validated outcomes that were reported to occur most likely during hospitalisation.
⇒ Accounting data lack information on patient history, medication, length of anaesthesia, staff-to-patient ratios, surgeon volumes, centralisation and which of the coded diagnoses had been present on admission.

INTRODUCTION

Measuring, assuring and improving patient safety are important objectives regarding patient outcome, payment and accreditation in colorectal resections. One of the most frequently used outcome indicator in colorectal resections is in-hospital mortality.[1] However, it has been stressed that patient safety is reflected in both mortality and non-mortality outcomes.[2 3] Therefore the measurement of outcomes beyond mortality is necessary for a comprehensive assessment of patient safety and care quality.[3] Additionally various risk factors for a poor patient safety outcome were analysed in previous studies. Besides patient characteristics (eg, age, sex, comorbidities), especially the influence of

healthcare (eg, weekend surgery, emergency, transfer from other hospital) and hospital variables (eg, volume, urbanisation degree) were widely discussed. Weekend surgery,[4–6] emergency admission,[7 8] transfer from other hospitals[9–11] and case volume[12 13] were found to have significant effects on mortality in colorectal resections. Analogous to patient outcomes, previous studies usually considered only subsets of these risk factors without analysing them together.

A comprehensive analysis of patient safety and its covariates in colorectal resections should take multiple outcomes and multiple risk factors into account.[14] To our knowledge, such comprehensive analyses have rarely been reported. Based on that assumption, our analysis aimed to investigate whether healthcare and hospital characteristics are associated with multiple patient safety outcomes in colorectal resections. Using a 3-year sample (2016–2018) of German inpatient claims data we investigated relationships between case, healthcare and hospital characteristics and the patient safety outcomes in-hospital death, postoperative respiratory failure, renal failure and post-operative wound infections in colorectal resections.

MATERIALS AND METHODS

This explorative cross-sectional analysis was embedded into the IMPRESS study. The IMPRESS study was a cluster-randomised trial evaluating the effects of clinical peer review on mortality in patients ventilated >24 hours nested in a prospective cohort study of 232 participating hospitals. Details, baseline, explorative and confirmatory results of the IMPRESS study were published previously.[15–18] The study has been registered at ISCRTN.[19] The identification of possible covariates of mortality and non-mortality outcomes in colorectal resections was a secondary aim of the IMPRESS study.

Data sources

The data used in this study were derived from two routine data sets. We used claims data according to German law regulating inpatient claims data (§21 Krankenhausentgeltgesetz) to gather information concerning age, sex, reason of admission, discharge destination, diagnoses/comorbidities (International Classification of Diseases, 10th Revision - German Modification (ICD-10-GM)) and medical/surgical procedures (Operationen- und Prozedurenschlüssel (OPS) codes). We applied the predefined groups of the Elixhauser comorbidity index and its coding modifications for ICD-10 (online supplemental file S1) to adjust for relevant comorbidities. The Elixhauser comorbidity index is a score used to adjust for chronic or non-acute comorbidities in routine data sets.[20 21] To assess hospital characteristics (ownership, university hospital status, urbanisation) we used data from the German hospital register ('Deutsches Krankenhausverzeichnis').

Study participation and privacy

All participating hospitals submitted a written consent regarding participation prior to the start of the IMPRESS study. The data trust site at Koordinierungszentrum für Klinische Studien (KKS) Dresden ensured the anonymisation of the data. The Center for Evidence-Based Healthcare (ZEGV) Dresden analysed the anonymised data.

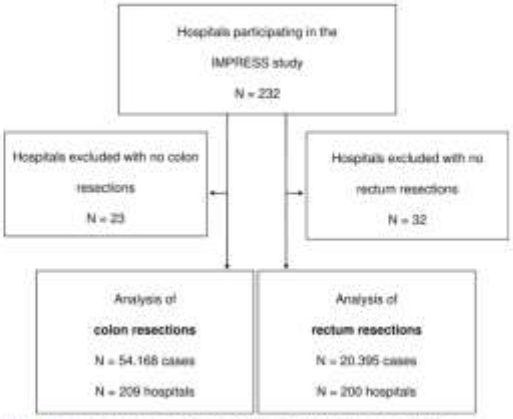

Figure 1 Flowchart of hospitals included for analysis.

Patient and public involvement

This cross-sectional analysis used observational routine data based on predefined outcomes and covariates without intervention and did not involve patients or the public in the design, conduct, reporting or dissemination plans of our research.

Population

Overall, 232 hospitals participated in the IMPRESS study (figure 1). We included all cases with a colon and/or rectum resection in the participating hospitals in 2016–2018. Due to anonymisation, the data do not contain a patient-relation. Therefore patients admitted more than once entered the analysis as multiple hospital cases. For each hospital case, all of the documented information in terms of diagnoses and medical/surgical procedures during hospitalisation was available. We used the definitions of the German Inpatient Quality Indicators to define and distinguish partial colon resections (online supplemental file S2), total colon resections (online supplemental file S3) and rectum resections (online supplemental file S4).[22] Hospitals without colon or rectum resections were excluded.

Outcomes and covariates

Following evidence from a previous study, in-hospital death, respiratory failure, renal failure and wound infection can be validly operationalised in hospital discharge data.[23] Hence, we analysed these outcomes in accordance with previously tested case definitions as presented in online supplemental file S5. The outcomes death, postoperative respiratory failure, renal failure and postoperative wound infections were selected as dependent variables.

The independent variables were classified into three groups:

1. Case (age, sex, Elixhauser comorbidities).[20 21]

2. Healthcare (admission date, surgical procedures/OPS codes, reason for admission, discharge destination).
3. Hospital (case volume, ownership, university hospital status, urbanisation degree rural/urban).

This study focused on healthcare and hospital variables. Case variables were primarily used for adjustment.

To adjust for all potentially relevant risk factors available in the data, the estimations included the full set of independent case, healthcare and hospital variables. Case level included age, sex and Elixhauser comorbidities.[23] Healthcare level included admission reason (referral/emergency case/transfer from other hospital), weekend surgery (identifiable via time stamp of the procedure) and total resection of the colon and resections of the colon and rectum. Hospital level included hospital case volume, degree of urbanisation (rural/urban), university hospital status and ownership (public/non-profit/private). Case volume entered the regression models in logarithmic form. This transformation of hospital volume data captures that volume-outcome relationships may be more pronounced at low case volumes.[24]

Statistical methods

We described case, healthcare and hospital characteristics using absolute and relative frequencies in case of categorical variables. For continuous variables, we reported median, first and third quartile. Relationships between patient safety outcomes and case-level, healthcare-level and hospital-level risk factors were estimated using multilevel logistic regression models. These models contained a random intercept at the hospital level to capture the correlation of patient outcomes within hospitals.[27] Estimations were conducted separately for cases with colon and rectum resection in bivariate and multivariate analyses. To improve interpretability of estimated effect sizes, we transformed the estimated regression coefficients into ORs. An estimated effect was considered statistically significant if its p value was below 5%. Statistical analysis was performed using Stata V.15.1.

Sensitivity analysis

In the preliminary research it became apparent that the literature distinguishes between colorectal cancer surgery and general colorectal resections.[1 12 13 26 27] Therefore, with respect to possible effect modifications, we explored differences between cases with and without a cancer diagnosis. The same applies to reported interactions between admission reason and the status of university hospitals compared with non-university hospitals.[16] Therefore we also reviewed these interactions to detect possible effect modifications.

RESULTS

Overall, 71 060 cases with colon and/or rectum resection were included in the analysis. Separating colon resections and rectum resections a total of 54 168 colon resection cases were treated in 209 hospitals. In total, 20 395 cases of rectum resections were treated in 200 hospitals. If both colon and rectum resection were documented (3503 cases), the case was analysed for both groups.

The minority of included cases received combined colorectal resections (partial and total colon, colon and rectum). Emergency case admission or transfer from other hospitals were less frequent than referral. Compared with rectum resections, colon resections were more often surgically treated on weekends (8.6% vs 3.8%), admitted as an emergency case (29.7% vs 18.3%) or transferred from other hospitals (3.5% vs 1.9%). The same applies to the rate of poor patient safety outcomes. Colon resection cases revealed higher rates of in-hospital death (9.6% vs 4.2%), postoperative respiratory failure (16.7% vs 12.2%), renal failure (15.2% vs 10.3%) and post-operative wound infections (11.3% vs 11.2%) than rectum resection cases.

The majority of the analysed hospitals were localised in urban regions (59%). Most were in private (40%) or public (40%) ownership. The annual median hospital case volume was 72 (Q1=38; Q3=116) for colon and 26 (Q1=11; Q3=42) for rectum resections.

The median age ranged from 67 to 68 years (table 1). Male and female sex in colon and rectum resections were approximately equally represented. For Elixhauser comorbidities, the most frequent codes were solid tumour without metastasis (colon: 47.3%, rectum: 67.0%), uncomplicated hypertension (colon and rectum: 47.6%) and fluid and electrolyte disorders (colon: 45.2%, rectum: 40.5%) in both procedure groups. Descriptive results for all Elixhauser comorbidities are presented in online supplemental file S6.

The bivariate analysis provided in online supplemental files S7 and S8 was performed to identify unadjusted effects of single covariates on the outcomes. The following multivariable analysis, focusing on healthcare and hospital level (tables 2 and 3), was performed to achieve adjusted and robust effects.

Healthcare covariates

Admission as an emergency case or transfer from another hospital were associated to multiple poor patient safety outcomes in both groups. For example, higher odds of in-hospital death were related to emergency admission in colon (OR 1.84 (95% CI 1.69 to 2.01) and rectum resections (OR 2.02 (95% CI 1.67 to 2.45) compared with referral hospital admissions. The same applies to transfer from other hospital, the odds of in-hospital death were higher in colon (OR 2.52 (95% CI 2.19 to 2.91)) and rectum resections (OR 2.67 (95% CI 1.87 to 3.82)). Except of postoperative wound infections, weekend surgery was associated with worsened patient safety outcome in both groups.

Hospital covariates

While most of the healthcare-level covariates showed similar associations in both groups, hospital covariates showed insignificant or heterogeneous effects.

A higher annual case volume of colon resections indicated a higher risk of postoperative wound infections (OR 1.16 (95% CI 1.03 to 1.32)). The remaining associations between annual case volume of colon resections

Table 1 Case and hospital characteristics of colon and rectum resections

	Colon resection		Rectum resection	
	n	% / Q1; Q3	n	% / Q1; Q3
Number of cases	54 168	(100.0)	20 395	(100.0)
Patient safety outcomes				
In-hospital death				
No	48 914	(90.31)	19 525	(95.73)
Yes	5254	(9.68)	870	(4.26)
Postoperative respiratory failure				
No	45 074	(83.21)	17 901	(87.77)
Yes	9094	(16.78)	2494	(12.22)
Renal failure				
No	45 920	(84.77)	18 279	(89.62)
Yes	8248	(15.22)	2116	(10.37)
Postoperative wound infections				
No	48 013	(88.63)	18 109	(88.79)
Yes	6155	(11.36)	2286	(11.20)
Healthcare characteristics				
Colon resection				
Total	2662	(4.91)	–	–
Partial	51 310	(94.72)	–	–
Both	196	(0.36)	–	–
Rectum resection				
No	50 665	(93.53)	–	–
Yes	3503	(6.46)	20 395	(100.00)
Colon and rectum resection				
No	50 665	(93.53)	16 892	(82.82)
Yes	3503	(6.46)	3503	(17.17)
Weekend surgery				
No	49 473	(91.33)	19 603	(96.11)
Yes	4695	(8.66)	792	(3.88)
Admission reason				
Referral	36 129	(66.69)	16 249	(79.67)
Emergency case	16 116	(29.75)	3744	(18.35)
Transfer from other hospital	1923	(3.55)	402	(1.97)
Hospital characteristics				
Hospitals included	209	(100.00)	200	(100.00)
Annual volume				
Colon resection cases (median)	72	(38; 119)	–	–
Total colon resection (median)	1	(0; 3)	–	–
Rectum resections (median)	–	–	26	(11; 42)
Urbanisation				
Urban	124	(59.33)	119	(59.50)
Tural	85	(40.66)	81	(40.50)
Ownership				
Public	82	(39.23)	80	(40.00)
Non-profit	41	(19.61)	39	(19.50)
Private	86	(41.14)	81	(40.50)
University hospital				
No	201	(96.17)	192	(96.00)
Yes	8	(3.82)	8	(4.00)
Case characteristics				
Age				
Median	68	(56; 77)	67	(57; 77)
Sex				
Male	26 954	(49.76)	10 367	(50.83)
Female	27 214	(50.23)	10 028	(49.16)
Elixhauser comorbidities (…)*				

Q1: first quartile. Q3: third quartile.
*Results of Elixhauser comorbidities (eg, alcohol abuse, blood loss anaemia, cardiac arrhythmias…) are presented in online supplemental file S6.

and patient safety outcomes were insignificant. A higher annual volume of rectum resections was associated with lower risks of in-hospital death (OR 0.70 (95% CI 0.61 to 0.80)), postoperative respiratory failure (OR 0.84 (95% CI 0.72 to 0.98)) and renal failure (OR 0.85 (95% CI 0.76 to 0.95)).

Rural localisation showed lower odds of renal failure (OR 0.77 (95% CI 0.63 to 0.93)) in cases with only colon resections.

Treatment in university hospitals was associated with increased odds of postoperative wound infections in colon (OR 1.98 (95% CI 1.17 to 3.35)) and rectum resections (OR 2.29 (95% CI 1.35 to 3.86)) compared with treatment in non-university hospitals.

The hospital ownership revealed differences between both groups and patient safety outcomes. Non-profit (OR 0.74 (95% CI 0.55 to 0.99)) or private (OR 0.77 (95% CI 0.60 to 0.99)) ownership was associated with lower risks of postoperative wound infections in colon resections. In contrast, odds of in-hospital death (OR 1.24 (95% CI 1.02 to 1.50)) and renal failure (OR 1.93 (95% CI 1.56 to 2.40)) in colon resections were higher in private hospitals. Rectum resections did not show significant associations of ownership and patient safety outcomes except for higher odds of renal failure (OR 1.59 (95% CI 1.25 to 2.03)) in private hospitals.

Table 2 Multivariate analysis of patient safety outcomes in 54 168 colon resections in 209 hospitals

	In-hospital death		Postoperative respiratory failure		Renal failure		Postoperative wound infection	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Healthcare covariates								
Admission reason								
Referral	Ref.		Ref.		Ref.		Ref.	
Emergency case	1.847***	(1.692 to 2.015)	1.413***	(1.320 to 1.513)	1.453***	(1.349 to 1.566)	1.145***	(1.067 to 1.228)
Transfer from other hospital	2.528***	(2.193 to 2.915)	1.982***	(1.749 to 2.245)	1.906***	(1.678 to 2.171)	1.223**	(1.071 to 1.397)
Weekend surgery								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.669***	(1.515 to 1.839)	1.426***	(1.312 to 1.550)	1.480***	(1.360 to 1.610)	1.080	(0.984 to 1.186)
Total colon resection								
No	Ref.		Ref.		Ref.		Ref.	
Yes	2.679***	(2.369 to 3.029)	1.639***	(1.472 to 1.825)	2.228***	(1.999 to 2.483)	1.022	(0.913 to 1.143)
Colon and rectum resection								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.103	(0.960 to 1.267)	1.524***	(1.378 to 1.686)	1.406***	(1.265 to 1.567)	1.579	(1.426 to 1.748)
Hospital covariates								
Case volume	0.968	(0.871 to 1.076)	0.919	(0.807 to 1.047)	0.992	(0.891 to 1.106)	1.168*	(1.030 to 1.325)
Area								
Urban	Ref.		Ref.		Ref.		Ref.	
Rural	1.061	(0.893 to 1.261)	0.863	(0.648 to 1.149)	0.772*	(0.635 to 0.939)	1.032	(0.824 to 1.292)
University hospital								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.303	(0.888 to 1.912)	0.687	(0.338 to 1.397)	1.412	(0.889 to 2.241)	1.981*	(1.171 to 3.352)
Ownership								
Public	Ref.		Ref.		Ref.		Ref.	
Non-profit	1.012	(0.811 to 1.262)	1.057	(0.726 to 1.540)	0.867	(0.670 to 1.122)	0.744*	(0.555 to 0.998)
Private	1.244*	(1.026 to 1.507)	1.329	(0.972 to 1.817)	1.937***	(1.563 to 2.400)	0.777*	(0.608 to 0.992)
Case covariates								
Sex								
Male	Ref.		Ref.		Ref.		Ref.	
Female	0.937	(0.873 to 1.006)	0.788***	(0.745 to 0.833)	0.683***	(0.645 to 0.725)	0.882***	(0.832 to 0.936)
Age	1.050***	(1.046 to 1.053)	1.014***	(1.012 to 1.017)	1.024***	(1.021 to 1.026)	0.998	(0.996 to 1.000)
Elixhauser comorbidities (…)†								

***p<0.001, **p<0.01, *p<0.05.
†Results of Elixhauser comorbidities (eg, alcohol abuse, blood loss anaemia, cardiac arrhythmias, chronic pulmonary disease…) are presented in online supplemental file S3.

Table 3 Multivariate analysis of patient safety outcomes in 20 395 rectum resections in 200 hospitals

	In-hospital death		Postoperative respiratory failure		Renal failure		Post-operative wound infection	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Healthcare covariates								
Admission reason								
Referral	Ref.		Ref.		Ref.		Ref.	
Emergency case	2.028***	(1.675 to 2.454)	1.335***	(1.170 to 1.523)	1.342***	(1.169 to 1.540)	1.291***	(1.138 to 1.466)
Transfer from other hospital	2.679***	(1.874 to 3.828)	1.859***	(1.406 to 2.459)	1.927***	(1.461 to 2.541)	1.484**	(1.131 to 1.948)
Weekend surgery								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.960***	(1.483 to 2.591)	1.427**	(1.150 to 1.770)	1.391**	(1.127 to 1.717)	0.985	(0.784 to 1.238)
Total colon resection								
No	Ref.		Ref.		Ref.		Ref.	
Yes	2.579***	(2.163 to 3.074)	2.164***	(1.921 to 2.438)	1.859***	(1.645 to 2.100)	1.522***	(1.356 to 1.708)
Hospital covariates								
Case volume	0.703***	(0.611 to 0.809)	0.844*	(0.725 to 0.982)	0.853**	(0.760 to 0.958)	0.973	(0.854 to 1.109)
Area								
Urban	Ref.		Ref.		Ref.		Ref.	
Rural	1.072	(0.817 to 1.407)	0.904	(0.639 to 1.281)	0.834	(0.670 to 1.037)	0.854	(0.663 to 1.101)
University hospital								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.616	(0.979 to 2.665)	0.853	(0.379 to 1.920)	1.299	(0.829 to 2.037)	2.292**	(1.358 to 3.869)
Ownership								
Public	Ref.		Ref.		Ref.		Ref.	
Non-profit	0.851	(0.614 to 1.179)	1.059	(0.674 to 1.664)	0.762	(0.576 to 1.008)	0.761	(0.553 to 1.048)
Private	0.925	(0.682 to 1.254)	1.267	(0.865 to 1.858)	1.597***	(1.256 to 2.030)	0.846	(0.642 to 1.117)
Case covariates								
Sex								
Male	Ref.		Ref		Ref		Ref	
Female	0.842*	(0.710 to 0.998)	0.842**	(0.759 to 0.934)	0.685***	(0.613 to 0.765)	0.826***	(0.748 to 0.912)
Age	1.068***	(1.059 to 1.078)	1.014***	(1.009 to 1.018)	1.021***	(1.016 to 1.026)	0.998	(0.995 to 1.002)
Elixhauser comorbidities (...)†								

***P<0.001; **p<0.01; *p<0.05.
†Results of Elixhauser comorbidities (eg, alcohol abuse, blood loss anaemia, cardiac arrhythmias, chronic pulmonary disease...) are presented in online supplemental file S10.

Case covariates

Female sex was consistently associated with better outcomes in both groups, except of a borderline-insignificant association with in-hospital death (OR 0.93 (95% CI 0.87 to 1.00)) in colon resections. Age was associated with higher risks of in-hospital death, postoperative respiratory failure and renal failure in both groups. Regarding postoperative wound infections, age was a borderline-insignificant protective factor in colon (OR 0.99 (95% CI 0.99 to 1.00)) and rectum (OR 0.99 (95% CI 0.99 to 1.00)) resections. Of all Elixhauser comorbidities analysed, coagulopathies showed the highest ORs for poor patient safety outcomes including higher ORs of death in colon (OR 4.17 (95% CI 3.864 to 4.509)) or rectum (OR 4.30 (95% CI 3.600 to 5.158)) resections. The same applies to other patient safety outcomes like postoperative respiratory failure in colon (OR 3.117 (95% CI 2.920 to 3.327)) or rectum (OR 3.052 (95% CI 2.697 to 3.455)) resections, renal failure in colon (OR 3.332 (95% CI 3.118 to 3.561)) and rectum (OR 2.886 (95% CI 2.541 to 3.277)) resections and postoperative wound infections in colon (OR 1.644 (95% CI 1.531 to 1.764)) or rectum (OR 1.770 (95% CI 1.570 to 1.996)) resections. Along with coagulopathies, fluid and electrolyte disorders, peripheral vascular disorders, congestive heart failure, chronic pulmonary disease, cardiac arrhythmias and pulmonary circulation disorders were also associated with multiple poor patient outcomes in both procedure groups. The multivariate results for the remaining Elixhauser groups can be found in online supplemental files S9 and S10.

We reviewed differences in results of stratified analyses for cases with and without cancerous colon and rectum resections. Significant effect reversals were not observed (online supplemental files S11–S14). The review also did not reveal differences between university and non-university hospitals in terms of emergency admission or transfer from other hospital (online supplemental files S15 and S16). Therefore, a stratification between cases with and without cancer or university and non-university hospitals has not been applied.

DISCUSSION

This large cross-sectional analysis of 54 168 colon resections and 20 395 rectum resections presents new and comprehensive findings for patient safety.

Healthcare-level covariates were significant risk factors for multiple patient safety outcomes. Preoperative transfer from other hospitals and emergency admission as possible proxy for case urgency were precursors of poor patient safety outcome in both groups. These findings confirm recent literature reporting associations between emergency admissions or transfers from other hospitals and 30-day-mortality, 5-year survival, complications, length of stay or morbidities.[7–11] Weekend surgery was associated with higher risks for death, postoperative respiratory and renal failure in both groups supported by the literature of mortality in colon[4] and general surgery.[5 6] Regarding rectum resections, the literature reported insignificant effects. These are most likely explained by a small number of included cases.[4] These findings underline the need for the consideration of healthcare contexts in risk-adjusted quality assurance.

The hospital covariates in this analysis showed conflicting effects. Inconclusive results were found for rural localisation, university hospital status and hospital ownership. The estimated effects were insignificant (rural hospitals) or conflicting (volume, ownership) and therefore did not strongly affect the considered patient safety outcomes. The literature discusses the influence of case volume,[12 13 17 28 29] rural hospitals,[30–32] ownership,[29 33] university hospital status[34] or hospital size in general[29] with confirming or contradicting results often explained by, for example, patient case-mix, staffing or surgeon experience differing between hospital sizes.[29 35] This may be due to outcome-relevant information like staffing,[36 37] expertise[38] or certification[39] not being included in claims data. For example, a German study reported insignificant associations between ownership and postoperative wound infections after colon surgery.[40] The differences compared with our analyses are the procedure-definitions (partial/total colon resections vs open/laparoscopic colon procedure), the sample size (54 168 colon resections vs 28 291 colon procedures) and the data. The claims data used in our analysis include individual information on age, sex and comorbidities. Infection surveillance data used by Schröder *et al* does not include individual patient data on age, sex or severity of a patient's illness.[40]

Additionally, some studies did not stratify colon and rectum resections.[41 42] However, the heterogeneous results for both procedure groups indicate the relevance of stratification as already reported for other indications.[16]

With respect to case covariates age, sex and comorbidities like coagulopathies, heart diseases, lung diseases or fluid and electrolyte disorders were risk factors for poor patient outcome in both groups in this analysis, which is supported by the literature as well.[26 43–48]

There are several strengths to this study. This study analysed a large and current sample providing a broad span of cases, hospital types, ownerships and locations. While previous studies emphasised specific covariates and/or outcomes, we considered combined sets of previously solitarily analysed outcomes and risk factors and, thus, provide a comprehensive analysis. The applied multilevel-regression model is able to simultaneously analyse individual covariates like comorbidities and hospital-level covariates like annual case volume. It also considers relationships between covariates (eg, weekend surgery and emergency admissions).[25]

There are several limitations to this study. Secondary data induce challenges for a reliable operationalisation of outcomes. First, the data are anonymised. The anonymisation makes it impossible to validate the coded diagnoses.[49] Second, claims data do not include information which of the coded diagnoses had been present on admission. To overcome these shortcomings, this study used a

set of previously validated outcomes that were reported to occur most likely during hospitalisation.[23] With respect to transfer from other hospitals, recent literature distinguishes between urgent and non-urgent inter-hospital transfers.[9–11] The data included in this analysis does not include details on the reasons for transfer from other hospital. However, our results were adjusted for age, sex, comorbidities and weekend surgery representing severity and complexity. The different results depending on adjustment, stratification, bivariate and multivariate analyses underline the need for careful and comprehensive statistical analysis. One weakness of German hospital discharge data is a lack of information on patient history, medication, length of anaesthesia, staff-to-patient ratios, surgeon volumes, acuity/reasons for inter-hospital transfers, validity of coding, centralisation and comorbidities present on admission.[37 39 50] This lacking information may lead to bias as these covariates may influence the outcome and could not be considered in our study. To overcome these challenges we sought to define colon and rectum resections,[22] outcomes[23] and comorbidities[20] based on study literature for transparency and consistency. The advantage of this process has its limits. These definitions do not involve specific distinctions referring to procedure (eg, type, localisation) or comorbidities (eg, bowel disease). To ensure transparency we decided against creating our own definitions of procedures or comorbidities. An additional limitation is the limited possibility to analyse some specific subgroups (eg, case volume stratified by ownership, weekend surgeries stratified by admission) in models using a large set of covariates. It poses the risk of separation due alone to the small sample size of specific subgroup-populations and outcomes.[51]

Conclusions

This study demonstrated that patient safety in colorectal resections is strongly related to specific healthcare covariates. Our results implicate a need to account for admission reasons and weekend surgery when measuring and comparing patient safety. Therefore a risk adjustment for these covariates in quality assurance measures should be pursued. Hospital volume, ownership, urbanisation degree and university hospital status could not be shown to be strongly associated with all patient safety outcomes of colorectal resections. Given these insights from an analysis of a large data set, this paper contributes reliable and comprehensive evidence to the ongoing debate on hospital- and healthcare-related influences on patient safety in general.

Contributors FW designed the concept, methods and investigation, visualised results and wrote the draft of the underlying analysis. MR undertook the formal analysis. MR and OS curated the data, supervised the methodology and project administration in general and revised the drafts. JS, ME-G, PS and RK acquired funding, supervised the concept and investigation and revised the drafts. FW is responsible for the overall content as the guarantor.

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Competing interests PS and RK are members of the scientific advisory board of IQM. ME-G serves as an external expert for IQM. The other authors declare that they have no conflict of interest.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the ethics committee of the TU Dresden: IRB00001473 and IORG0001076.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The data are not publicly available due to containing information that could compromise research participant privacy/consent. The consent given from the research participants included the obligation to analyse the data anonymously without disclosure to other parties.

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Anlagen Publikation (2) – Supplemental Material

S1: ICD-10 Codes of Elixhauser Comorbidity Groups [20]

Congestive heart failure: I099, I110, I130, I132, I255, I420, I425, I426, I427, I428, I429, I43, I50, P290

Cardiac arrhythmias: I441, I442, I443, I456, I459, I47, I48, I49, R000, R001, R008, T821, Z450, Z950

Valvular disease : A520, I05, I06, I07, I08, I091, I098, I34, I35, I36, I37, I38, I39, Q230, Q231, Q232, Q233, Z952, Z953 Z954

Pulmonary circulation Disorders: I26, I27, I280, I288, I289

Peripheral vascular disorders: I70, I71, I731, I738, I739, I771, I790, I792, K551, K558, K559, Z958, Z959

Hypertension, uncomplicated: I10

Hypertension, complicated: I11, I12, I13, I15

Paralysis: G041, G114, G801, G802, G81, G82, G830, G831, G832, G833, G834, G839

Other neurological disorders: G10, G11, G12, G13, G20, G21, G22, G254, G255, G312, G318, G319, G32, G35, G36, G37, G40, G41, G931, G934, R470, R56

Chronic pulmonary disease: I278, I279, J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J684, J701, J703

Diabetes, uncomplicated: E100, E101, E109, E110, E111, E119, E120, E121, E129, E130, E131, E139, E140, E141, E149

Diabetes, complicated: E102, E103, E104, E105, E106, E107, E108, E112, E113, E114, E115, E116, E117, E118, E122, E123, E124, E125, E126, E127, E128, E132, E133, E134, E135, E136, E137, E138, E142, E143, E144, E145, E146, E147, E148

Hypothyroidism: E00, E01, E02, E03, E890

Renal failure: I120, I131, N18, N19, N250, Z490, Z491, Z492, Z940, Z992

Peptic ulcer disease excluding bleeding: K257, K259, K267, K269, K277, K279, K287, K289

AIDS/HIV: B20, B21, B22, B24

Lymphoma: C81, C82, C83, C84, C85, C88, C96, C900, C902

Metastatic cancer: C77, C78, C79, C80

Solid tumor without metastasis: C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C1 0, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C97

Rheumatoid arthritis/collagen vascular diseases: L940, L941, L943, M05, M06, M08, M120, M123, M30, M310, M311, M312, M313, M32, M33, M34, M35, M45, M461, M468, M469

Coagulopathy: D65, D66, D67, D68, D691, D693, D694, D695, D696

Obesity: E66

Weight loss: E40, E41, E42, E43, E44, E45, E46, R634, R64

Fluid and electrolyte disorders: E222, E86, E87

Blood loss anemia: D500

S2: OPS-codes for partial colon resections according to GIQI [21]

OPS-CODE	TRANSLATION (BY AUTHOR)
5-455.01	Partial resection of the colon: segmental resection: open surgery with anastomosis
5-455.02	Partial resection of the colon: segmental resection: open surgery with enterostoma and blind closure
5-455.03	Partial Resection of the Colon: Segment Resection: Open Surgery with Two Enterostomata
5-455.04	Partial Resection of the Colon: Segment Resection: Open Surgery with Anastomosis Anus praeter
5-455.05	Partial Resection of the Colon: Segmental Resection: Laparoscopic with Anastomosis
5-455.06	Partial Resection of the Colon: Segmental Resection: Laparoscopic with Enterostomy
5-455.07	Partial resection of the colon: segmental resection: change laparoscopic - open surgical
5-455.0X	Partial resection of the colon: Segment resection: Other
5-455.11	Partial resection of the colon: multiple segment resections: Open surgery with anastomosis
5-455.12	Partial resection of the colon: multiple segment resections: Open surgery with enterostoma and blind closure
5-455.13	Partial resection of the colon: multiple segment resections: Open surgery with two enterostomata
5-455.14	Partial resection of the colon: multiple segment resections: Open surgery with anastomosis anus praeter
5-455.15	Partial resection of the colon: multiple segment resections: Laparoscopic with anastomosis
5-455.16	Partial resection of the colon: multiple segment resections: Laparoscopic with enterostomy
5-455.17	Partial resection of the colon: multiple segment resections: Transfer laparoscopic - open surgery
5-455.1X	Partial resection of the colon: multiple segment resections: Other
5-455.21	Partial Resection of the Colon: Ileocecal Resection: Open Surgery with Anastomosis
5-455.22	Partial Resection of the Colon: Ileocecal Resection: Open surgery with enterostoma and blind closure
5-455.23	Partial Resection of the Colon: Ileocecal Resection: Open Surgery with Two Enterostomata
5-455.24	Partial Resection of the Colon: Ileocecal Resection: Open Surgery with Anastomosis Anus praeter
5-455.25	Partial Resection of the Colon: Ileocecal Resection: Laparoscopic with Anastomosis
5-455.26	Partial Resection of the Colon: Ileocecal Resection: Laparoscopic with Enterostoma
5-455.27	Partial resection of the colon: Ileocecal resection: change laparoscopic - open surgical
5-455.2X	Partial resection of the colon: Ileocecal resection: Other
5-455.31	Partial resection of the colon: Caecal resection: Open surgery
5-455.35	Partial resection of the colon: Caecal resection: Laparoscopic
5-455.37	Partial resection of the colon: Caecal resection: change laparoscopic - open surgical
5-455.41	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure [hemicolectomy right]: Open surgery with anastomosis
5-455.42	Partial Resection of the Colon: Resection of the ascending colon with coecum and right flexure [Hemicolectomy right]: Open surgery with enterostoma and
5-455.43	Partial Resection of the Colon: Resection of the ascending colon with coecum and right flexure [Hemicolectomy right]: Open surgery with two enterostomata
5-455.44	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure [hemicolectomy right]: Open surgery with anastomosis anus praeter
5-455.45	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure [hemicolectomy right]: Laparoscopic with anastomosis
5-455.46	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure [hemicolectomy right]: Laparoscopically with enterostoma
5-455.47	Partial resection of the colon: resection of the ascending colon with coecum and right flexure [hemicolectomy right]: change laparoscopic - open surgical
5-455.4X	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure [right hemicolectomy]: Other
5-455.51	Partial resection of the colon: Resection of the transverse colon: Open surgery with anastomosis
5-455.52	Partial resection of the colon: Resection of the transverse colon: open surgery with enterostoma and blind closure
5-455.53	Partial Resection of the Colon: Resection of the Transverse Colon: Open Surgery with Two Enterostomata
5-455.54	Partial resection of the colon: resection of the transverse colon: open surgery with anastomosis anus praeter
5-455.55	Partial resection of the colon: Resection of the transverse colon: Laparoscopic with anastomosis
5-455.56	Partial Resection of the Colon: Resection of the Transverse Colon: Laparoscopic with Enterostoma
5-455.57	Partial resection of the colon: resection of the transverse colon: change laparoscopic - open surgical
5-455.5X	Partial resection of the colon: Resection of the transverse colon: Other
5-455.61	Partial resection of the colon: resection of the descending colon with left flexure [hemicolectomy left]: open surgery with anastomosis
5-455.62	Partial resection of the colon: resection of the descending colon with left flexure [hemicolectomy left]: open surgery with enterostoma and blind closure
5-455.63	Partial resection of the colon: resection of the descending colon with left flexure [hemicolectomy left]: open surgery with two enterostomata
5-455.64	Partial resection of the colon: resection of the descending colon with left flexure [hemicolectomy left]: open surgery with anastomosis anus praeter
5-455.65	Partial resection of the colon: Resection of the descending colon with left flexure [Hemicolectomy left]: Laparoscopic with anastomosis
5-455.66	Partial Resection of the Colon: Resection of the descending colon with left flexure [Hemicolectomy left]: Laparoscopic with Enterostoma
5-455.67	Partial resection of the colon: resection of the descending colon with left flexure [hemicolectomy left]: change laparoscopic - open surgical
5-455.6X	Partial resection of the colon: Resection of the descending colon with left flexure [Hemicolectomy left]: Other
5-455.71	Partial resection of the colon: sigmoid resection: open surgery with anastomosis
5-455.72	Partial resection of the colon: sigmoid resection: open surgery with enterostoma and blind closure
5-455.73	Partial resection of the colon: sigmoid resection: open surgery with two enterostomata
5-455.74	Partial resection of the colon: sigmoid resection: open surgery with anastomosis anus praeter

5-455.75	Partial resection of the colon: sigmoid resection: laparoscopic with anastomosis
5-455.76	Partial resection of the colon: Sigmoid resection: laparoscopic with enterostoma
5-455.77	Partial resection of the colon: sigmoid resection: change laparoscopic - open surgical
5-455.7X	Partial resection of the colon: Sigmoid resection: Other
5-455.91	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.92	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.93	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.94	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.95	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.96	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.97	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.9X	Partial resection of the colon: Resection of the ascending colon with coecum and right flexure and transverse colon [right hemicolectomy with transverse resection]:
5-455.A1	Partial resection of the colon: Resection of the descending colon with left flexure and transverse colon [left hemicolectomy with transverse resection]: Open
5-455.A2	Partial resection of the colon: Resection of the descending colon with left flexure and transverse colon [left hemicolectomy with transverse resection]: Open
5-455.A3	Partial resection of the colon: Resection of the descending colon with left flexure and transverse colon [left hemicolectomy with transverse resection]: Open
5-455.A4	Partial resection of the colon: Resection of the descending colon with left flexure and transverse colon [left hemicolectomy with transverse resection]: Open
5-455.A5	Partial Resection of the Colon: Resection of the descending colon with left flexure and transverse colon [Hemicolectomy left with transverse resection]: Laparoscopic
5-455.A6	Partial Resection of the Colon: Resection of the descending colon with left flexure and transverse colon [Hemicolectomy left with transverse resection]: Laparoscopic
5-455.A7	Partial resection of the colon: resection of the descending colon with left flexure and transverse colon [hemicolectomy left with transverse resection]: change
5-455.AX	Partial resection of the colon: Resection of the descending colon with left flexure and transverse colon [left hemicolectomy with transverse resection]: Other
5-455.B1	Partial resection of the colon: resection of the descending colon and sigmoid colon: open surgery with anastomosis
5-455.B2	Partial resection of the colon: resection of the descending colon and sigmoid colon: open surgery with enterostoma and blind closure
5-455.B3	Partial Resection of the Colon: Resection of the descending colon and sigmoid colon: Open surgery with two enterostomata
5-455.B4	Partial Resection of the Colon: Resection of the descending colon and sigmoid colon: Open surgery with anastomosis anus praeter
5-455.B5	Partial resection of the colon: resection of the descending colon and sigmoid colon: laparoscopic with anastomosis
5-455.B6	Partial resection of the colon: resection of the descending colon and sigmoid colon: laparoscopic with enterostoma
5-455.B7	Partial Resection of the Colon: Resection of the descending colon and sigmoid colon: transfer laparoscopically - open surgery
5-455.BX	Partial resection of the colon: Resection of the descending colon and sigmoid colon: Other
5-455.C1	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C2	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C3	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C4	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C5	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C6	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.C7	Partial resection of the colon: resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.CX	Partial resection of the colon: Resection of the ascending, transverse and descending colon with coecum and right and left flexure [hemicolectomy right and left
5-455.D1	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D2	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D3	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D4	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D5	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D6	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.D7	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [hemicolectomy left with
5-455.DX	Partial resection of the colon: resection of the transverse colon, descending colon with left flexure and sigmoid colon [left hemicolectomy with
5-455.X1	Partial resection of the colon: Other: Open surgery with anastomosis
5-455.X2	Partial resection of the colon: Other: Open surgery with enterostoma and blind closure
5-455.X3	Partial resection of the colon: Other: Open surgery with two enterostomata
5-455.X4	Partial resection of the colon: Other: Open surgery with anastomosis anus praeter
5-455.X5	Partial resection of the colon: Other: Laparoscopic with anastomosis
5-455.X6	Partial resection of the colon: Other: Laparoscopic with enterostoma
5-455.X7	Partial resection of the colon: Other: transfer laparoscopic - open surgical
5-455.XX	Partial resection of the colon: Other: Other
5-455.Y	Partial resection of the colon: N.n.ref.

S3: OPS-codes for total colon resections according to GIQI [21]

OPS-CODE	TRANSLATION (BY AUTHOR)
5-456.00	(Total) Colectomy and Proctocolectomy: Colectomy: Open surgery with ileostoma
5-456.01	(Total) Colectomy and Proctocolectomy: Colectomy: Open surgery with ileorectal anastomosis with reservoir (pouch)
5-456.02	(Total) Colectomy and Proctocolectomy: Colectomy: Open surgery with ileorectal anastomosis without reservoir (pouch)
5-456.03	(Total) Colectomy and Proctocolectomy: Colectomy: Open surgery with ileoanal anastomosis with reservoir (pouch)
5-456.04	(Total) Colectomy and Proctocolectomy: Colectomy: Open surgery with ileoanal anastomosis without reservoir (pouch)
5-456.05	(Total) Colectomy and Proctocolectomy: Colectomy: Laparoscopic with reservoir anastomosis (Pouch)
5-456.06	(Total) Colectomy and Proctocolectomy: Colectomy: Laparoscopic with Anastomosis without reservoir (Pouch)
5-456.07	(Total) Colectomy and Proctocolectomy: Colectomy: Laparoscopic with Ileostoma
5-456.08	(Total) Colectomy and Proctocolectomy: Colectomy: change laparoscopic - open surgical
5-456.0X	(Total) Colectomy and Proctocolectomy: Colectomy: Other
5-456.10	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Open surgery with ileostoma
5-456.11	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Open surgery with ileorectal anastomosis with reservoir (pouch)
5-456.12	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Open surgery with ileorectal anastomosis without reservoir (pouch)
5-456.13	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Open surgery with ileoanal anastomosis with reservoir (pouch)
5-456.14	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Open surgery with ileoanal anastomosis without reservoir (pouch)
5-456.15	(Total) colectomy and proctocolectomy: Proctocolectomy: Laparoscopic with reservoir anastomosis (pouch)
5-456.16	(Total) Colectomy and Proctocolectomy: Proctocolectomy: Laparoscopic with anastomosis without reservoir (pouch)
5-456.17	(Total) colectomy and proctocolectomy: proctocolectomy: laparoscopic with ileostomy
5-456.18	(Total) colectomy and proctocolectomy: proctocolectomy: change laparoscopic - open surgical
5-456.1X	(Total) colectomy and proctocolectomy: Proctocolectomy: Other
5-456.20	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: open surgery with ileostoma
5-456.21	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: open surgery with ileorectal anastomosis with reservoir (pouch)
5-456.22	(Total) Colectomy and Proctocolectomy: Colectomy with Proctomucosectomy: Open surgery with ileorectal anastomosis without reservoir (pouch)
5-456.23	(Total) Colectomy and Proctocolectomy: Colectomy with proctomucosectomy: Open surgery with ileoanal anastomosis with reservoir (pouch)
5-456.24	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: open surgery with ileoanal anastomosis without reservoir (pouch)
5-456.25	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: laparoscopic with reservoir anastomosis (pouch)
5-456.26	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: laparoscopic with anastomosis without reservoir (pouch)
5-456.27	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: laparoscopic with ileostomy
5-456.28	(Total) colectomy and proctocolectomy: colectomy with proctomucosectomy: change laparoscopic - open surgical
5-456.2X	(total) colectomy and proctocolectomy: colectomy with proctomucosectomy: other
5-456.X0	(Total) colectomy and proctocolectomy: Other: Open surgery with ileostomy
5-456.X1	(Total) colectomy and proctocolectomy: Other: Open surgery with ileorectal anastomosis with reservoir (pouch)
5-456.X2	(total) colectomy and proctocolectomy: Other: Open surgery with ileorectal anastomosis without reservoir (pouch)
5-456.X3	(Total) colectomy and proctocolectomy: Other: Open surgery with ileoanal anastomosis with reservoir (pouch)
5-456.X4	(Total) colectomy and proctocolectomy: Other: Open surgery with ileoanal anastomosis without reservoir (pouch)
5-456.X5	(total) colectomy and proctocolectomy: Other: Laparoscopic with reservoir anastomosis (pouch)
5-456.X6	(Total) colectomy and proctocolectomy: Other: Laparoscopic with anastomosis without reservoir (pouch)
5-456.X7	(Total) colectomy and proctocolectomy: Other: Laparoscopic with ileostomy
5-456.X8	(total) colectomy and proctocolectomy: Other: change laparoscopic - open surgical
5-456.XX	(Total) colectomy and proctocolectomy: Other: Other
5-456.Y	(Total) colectomy and proctocolectomy: N.n.d.

S4: OPS-codes for rectum resections according to GIQI [21]

OPS-CODE	TRANSLATION (BY AUTHOR)
5-484.01	Rectum resection with sphincter preservation: Anterior cuff resection: Open surgery with anastomosis
5-484.02	Rectum resection with sphincter preservation: Anterior cuff resection: Open surgery with enterostoma and blind closure
5-484.05	Rectum resection with sphincter preservation: Anterior cuff resection: Laparoscopic with anastomosis
5-484.06	Rectum resection with sphincter preservation: Anterior cuff resection: Laparoscopic with enterostomy and blind closure
5-484.08	Rectum resection with sphincter preservation: Anterior cuff resection: change laparoscopic - open surgery with anastomosis
5-484.09	Rectum resection with sphincter preservation: Anterior cuff resection: change laparoscopic - open surgery with enterostoma and blind closure
5-484.0X	Rectum resection with sphincter preservation: Anterior cuff resection: Other
5-484.11	Rectum resection with sphincter preservation: Posterior rectotomy [Rectotomia posterior]: Open surgery with anastomosis
5-484.12	Rectum resection with sphincter preservation: Posterior rectotomy [Rectotomia posterior]: Open surgery with enterostoma and blind closure
5-484.15	Rectum resection with sphincter preservation: Posterior cuff resection [Rectotomia posterior]: Laparoscopic with anastomosis
5-484.16	Rectum resection with sphincter preservation: Posterior cuff resection [Rectotomia posterior]: Laparoscopic with enterostoma and blind closure
5-484.18	Rectum resection with sphincter preservation: posterior cuff resection [Rectotomia posterior]: change laparoscopic - open surgery with anastomosis
5-484.19	Rectum resection with sphincter preservation: posterior cuff resection [rectotomia posterior]: change laparoscopically - open surgically with enterostoma and
5-484.1X	Rectum resection with sphincter preservation: Posterior cuff resection [Rectotomia posterior]: Other
5-484.21	Rectum resection with preservation of sphincter: Tubular resection with paraproctica left intact: Open surgery with anastomosis
5-484.22	Rectum resection with preservation of sphincter: Tubular resection with paraproktium left in place: Open surgery with enterostoma and blind closure
5-484.25	Rectum resection with preservation of sphincter: Tubular resection with paraproctica left in place: Laparoscopic with anastomosis
5-484.26	Rectum resection with preservation of sphincter: Tubular resection with paraproktium: Laparoscopic with enterostoma and blind closure
5-484.27	Rectum resection with sphincter preservation: Tubular resection with paraprotic left in place: Peranal
5-484.28	Rectum resection with sphincter preservation: Tubular resection with paraproctium left in place: change laparoscopic - open surgery with anastomosis
5-484.29	Rectum resection with preservation of sphincter: Tubular resection with preservation of paraproktium: change laparoscopically - open surgically with enterostoma and
5-484.2X	Rectum resection with preservation of sphincter: Tubular resection with preservation of paraproktium: Other
5-484.31	Rectum resection with sphincter preservation: Anterior resection: Open surgery with anastomosis
5-484.32	Rectum resection with sphincter preservation: Anterior resection: open surgery with enterostoma and blind closure
5-484.35	Rectum resection with sphincter preservation: Anterior resection: Laparoscopic with anastomosis
5-484.36	Rectum resection with sphincter preservation: Anterior resection: Laparoscopic with enterostoma and blind closure
5-484.38	Rectum resection with sphincter preservation: Anterior resection: change laparoscopic - open surgical with anastomosis
5-484.39	Rectum resection with sphincter preservation: anterior resection: change laparoscopically - open surgically with enterostoma and blind closure
5-484.3X	Rectum resection with sphincter preservation: Anterior resection: Other
5-484.51	Rectum resection with sphincter preservation: deep anterior resection: open surgery with anastomosis
5-484.52	Rectum resection with sphincter preservation: deep anterior resection: open surgery with enterostoma and blind closure
5-484.55	Rectum resection with sphincter preservation: Deep anterior resection: Laparoscopic with anastomosis
5-484.56	Rectum resection with sphincter preservation: Deep anterior resection: Laparoscopic with enterostoma and blind closure
5-484.58	Rectum resection with sphincter preservation: deep anterior resection: change laparoscopic - open surgery with anastomosis
5-484.59	Rectum resection with sphincter preservation: deep anterior resection: change laparoscopic - open surgical with enterostoma and blind closure
5-484.5X	Rectum resection with sphincter preservation: Deep anterior resection: Other
5-484.61	Rectum resection with sphincter preservation: deep anterior resection with peranal anastomosis: open surgery with anastomosis
5-484.65	Rectum resection with sphincter preservation: deep anterior
5-484.68	Rectum resection with sphincter preservation: deep anterior resection with peranal anastomosis: change laparoscopic - open surgical with anastomosis
5-484.6X	Rectum resection with sphincter preservation: Deep anterior resection with peranal anastomosis: Other
5-484.X1	Rectum resection with sphincter preservation: Other: Open surgery with anastomosis
5-484.X2	Rectum resection with sphincter preservation: Other: Open surgery with enterostoma and blind closure
5-484.X5	Rectum resection with sphincter preservation: Other: Laparoscopic with anastomosis
5-484.X6	Rectum resection with sphincter preservation: Other: Laparoscopic with enterostoma and blind closure

5-484.X8	Rectum resection with sphincter preservation: Other: change laparoscopic - open surgery with anastomosis
5-484.X9	Rectum resection with sphincter preservation: Other: change laparoscopically - open surgically with enterostoma and blind closure
5-484.XX	Rectum resection with sphincter preservation: Other: Other
5-484.Y	Rectum resection with sphincter preservation: N.n.ref.
5-485.01	Rectum resection without preservation of sphincter: Abdominoperineal: Open surgery
5-485.02	Rectum resection without sphincter preservation: Abdominoperineal: Combined open surgical-laparoscopic
5-485.0X	Rectum resection without sphincter preservation: Abdominoperineal: Other
5-485.1	Rectum resection without preservation of sphincter: Abdominoperineal with removal of adjacent organs
5-485.21	Rectum resection without sphincter preservation: Sacroiliac abdomen: Open surgery
5-485.22	Rectum resection without sphincter preservation: Sacroiliac abdomen: Combined open surgical-laparoscopic
5-485.2X	Rectum resection without sphincter preservation: Sacroiliac abdomen: Other
5-485.3	Rectum resection without sphincter preservation: Sacral abdominosacral with removal of neighboring organs
5-485.4	Rectum resection without sphincter preservation: sacroperineal
5-485.5	Rectum resection without sphincter preservation: Perineal
5-485.X	Rectum resection without sphincter preservation: Other
5-485.Y	Rectum resection without sphincter preservation: N.n.ref.

S5: Definitions of patient safety outcomes

PATIENT SAFETY OUTCOME	DEFINITION ACCORDING TO ICD-10 GM
IN-HOSPITAL DEATH	Discharge destination: death (included in accounting data derived)
POST-OPERATIVE RESPIRATORY FAILURE [15]	ICD-10: J96 .0 - Respiratory failure, not elsewhere classified
POST-OPERATIVE WOUND INFECTION [15]	ICD-10: T81.4 - Infection following a procedure, not elsewhere classified
	ICD-10: T82.6 - Infection and inflammatory reaction due to cardiac valve prosthesis
	ICD-10: T82.7 - Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts
	ICD-10: T83.5 - Infection and inflammatory reaction due to prosthetic device, implant and graft in urinary system
	ICD-10: T83.6 - Infection and inflammatory reaction due to prosthetic device, implant and graft in genital tract
	ICD-10: T84.5 - Infection and inflammatory reaction due to internal joint prosthesis
	ICD-10: T84.6 - Infection and inflammatory reaction due to internal fixation device [any site]
	ICD-10: T84.7 - Infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants and grafts
	ICD-10: T87.4 - Infection of amputation stump
RENAL FAILURE [15]	ICD-10: N17.0 - Acute renal failure with tubular necrosis
	ICD-10: N17.1 - Acute renal failure with acute cortical necrosis
	ICD-10: N17.2 - Acute renal failure with medullary necrosis
	ICD-10: N17.8 - Other acute renal failure
	ICD-10: N17.9 - Acute renal failure, unspecified
	ICD-10: N99.0- Postprocedural renal failure
	Procedure code: 8-853.7- Continuous, venovenous, pump-driven (CVVH), anticoagulation with heparin or without anticoagulation

S6: Case-, care- and hospital related characteristics

	COLON RESECTIONS		RECTUM RESECTIONS	
PATIENT SAFETY OUTCOMES	n	% / Q1; Q3	n	% / Q1; Q3
Outcome in-hospital death				
no	48,914	(90.30 %)	19,525	(95.73 %)
yes	5,254	(9.69 %)	870	(4.26 %)
Outcome post-operative respiratory failure				
no	45,074	(83.21 %)	17,901	(87.77 %)
yes	9,094	(16.78 %)	2,494	(12.22 %)
Outcome post-operative wound infections				
no	48,013	(88.63 %)	18,109	(88.79 %)
yes	6,155	(11.36 %)	2,286	(11.2 %)
Outcome renal failure				
no	45,920	(84.77 %)	18,279	(89.62 %)
yes	8,248	(15.22 %)	2,116	(10.37 %)
CASE CHARACTERISTICS				
age (median)	68	(56; 77)	67	(57; 77)
elixhauser groups per case (median)	3	(2; 5)	3	(2; 5)
sex				
male	26,954	(49.76 %)	10,367	(50.83 %)
female	27,214	(50.23 %)	10,028	(49.16 %)
AIDS/HIV				
no	54,142	(99.95 %)	20,383	(99.94 %)
yes	26	(0.04 %)	12	(0.05 %)
alcohol abuse				
no	53,025	(97.88 %)	20,088	(98.49 %)
yes	1,143	(2.11 %)	307	(1.5 %)
blood loss anemia				
no	53,022	(97.88 %)	20,134	(98.72 %)
yes	1,146	(2.11 %)	261	(1.27 %)
cardiac arrhythmias				
no	43,241	(79.82 %)	17,135	(84.01 %)
yes	10,927	(20.17 %)	3,260	(15.98 %)
chronic pulmonary disease				
no	49,042	(90.53 %)	18,792	(92.14 %)
yes	5,126	(9.46 %)	1,603	(7.85 %)
coagulopathy				
no	44,935	(82.95 %)	17,598	(86.28 %)
yes	9,233	(17.04 %)	2,797	(13.71 %)
congestive heart failure				
no	47,447	(87.59 %)	18,608	(91.23 %)
yes	6,721	(12.4 %)	1,787	(8.76 %)
deficiency anemia				
no	51,887	(95.78 %)	19,852	(97.33 %)
yes	2,281	(4.21 %)	543	(2.66 %)
depression				
no	51,232	(94.57 %)	19,318	(94.71 %)
yes	2,936	(5.42 %)	1,077	(5.28 %)
diabetes, complicated				
no	51,887	(95.78 %)	19,754	(96.85 %)
yes	2,281	(4.21 %)	641	(3.14 %)
diabetes, uncomplicated				
no	46,491	(85.82 %)	17,664	(86.6 %)
yes	7,677	(14.17 %)	2,731	(13.39 %)
drug abuse				
no	53,911	(99.52 %)	20,321	(99.63 %)
yes	257	(0.47 %)	74	(0.36 %)
fluid and electrolyte disorders				
no	29,678	(54.78 %)	12,122	(59.43 %)
yes	24,490	(45.21 %)	8,273	(40.56 %)
hypertension, complicated				
no	51,632	(95.31 %)	19,680	(96.49 %)
yes	2,536	(4.68 %)	715	(3.51 %)
hypertension, uncomplicated				
no	28,369	(52.37 %)	10,692	(52.42 %)
yes	25,799	(47.62 %)	9,703	(47.57 %)

hypothyroidism				
no	47,235	(87.2 %)	18,008	(88.29 %)
yes	6,933	(12.79 %)	2,387	(11.7 %)
liver disease				
no	50,277	(92.81 %)	19,433	(95.28 %)
yes	3,891	(7.18 %)	962	(4.71 %)
lymphoma				
no	53,762	(99.25 %)	20,315	(99.6 %)
yes	406	(0.74 %)	80	(0.39 %)
metastatic cancer				
no	43,637	(80.55 %)	15,149	(74.27 %)
yes	10,531	(19.44 %)	5,246	(25.72 %)
obesity				
no	47,727	(88.11 %)	18,046	(88.48 %)
yes	6,441	(11.89 %)	2,349	(11.51 %)
other neurological disorders				
no	51,956	(95.91 %)	19,747	(96.82 %)
yes	2,212	(4.08 %)	648	(3.17 %)
paralysis				
no	52,765	(97.4 %)	19,989	(98.01 %)
yes	1,403	(2.59 %)	406	(1.99 %)
peptic ulcer disease excluding bleeding				
no	54,004	(99.69 %)	20,348	(99.76 %)
yes	164	(0.31 %)	47	(0.23 %)
peripheral vascular disorders				
no	49,190	(90.81 %)	18,228	(89.37 %)
yes	4,978	(9.18 %)	2,167	(10.62 %)
psychoses				
no	53,889	(99.48 %)	20,330	(99.68 %)
yes	279	(0.51 %)	65	(0.31 %)
pulmonary circulation disorders				
no	52,476	(96.87 %)	19,929	(97.71 %)
yes	1,692	(3.12 %)	466	(2.28 %)
renal Diseases				
no	45,739	(84.43 %)	17,896	(87.74 %)
yes	8,429	(15.56 %)	2,499	(12.25 %)
rheumatoid arthritis/ collagen vascular diseases				
no	53,262	(98.32 %)	20,115	(98.62 %)
yes	906	(1.67 %)	280	(1.37 %)
solid tumor without metastasis				
no	28,520	(52.65 %)	6,722	(32.95 %)
yes	25,648	(47.34 %)	13,673	(67.04 %)
valvular disease				
no	51,473	(95.02 %)	19,591	(96.05 %)
yes	2,695	(4.97 %)	804	(3.94 %)
weight loss				
no	46,134	(85.16 %)	17,442	(85.52 %)
yes	8,034	(14.83 %)	2,953	(14.47 %)
HEALTHCARE CHARACTERISTICS				
total colon resections				
no	51,310	(94.72 %)	20,173	(98.91 %)
yes	2,858	(5.27 %)	222	(1.08 %)
partial colon resections				
no	2,662	(4.91 %)	17,088	(83.78 %)
yes	51,506	(95.08 %)	3,307	(16.21 %)
rectum resections				
no	50,665	(93.53 %)	-	-
yes	3,503	(6.46 %)	20,395	(100.00 %)
colon and rectum resection				
no	50,665	(93.53 %)	16,892	(82.82 %)
yes	3,503	(6.46 %)	3,503	(17.17 %)
weekend surgery				
no	49,473	(91.33 %)	19,603	(96.11 %)
yes	4,695	(8.66 %)	792	(3.88 %)
admission				
referral	36,129	(66.69 %)	16,249	(79.67 %)
emergency case	16,116	(29.75 %)	3,744	(18.35 %)
transfer from other hospital	1,923	(3.55 %)	402	(1.97 %)

HOSPITAL CHARACTERISTICS				
annual volume				
colon resection cases (median)	72	(38; 119)	-	-
total colon resection (median)	1	(0;3)	-	-
rectum resections (median)	-	-	26	(11;42)
urbanization				
urban	124	(59.33 %)	119	(59.50 %)
rural	85	(40.66 %)	81	(40.50 %)
ownership				
public	82	(39.23 %)	80	(40.00 %)
non-profit	41	(19.61 %)	39	(19.50 %)
private	86	(41.14 %)	81	(40.50 %)
university hospital				
no	201	(96.17 %)	192	(96.00 %)
yes	8	(3.82 %)	8	(4.00 %)

S7: Bivariate analysis of case-, care- and hospital-related covariates of patient safety including all 54.168 colon resections in 209 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
PATIENT COVARIATES	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
sex								
male	Ref.		Ref.		Ref.		Ref.	
female	0.876***	(0.827 - 0.928)	0.828***	(0.790 - 0.868)	0.742***	(0.707 - 0.778)	0.931**	(0.881 - 0.983)
age	1.052***	(1.049 - 1.055)	1.030***	(1.028 - 1.031)	1.037***	(1.035 - 1.039)	1.008***	(1.006 - 1.009)
alcohol abuse	3.845***	(3.363 - 4.396)	3.862***	(3.400 - 4.387)	3.860***	(3.406 - 4.374)	1.945***	(1.669 - 2.266)
blood loss anemia	0.715**	(0.570 - 0.896)	1.355***	(1.159 - 1.585)	1.200*	(1.025 - 1.405)	1.387***	(1.159 - 1.659)
cardiac arrhythmias	4.338***	(4.084 - 4.608)	3.544***	(3.364 - 3.734)	3.995***	(3.791 - 4.209)	1.766***	(1.660 - 1.878)
chronic pulmonary disease	2.025***	(1.867 - 2.196)	2.120***	(1.978 - 2.273)	1.793***	(1.668 - 1.927)	1.554***	(1.431 - 1.689)
coagulopathy	9.015***	(8.439 - 9.630)	6.370***	(6.011 - 6.751)	7.207***	(6.798 - 7.640)	2.483***	(2.331 - 2.646)
congestive heart failure	4.645***	(4.342 - 4.969)	4.294***	(4.042 - 4.563)	4.382***	(4.127 - 4.652)	1.899***	(1.765 - 2.044)
deficiency anemia	1.013	(0.878 - 1.169)	1.448***	(1.302 - 1.610)	1.416***	(1.268 - 1.582)	1.250***	(1.101 - 1.418)
depression	0.888	(0.779 - 1.012)	1.827***	(1.669 - 2.000)	1.372***	(1.244 - 1.513)	1.923***	(1.741 - 2.125)
diabetes, complicated	2.766***	(2.481 - 3.084)	2.339***	(2.121 - 2.578)	2.946***	(2.678 - 3.240)	1.705***	(1.514 - 1.921)
diabetes, uncomplicated	1.485***	(1.378 - 1.600)	1.559***	(1.465 - 1.659)	1.594***	(1.497 - 1.698)	1.300***	(1.208 - 1.399)
fluid and electrolyte disorders	4.072***	(3.809 - 4.354)	4.463***	(4.229 - 4.709)	5.033***	(4.756 - 5.328)	2.650***	(2.497 - 2.812)
hypertension, complicated	2.124***	(1.896 - 2.380)	2.156***	(1.957 - 2.375)	2.446***	(2.225 - 2.688)	1.453***	(1.288 - 1.638)
hypertension, uncomplicated	0.961	(0.906 - 1.020)	1.266***	(1.207 - 1.329)	1.294***	(1.232 - 1.360)	1.198***	(1.132 - 1.267)
hypothyroidism	0.964	(0.883 - 1.052)	1.227***	(1.147 - 1.312)	1.176***	(1.096 - 1.261)	1.316***	(1.219 - 1.421)
liver disease	6.486***	(6.007 - 7.004)	2.844***	(2.635 - 3.069)	4.573***	(4.254 - 4.917)	1.345***	(1.223 - 1.478)
lymphoma	1.869***	(1.441 - 2.424)	1.319*	(1.030 - 1.690)	1.850***	(1.470 - 2.327)	1.246	(0.939 - 1.654)
metastatic cancer	0.948	(0.881 - 1.021)	1.004	(0.946 - 1.065)	0.827***	(0.777 - 0.881)	1.069	(1.000 - 1.143)
obesity	0.780***	(0.707 - 0.860)	1.173***	(1.092 - 1.259)	1.419***	(1.324 - 1.521)	1.556***	(1.533 - 1.789)
other neurological disorders	2.854***	(2.567 - 3.174)	3.417***	(3.109 - 3.754)	2.834***	(2.575 - 3.119)	1.860***	(1.660 - 2.084)
paralysis	2.709***	(2.373 - 3.092)	3.030***	(2.692 - 3.410)	2.435***	(2.156 - 2.751)	1.874***	(1.629 - 2.156)
peripheral vascular disorders	3.572***	(3.316 - 3.848)	2.745***	(2.562 - 2.941)	3.001***	(2.804 - 3.213)	1.741***	(1.606 - 1.889)
psychoses	1.004	(0.676 - 1.492)	2.578***	(1.978 - 3.361)	1.232	(0.903 - 1.679)	1.845***	(1.352 - 2.517)
pulmonary circulation disorders	3.533***	(3.150 - 3.964)	3.959***	(3.562 - 4.401)	3.185***	(2.863 - 3.543)	1.721***	(1.511 - 1.960)
renal failure	2.772***	(2.592 - 2.966)	2.261***	(2.132 - 2.398)	2.982***	(2.815 - 3.158)	1.524***	(1.419 - 1.636)
rheumatoid arthritis/collagen vascular diseases	1.393**	(1.141 - 1.702)	1.283***	(1.079 - 1.524)	1.373***	(1.156 - 1.630)	1.196	(0.980 - 1.461)
solid tumor without metastasis	0.660***	(0.622 - 0.701)	0.845***	(0.806 - 0.886)	0.760***	(0.724 - 0.798)	0.949	(0.898 - 1.002)
valvular disease	2.580***	(2.332 - 2.855)	2.355***	(2.151 - 2.579)	2.632***	(2.409 - 2.876)	1.426***	(1.275 - 1.594)
weight loss	1.439***	(1.328 - 1.560)	2.418***	(2.269 - 2.576)	2.091***	(1.963 - 2.228)	2.230***	(2.073 - 2.398)
HEALTHCARE COVARIATES								
admission								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	3.066***	(2.852 - 3.297)	2.263***	(2.133 - 2.401)	2.409***	(2.260 - 2.567)	1.461***	(1.368 - 1.559)
transfer from other hospital	5.722***	(5.105 - 6.412)	4.200***	(3.768 - 4.680)	4.308***	(3.870 - 4.795)	1.865***	(1.645 - 2.115)
weekend Surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.704***	(2.498 - 2.927)	2.148***	(1.999 - 2.308)	2.254***	(2.099 - 2.419)	1.382***	(1.265 - 1.509)

total colon resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	3.687***	(3.351 - 4.057)	2.395***	(2.186 - 2.625)	2.954***	(2.704 - 3.227)	1.340***	(1.204 - 1.493)
colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.114	(0.991 - 1.252)	1.563***	(1.429 - 1.710)	1.390***	(1.267 - 1.525)	1.757***	(1.593 - 1.937)
HOSPITAL COVARIATES								
case volume	1.071	(0.978 - 1.173)	0.934	(0.837 - 1.043)	1.044	(0.944 - 1.155)	1.265***	(1.117 - 1.432)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	0.830*	(0.711 - 0.969)	0.849	(0.665 - 1.085)	0.760**	(0.624 - 0.927)	0.837	(0.661 - 1.059)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.946***	(1.411 - 2.683)	1.003	(0.555 - 1.814)	1.767*	(1.113 - 2.806)	3.178***	(1.894 - 5.333)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	0.774*	(0.634 - 0.945)	0.915	(0.657 - 1.272)	0.691**	(0.534 - 0.895)	0.615**	(0.452 - 0.835)
private	0.748***	(0.636 - 0.880)	1.025	(0.785 - 1.338)	1.226	(0.999 - 1.504)	0.662**	(0.518 - 0.847)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to low case numbers
*** p<0.001
** p <0.01
* p<0.05

S8: Bivariate analysis of case-, care- and hospital-related covariates of patient safety including all 20.395 rectum resections in 200 hospitals

-	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
PATIENT COVARIATES	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
sex								
male	Ref.		Ref.		Ref.		Ref.	
female	0.915	(0.796 - 1.050)	0.913*	(0.836 - 0.998)	0.787***	(0.717 - 0.864)	0.877**	(0.801 - 0.960)
age	1.075***	(1.067 - 1.082)	1.031***	(1.027 - 1.034)	1.039***	(1.035 - 1.043)	1.007***	(1.004 - 1.010)
alcohol abuse	2.767***	(1.915 - 3.997)	2.705***	(2.050 - 3.570)	2.531***	(1.916 - 3.345)	1.826***	(1.356 - 2.459)
blood loss anemia	1.984**	(1.270 - 3.100)	1.769**	(1.256 - 2.493)	2.637***	(1.942 - 3.581)	2.264***	(1.619 - 3.165)
cardiac arrhythmias	5.465***	(4.741 - 6.299)	3.457***	(3.124 - 3.825)	3.777***	(3.410 - 4.183)	1.564***	(1.399 - 1.748)
chronic pulmonary disease	2.213***	(1.820 - 2.690)	2.185***	(1.905 - 2.506)	1.835***	(1.587 - 2.122)	1.690***	(1.463 - 1.952)
coagulopathy	9.352***	(8.020 - 10.906)	5.781***	(5.171 - 6.463)	5.702***	(5.091 - 6.386)	2.680***	(2.401 - 2.993)
congestive heart failure	5.853***	(4.995 - 6.858)	4.275***	(3.781 - 4.834)	4.272***	(3.787 - 4.820)	1.793***	(1.560 - 2.060)
deficiency anemia	1.741**	(1.241 - 2.442)	2.119***	(1.696 - 2.648)	2.275***	(1.810 - 2.858)	1.893***	(1.499 - 2.391)
depression	0.872	(0.637 - 1.192)	1.675***	(1.409 - 1.991)	1.686***	(1.411 - 2.014)	1.701***	(1.436 - 2.014)
diabetes, complicated	3.196***	(2.455 - 4.160)	2.073***	(1.692 - 2.540)	3.187***	(2.635 - 3.854)	1.730***	(1.390 - 2.154)
diabetes, uncomplicated	1.653***	(1.388 - 1.969)	1.613***	(1.435 - 1.813)	1.660***	(1.472 - 1.873)	1.341***	(1.184 - 1.518)
fluid and electrolyte disorders	3.961***	(3.387 - 4.633)	4.043***	(3.660 - 4.467)	4.586***	(4.122 - 5.102)	2.563***	(2.324 - 2.826)
hypertension, complicated	2.656***	(2.033 - 3.470)	2.366***	(1.947 - 2.876)	2.681***	(2.225 - 3.230)	1.480***	(1.188 - 1.844)
hypertension, uncomplicated	1.094	(0.951 - 1.257)	1.358***	(1.241 - 1.486)	1.449***	(1.318 - 1.593)	1.159***	(1.057 - 1.271)
hypothyroidism	0.980	(0.790 - 1.215)	1.164*	(1.019 - 1.329)	1.170*	(1.019 - 1.344)	1.125	(0.981 - 1.290)
liver disease	5.887***	(4.864 - 7.124)	2.298***	(1.937 - 2.725)	3.606***	(3.084 - 4.216)	1.539***	(1.279 - 1.850)
lymphoma	2.350*	(1.112 - 4.967)	1.618	(0.882 - 2.967)	1.766	(0.972 - 3.208)	1.683	(0.946 - 2.992)
metastatic cancer	0.979	(0.835 - 1.148)	1.298***	(1.177 - 1.431)	0.978	(0.879 - 1.087)	1.187***	(1.075 - 1.311)
obesity	0.908	(0.726 - 1.135)	1.500***	(1.320 - 1.704)	1.632***	(1.435 - 1.855)	1.653***	(1.455 - 1.878)
other neurological disorders	3.942***	(3.107 - 5.001)	3.107***	(2.569 - 3.757)	2.277***	(1.860 - 2.788)	1.887***	(1.530 - 2.327)
paralysis	3.060***	(2.244 - 4.173)	2.958***	(2.336 - 3.745)	2.816***	(2.220 - 3.572)	1.849***	(1.425 - 2.399)
peripheral vascular disorders	2.521***	(2.118 - 3.000)	1.673***	(1.469 - 1.905)	1.924***	(1.690 - 2.189)	1.531***	(1.341 - 1.748)
psychoses	0.943	(0.291 - 3.056)	0.843	(0.371 - 1.914)	1.865	(0.969 - 3.592)	1.337	(0.660 - 2.707)
pulmonary circulation disorders	6.535***	(5.123 - 8.336)	4.514***	(3.663 - 5.563)	3.734***	(3.022 - 4.613)	2.041***	(1.619 - 2.573)
renal failure	2.984***	(2.532 - 3.518)	2.416***	(2.147 - 2.718)	3.393***	(3.031 - 3.797)	1.688***	(1.488 - 1.915)
rheumatoid arthritis/collagen vascular diseases	1.521	(0.932 - 2.482)	1.582**	(1.140 - 2.196)	1.471*	(1.043 - 2.076)	0.868	(0.580 - 1.301)
solid tumor without metastasis	0.571***	(0.494 - 0.659)	1.002	(0.906 - 1.107)	0.836***	(0.755 - 0.924)	1.090	(0.984 - 1.207)
valvular disease	3.682***	(2.935 - 4.619)	2.693***	(2.257 - 3.214)	2.803***	(2.351 - 3.341)	1.364**	(1.113 - 1.672)
weight loss	1.408***	(1.165 - 1.702)	2.522***	(2.244 - 2.834)	2.072***	(1.842 - 2.331)	2.079***	(1.843 - 2.346)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	4.038***	(3.450 - 4.727)	2.200***	(1.963 - 2.465)	2.272***	(2.013 - 2.563)	1.656***	(1.474 - 1.862)
transfer from other hospital	6.550***	(4.887 - 8.780)	3.944***	(3.088 - 5.038)	4.248***	(3.337 - 5.406)	2.208***	(1.705 - 2.861)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	3.693***	(2.927 - 4.659)	2.215***	(1.831 - 2.678)	2.177***	(1.809 - 2.620)	1.281*	(1.030 - 1.593)
colon and rectum resection								

no	Ref.		Ref.		Ref.		Ref.	
yes	4.015***	(3.458 - 4.663)	3.095***	(2.781 - 3.444)	2.706***	(2.428 - 3.016)	2.014***	(1.805 - 2.247)
HOSPITAL COVARIATES								
case volume	0.743***	(0.661 - 0.835)	0.828**	(0.730 - 0.940)	0.830***	(0.746 - 0.924)	1.079	(0.946 - 1.232)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	0.882	(0.680 - 1.143)	0.925	(0.684 - 1.251)	0.895	(0.709 - 1.129)	0.726*	(0.554 - 0.951)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.439	(0.890 - 2.324)	0.857	(0.435 - 1.690)	1.134	(0.696 - 1.847)	3.037***	(1.778 - 5.186)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	0.691*	(0.500 - 0.954)	0.887	(0.594 - 1.324)	0.633**	(0.472 - 0.848)	0.605**	(0.428 - 0.854)
private	0.631***	(0.480 - 0.830)	1.070	(0.773 - 1.482)	1.245	(0.988 - 1.571)	0.673**	(0.508 - 0.893)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers
*** p<0.001
** p <0.01
* p<0.05

S9: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including all 54.168 colon resections in 209 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref		Ref		Ref	
female	0.937	(0.873 - 1.006)	0.788***	(0.745 - 0.833)	0.683***	(0.645 - 0.725)	0.882***	(0.832 - 0.936)
age	1.050***	(1.046 - 1.053)	1.014***	(1.012 - 1.017)	1.024***	(1.021 - 1.026)	0.998	(0.996 - 1.000)
alcohol abuse	1.484***	(1.250 - 1.761)	1.948***	(1.677 - 2.263)	1.574***	(1.352 - 1.833)	1.304***	(1.106 - 1.539)
blood loss anemia	0.472***	(0.365 - 0.609)	0.982	(0.823 - 1.172)	0.831*	(0.695 - 0.995)	1.154	(0.958 - 1.390)
cardiac arrhythmias	1.640***	(1.518 - 1.772)	1.585***	(1.487 - 1.690)	1.627***	(1.524 - 1.737)	1.183***	(1.100 - 1.271)
chronic pulmonary disease	1.362***	(1.234 - 1.503)	1.459***	(1.347 - 1.581)	1.113*	(1.022 - 1.212)	1.242***	(1.138 - 1.356)
coagulopathy	4.174***	(3.864 - 4.509)	3.117***	(2.920 - 3.327)	3.332***	(3.118 - 3.561)	1.644***	(1.531 - 1.764)
congestive heart failure	1.748***	(1.597 - 1.914)	1.902***	(1.759 - 2.056)	1.678***	(1.551 - 1.815)	1.218***	(1.114 - 1.332)
deficiency anemia	0.778**	(0.660 - 0.918)	1.058	(0.937 - 1.194)	1.096	(0.965 - 1.245)	1.024	(0.897 - 1.169)
depression	0.658***	(0.566 - 0.765)	1.425***	(1.286 - 1.580)	1.070	(0.956 - 1.197)	1.569***	(1.414 - 1.741)
diabetes, complicated	1.297***	(1.131 - 1.487)	1.181**	(1.051 - 1.328)	1.274***	(1.135 - 1.431)	1.191**	(1.045 - 1.358)
diabetes, uncomplicated	1.128*	(1.029 - 1.237)	1.201***	(1.117 - 1.291)	1.151***	(1.067 - 1.241)	1.113***	(1.028 - 1.204)
fluid and electrolyte disorders	1.884***	(1.743 - 2.038)	2.561***	(2.412 - 2.719)	2.882***	(2.704 - 3.072)	1.991***	(1.867 - 2.123)
hypertension, complicated	0.507***	(0.437 - 0.589)	0.735***	(0.649 - 0.832)	0.805***	(0.712 - 0.911)	0.928	(0.807 - 1.067)
hypertension, uncomplicated	0.551***	(0.511 - 0.595)	0.945	(0.890 - 1.003)	0.921*	(0.865 - 0.981)	1.045	(0.980 - 1.115)
hypothyroidism	0.795***	(0.716 - 0.884)	1.110**	(1.027 - 1.200)	1.046	(0.963 - 1.137)	1.206***	(1.112 - 1.309)
liver disease	4.411***	(3.999 - 4.865)	1.373***	(1.253 - 1.506)	2.588***	(2.368 - 2.829)	0.831***	(0.749 - 0.923)
lymphoma	0.983	(0.717 - 1.349)	0.810	(0.613 - 1.070)	1.111	(0.846 - 1.458)	1.029	(0.767 - 1.382)
metastatic cancer	1.524***	(1.376 - 1.687)	1.120**	(1.036 - 1.211)	0.984	(0.906 - 1.070)	1.058	(0.974 - 1.149)
obesity	0.766***	(0.682 - 0.862)	1.165***	(1.073 - 1.265)	1.498***	(1.379 - 1.627)	1.634***	(1.506 - 1.773)
other neurological disorders	1.504***	(1.319 - 1.714)	1.903***	(1.706 - 2.123)	1.515***	(1.352 - 1.699)	1.259***	(1.114 - 1.422)
paralysis	1.481***	(1.261 - 1.740)	1.468***	(1.281 - 1.682)	1.142	(0.989 - 1.318)	1.231**	(1.060 - 1.429)
peripheral vascular disorders	1.926***	(1.757 - 2.111)	1.493***	(1.378 - 1.618)	1.518***	(1.399 - 1.647)	1.239***	(1.136 - 1.351)
psychoses	0.707	(0.449 - 1.113)	2.052***	(1.516 - 2.778)	0.859	(0.600 - 1.229)	1.493*	(1.081 - 2.061)
pulmonary circulation disorders	1.593***	(1.380 - 1.838)	1.864***	(1.649 - 2.108)	1.336***	(1.174 - 1.519)	1.071	(0.933 - 1.231)
renal failure	1.308***	(1.200 - 1.425)	1.112**	(1.035 - 1.196)	1.505***	(1.401 - 1.616)	1.067	(0.984 - 1.156)
rheumatoid arthritis/collagen vascular diseases	1.001	(0.793 - 1.264)	0.971	(0.798 - 1.182)	0.982	(0.806 - 1.197)	1.056	(0.858 - 1.298)
solid tumor without metastasis	0.573***	(0.525 - 0.625)	0.764***	(0.715 - 0.816)	0.707***	(0.660 - 0.757)	0.907***	(0.845 - 0.975)
valvular disease	0.817**	(0.719 - 0.929)	0.862**	(0.772 - 0.961)	0.927	(0.831 - 1.033)	0.927	(0.820 - 1.048)
weight loss	0.891*	(0.809 - 0.980)	1.658***	(1.542 - 1.783)	1.426***	(1.324 - 1.535)	1.774***	(1.643 - 1.916)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	1.847***	(1.692 - 2.015)	1.413***	(1.320 - 1.513)	1.453***	(1.349 - 1.566)	1.145***	(1.067 - 1.228)
transfer from other hospital	2.528***	(2.193 - 2.915)	1.982***	(1.749 - 2.245)	1.908***	(1.678 - 2.171)	1.223***	(1.071 - 1.397)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.669***	(1.515 - 1.839)	1.426***	(1.312 - 1.550)	1.480***	(1.360 - 1.610)	1.080	(0.984 - 1.186)

total colon resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.679***	(2.369 - 3.029)	1.639***	(1.472 - 1.825)	2.228***	(1.999 - 2.483)	1.022	(0.913 - 1.143)
colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.103	(0.960 - 1.267)	1.524***	(1.378 - 1.686)	1.408***	(1.265 - 1.567)	1.579***	(1.426 - 1.748)
HOSPITAL COVARIATES								
case volume	0.968	(0.871 - 1.076)	0.919	(0.807 - 1.047)	0.992	(0.891 - 1.106)	1.168*	(1.030 - 1.325)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	1.061	(0.893 - 1.261)	0.863	(0.648 - 1.149)	0.772**	(0.635 - 0.939)	1.032	(0.824 - 1.292)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.303	(0.888 - 1.912)	0.687	(0.338 - 1.397)	1.412	(0.889 - 2.241)	1.981*	(1.171 - 3.352)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	1.012	(0.811 - 1.262)	1.057	(0.726 - 1.540)	0.867	(0.670 - 1.122)	0.744*	(0.555 - 0.998)
private	1.244*	(1.026 - 1.507)	1.329	(0.972 - 1.817)	1.937***	(1.563 - 2.400)	0.777*	(0.608 - 0.992)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers
*** p<0.001
** p <0.01
* p<0.05

S10: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including all 20.395 rectum resections in 200 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref.		Ref.		Ref.	
female	0.842*	(0.710 - 0.998)	0.842**	(0.759 - 0.934)	0.685***	(0.613 - 0.765)	0.826***	(0.748 - 0.912)
age	1.068***	(1.059 - 1.078)	1.014***	(1.009 - 1.018)	1.021***	(1.016 - 1.026)	0.998	(0.995 - 1.002)
alcohol abuse	1.410	(0.891 - 2.231)	1.656**	(1.200 - 2.286)	1.207	(0.869 - 1.676)	1.143	(0.828 - 1.578)
blood loss anemia	0.829	(0.486 - 1.413)	0.890	(0.607 - 1.305)	1.383	(0.976 - 1.959)	1.579*	(1.113 - 2.241)
cardiac arrhythmias	1.832***	(1.535 - 2.188)	1.662***	(1.471 - 1.878)	1.639***	(1.448 - 1.854)	1.034	(0.909 - 1.176)
chronic pulmonary disease	1.303*	(1.030 - 1.648)	1.510***	(1.291 - 1.766)	1.156	(0.979 - 1.366)	1.369***	(1.175 - 1.594)
coagulopathy	4.309***	(3.600 - 5.158)	3.052***	(2.697 - 3.455)	2.886***	(2.541 - 3.277)	1.770***	(1.570 - 1.996)
congestive heart failure	1.825***	(1.481 - 2.248)	1.849***	(1.583 - 2.159)	1.536***	(1.317 - 1.792)	1.099	(0.929 - 1.300)
deficiency anemia	0.880	(0.593 - 1.304)	1.242	(0.967 - 1.595)	1.357*	(1.052 - 1.750)	1.332*	(1.043 - 1.700)
depression	0.629*	(0.439 - 0.900)	1.222*	(1.005 - 1.486)	1.290*	(1.056 - 1.577)	1.386***	(1.161 - 1.654)
diabetes, complicated	1.584**	(1.145 - 2.192)	1.045	(0.824 - 1.326)	1.441**	(1.153 - 1.801)	1.172	(0.922 - 1.490)
diabetes, uncomplicated	1.124	(0.911 - 1.388)	1.194*	(1.043 - 1.368)	1.191*	(1.036 - 1.369)	1.164*	(1.018 - 1.331)
fluid and electrolyte disorders	1.704***	(1.425 - 2.039)	2.432***	(2.181 - 2.712)	2.855***	(2.542 - 3.206)	1.952***	(1.759 - 2.166)
hypertension, complicated	0.461***	(0.324 - 0.656)	0.757*	(0.591 - 0.970)	0.836	(0.659 - 1.060)	0.911	(0.704 - 1.178)
hypertension, uncomplicated	0.584***	(0.490 - 0.695)	0.980	(0.878 - 1.093)	0.999	(0.890 - 1.121)	0.993	(0.893 - 1.104)
hypothyroidism	0.812	(0.632 - 1.043)	0.993	(0.854 - 1.155)	1.002	(0.856 - 1.174)	1.035	(0.895 - 1.198)
liver disease	4.027***	(3.155 - 5.139)	1.268*	(1.036 - 1.553)	2.312***	(1.920 - 2.783)	1.036	(0.848 - 1.267)
lymphoma	1.308	(0.563 - 3.042)	1.028	(0.532 - 1.986)	0.930	(0.476 - 1.814)	1.320	(0.718 - 2.427)
metastatic cancer	1.376**	(1.118 - 1.694)	1.211**	(1.073 - 1.367)	0.983	(0.863 - 1.121)	1.051	(0.937 - 1.179)
obesity	0.922	(0.708 - 1.202)	1.501***	(1.296 - 1.738)	1.563***	(1.348 - 1.812)	1.638***	(1.431 - 1.876)
other neurological disorders	2.306***	(1.722 - 3.089)	1.879***	(1.507 - 2.343)	1.184	(0.936 - 1.498)	1.376**	(1.098 - 1.725)
paralysis	1.153	(0.785 - 1.695)	1.391*	(1.056 - 1.833)	1.320	(0.999 - 1.744)	1.110	(0.839 - 1.469)
peripheral vascular disorders	1.908***	(1.548 - 2.353)	1.253**	(1.083 - 1.450)	1.369***	(1.181 - 1.587)	1.283***	(1.117 - 1.475)
psychoses	0.867	(0.205 - 3.672)	0.618	(0.246 - 1.551)	2.075	(0.986 - 4.369)	1.072	(0.507 - 2.264)
pulmonary circulation disorders	2.816***	(2.076 - 3.821)	1.935***	(1.522 - 2.460)	1.460**	(1.140 - 1.870)	1.208	(0.941 - 1.551)
renal failure	1.124	(0.917 - 1.377)	1.252**	(1.087 - 1.442)	1.766***	(1.544 - 2.020)	1.278***	(1.108 - 1.473)
rheumatoid arthritis/collagen vascular diseases	0.954	(0.531 - 1.713)	1.248	(0.860 - 1.812)	1.014	(0.683 - 1.507)	0.761	(0.501 - 1.158)
solid tumor without metastasis	0.599***	(0.491 - 0.731)	0.962	(0.846 - 1.094)	0.798***	(0.700 - 0.909)	1.070	(0.946 - 1.211)
valvular disease	1.000	(0.750 - 1.333)	1.075	(0.870 - 1.328)	1.042	(0.844 - 1.287)	0.893	(0.713 - 1.117)
weight loss	0.906	(0.729 - 1.127)	1.810***	(1.590 - 2.060)	1.448***	(1.268 - 1.653)	1.679***	(1.479 - 1.905)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	2.028***	(1.675 - 2.454)	1.335***	(1.170 - 1.523)	1.342***	(1.169 - 1.540)	1.291***	(1.138 - 1.466)
transfer from other hospital	2.679***	(1.874 - 3.828)	1.859***	(1.406 - 2.459)	1.927***	(1.461 - 2.541)	1.484**	(1.131 - 1.948)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.960***	(1.483 - 2.591)	1.427**	(1.150 - 1.770)	1.391**	(1.127 - 1.717)	0.985	(0.784 - 1.238)

colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.579***	(2.163 - 3.074)	2.164***	(1.921 - 2.438)	1.859***	(1.645 - 2.100)	1.522***	(1.356 - 1.708)
HOSPITAL COVARIATES								
case volume	0.703***	(0.611 - 0.809)	0.844*	(0.725 - 0.982)	0.853**	(0.760 - 0.958)	0.973	(0.854 - 1.109)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	1.072	(0.817 - 1.407)	0.904	(0.639 - 1.281)	0.834	(0.670 - 1.037)	0.854	(0.663 - 1.101)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.616	(0.979 - 2.665)	0.853	(0.379 - 1.920)	1.299	(0.829 - 2.037)	2.292**	(1.358 - 3.869)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	0.851	(0.614 - 1.179)	1.059	(0.674 - 1.664)	0.762	(0.576 - 1.008)	0.761	(0.553 - 1.048)
private	0.925	(0.682 - 1.254)	1.267	(0.865 - 1.858)	1.597***	(1.256 - 2.030)	0.846	(0.642 - 1.117)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers

*** p<0.001

** p <0.01

* p<0.05

S11: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including 25.805 colon cancer resections in 201 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref		Ref		Ref	
female	0.867***	(0.780 - 0.963)	0.810***	(0.747 - 0.878)	0.623***	(0.572 - 0.678)	0.879**	(0.807 - 0.959)
age	1.039***	(1.034 - 1.045)	1.008***	(1.005 - 1.012)	1.018***	(1.014 - 1.022)	0.998	(0.994 - 1.002)
alcohol abuse	1.448*	(1.087 - 1.928)	1.273	(0.982 - 1.650)	1.297*	(1.006 - 1.672)	1.222	(0.919 - 1.624)
blood loss anemia	0.552***	(0.405 - 0.752)	0.926	(0.743 - 1.153)	0.720**	(0.576 - 0.899)	1.199	(0.953 - 1.507)
cardiac arrhythmias	1.616***	(1.440 - 1.814)	1.560***	(1.422 - 1.712)	1.639***	(1.492 - 1.800)	1.229***	(1.108 - 1.363)
chronic pulmonary disease	1.329***	(1.142 - 1.546)	1.450***	(1.288 - 1.632)	1.059	(0.931 - 1.204)	1.213**	(1.064 - 1.384)
coagulopathy	4.057***	(3.617 - 4.550)	3.121***	(2.837 - 3.434)	3.066***	(2.780 - 3.383)	1.679***	(1.515 - 1.861)
congestive heart failure	1.766***	(1.539 - 2.026)	1.848***	(1.649 - 2.071)	1.629***	(1.453 - 1.827)	1.143*	(1.000 - 1.306)
deficiency anemia	0.687***	(0.550 - 0.858)	1.027	(0.880 - 1.198)	0.894	(0.756 - 1.057)	0.945	(0.793 - 1.126)
depression	0.760*	(0.610 - 0.946)	1.409***	(1.212 - 1.637)	1.053	(0.891 - 1.243)	1.557***	(1.336 - 1.813)
diabetes, complicated	1.213	(0.986 - 1.491)	0.969	(0.817 - 1.149)	1.351***	(1.150 - 1.587)	1.077	(0.891 - 1.302)
diabetes, uncomplicated	1.100	(0.965 - 1.253)	1.125*	(1.017 - 1.243)	1.090	(0.982 - 1.210)	1.074	(0.963 - 1.198)
fluid and electrolyte disorders	1.873***	(1.670 - 2.100)	2.338***	(2.145 - 2.547)	2.755***	(2.512 - 3.021)	2.038***	(1.857 - 2.236)
hypertension, complicated	0.511***	(0.409 - 0.639)	0.846	(0.711 - 1.008)	0.795*	(0.667 - 0.947)	0.941	(0.770 - 1.151)
hypertension, uncomplicated	0.624***	(0.559 - 0.698)	0.960	(0.861 - 1.047)	0.996	(0.909 - 1.090)	0.997	(0.909 - 1.094)
hypothyroidism	0.879	(0.752 - 1.028)	1.071	(0.955 - 1.201)	1.018	(0.900 - 1.151)	1.200**	(1.064 - 1.354)
liver disease	3.393***	(2.941 - 3.914)	1.375***	(1.202 - 1.571)	2.346***	(2.065 - 2.664)	0.906	(0.777 - 1.056)
lymphoma	0.816	(0.463 - 1.437)	0.766	(0.477 - 1.231)	1.366	(0.891 - 2.093)	1.283	(0.798 - 2.063)
metastatic cancer	1.414***	(1.273 - 1.571)	1.089*	(1.005 - 1.181)	0.986	(0.905 - 1.073)	1.053	(0.966 - 1.148)
obesity	0.745***	(0.621 - 0.894)	1.123	(0.994 - 1.269)	1.431***	(1.266 - 1.616)	1.513***	(1.337 - 1.713)
other neurological disorders	1.337**	(1.080 - 1.655)	1.818***	(1.532 - 2.157)	1.512***	(1.263 - 1.810)	1.214	(0.997 - 1.479)
paralysis	1.754***	(1.367 - 2.250)	1.402**	(1.135 - 1.733)	1.114	(0.889 - 1.395)	1.209	(0.951 - 1.537)
peripheral vascular disorders	1.644***	(1.420 - 1.904)	1.295***	(1.144 - 1.465)	1.290***	(1.138 - 1.462)	1.217**	(1.068 - 1.387)
psychoses	1.170	(0.607 - 2.253)	1.520	(0.948 - 2.437)	1.222	(0.731 - 2.045)	1.359	(0.820 - 2.252)
pulmonary circulation disorders	1.840***	(1.511 - 2.240)	1.977***	(1.675 - 2.333)	1.360***	(1.141 - 1.620)	1.088	(0.898 - 1.318)
renal failure	1.248***	(1.098 - 1.420)	1.162***	(1.047 - 1.289)	1.538***	(1.389 - 1.702)	1.143*	(1.018 - 1.282)
rheumatoid arthritis/collagen vascular diseases	0.883	(0.559 - 1.395)	0.647*	(0.441 - 0.949)	0.894	(0.626 - 1.277)	0.884	(0.599 - 1.305)
solid tumor without metastasis	0.329***	(0.212 - 0.511)	0.806	(0.520 - 1.252)	0.507**	(0.332 - 0.773)	1.526	(0.894 - 2.605)
valvular disease	0.671***	(0.548 - 0.821)	0.875	(0.747 - 1.024)	0.914	(0.781 - 1.069)	0.920	(0.769 - 1.100)
weight loss	1.007	(0.882 - 1.150)	1.586***	(1.434 - 1.753)	1.366***	(1.233 - 1.514)	1.583***	(1.421 - 1.763)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	1.822***	(1.613 - 2.058)	1.202***	(1.089 - 1.326)	1.407***	(1.266 - 1.564)	1.091	(0.983 - 1.211)
transfer from other hospital	2.491***	(1.962 - 3.161)	1.697***	(1.371 - 2.101)	1.556***	(1.247 - 1.941)	1.389**	(1.112 - 1.734)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.949***	(1.650 - 2.303)	1.377***	(1.187 - 1.598)	1.578***	(1.365 - 1.824)	1.049	(0.885 - 1.244)

total colon resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.046***	(1.669 - 2.509)	1.691***	(1.420 - 2.014)	1.703***	(1.422 - 2.038)	1.182	(0.986 - 1.417)
colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.025	(0.853 - 1.232)	1.617***	(1.422 - 1.837)	1.394***	(1.214 - 1.600)	1.753***	(1.542 - 1.993)
HOSPITAL COVARIATES								
case volume	0.926	(0.810 - 1.058)	0.939	(0.795 - 1.110)	0.994	(0.865 - 1.142)	1.146	(0.975 - 1.348)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	1.042	(0.857 - 1.267)	0.815	(0.605 - 1.099)	0.793*	(0.639 - 0.983)	0.964	(0.750 - 1.239)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.301	(0.877 - 1.931)	0.650	(0.318 - 1.328)	1.280	(0.790 - 2.076)	2.209**	(1.281 - 3.807)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	1.146	(0.898 - 1.463)	1.098	(0.745 - 1.618)	0.876	(0.660 - 1.162)	0.767	(0.557 - 1.056)
private	1.207	(0.970 - 1.502)	1.316	(0.951 - 1.821)	1.993***	(1.572 - 2.526)	0.776	(0.591 - 1.018)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers
*** p<0.001
** p <0.01
* p<0.05

S12: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including 13.703 rectum cancer resections in 197 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref.		Ref.		Ref.	
female	0.912	(0.738 - 1.127)	0.892	(0.789 - 1.009)	0.685***	(0.599 - 0.783)	0.888	(0.789 - 1.000)
age	1.066***	(1.054 - 1.079)	1.013***	(1.007 - 1.019)	1.019***	(1.013 - 1.026)	0.998	(0.993 - 1.003)
alcohol abuse	1.807*	(1.034 - 3.156)	1.603*	(1.076 - 2.389)	1.156	(0.770 - 1.736)	1.138	(0.768 - 1.687)
blood loss anemia	0.823	(0.426 - 1.589)	0.677	(0.415 - 1.102)	1.231	(0.812 - 1.867)	1.466	(0.961 - 2.236)
cardiac arrhythmias	1.704***	(1.361 - 2.135)	1.714***	(1.484 - 1.981)	1.628***	(1.402 - 1.890)	1.050	(0.901 - 1.223)
chronic pulmonary disease	1.540**	(1.149 - 2.065)	1.473***	(1.218 - 1.781)	1.209	(0.986 - 1.482)	1.389***	(1.153 - 1.673)
coagulopathy	3.691***	(2.941 - 4.632)	2.783***	(2.396 - 3.233)	2.487***	(2.126 - 2.909)	1.723***	(1.493 - 1.990)
congestive heart failure	1.784***	(1.363 - 2.335)	1.798***	(1.488 - 2.172)	1.557***	(1.287 - 1.885)	1.028	(0.837 - 1.262)
deficiency anemia	1.008	(0.631 - 1.610)	1.404*	(1.049 - 1.879)	1.527**	(1.129 - 2.066)	1.269	(0.945 - 1.703)
depression	0.665	(0.418 - 1.058)	1.299*	(1.026 - 1.646)	1.359*	(1.060 - 1.742)	1.449***	(1.170 - 1.793)
diabetes, complicated	1.285	(0.830 - 1.990)	1.061	(0.798 - 1.409)	1.190	(0.906 - 1.562)	1.146	(0.860 - 1.528)
diabetes, uncomplicated	1.060	(0.817 - 1.375)	1.194*	(1.022 - 1.396)	1.075	(0.913 - 1.267)	1.243***	(1.067 - 1.448)
fluid and electrolyte disorders	1.693***	(1.353 - 2.117)	2.162***	(1.903 - 2.456)	2.720***	(2.367 - 3.126)	1.966***	(1.738 - 2.223)
hypertension, complicated	0.590*	(0.379 - 0.918)	0.844	(0.627 - 1.137)	0.844	(0.630 - 1.130)	0.894	(0.652 - 1.226)
hypertension, uncomplicated	0.625***	(0.502 - 0.780)	0.994	(0.873 - 1.132)	1.106	(0.962 - 1.272)	0.995	(0.877 - 1.129)
hypothyroidism	0.878	(0.633 - 1.217)	1.032	(0.860 - 1.239)	0.965	(0.791 - 1.177)	0.995	(0.832 - 1.191)
liver disease	3.342***	(2.461 - 4.538)	1.126	(0.879 - 1.443)	2.363***	(1.894 - 2.949)	1.171	(0.924 - 1.486)
lymphoma	1.440	(0.468 - 4.431)	1.006	(0.429 - 2.360)	1.225	(0.519 - 2.893)	1.918	(0.891 - 4.126)
metastatic cancer	1.280*	(1.035 - 1.581)	1.212**	(1.071 - 1.371)	1.015	(0.889 - 1.158)	1.041	(0.925 - 1.172)
obesity	0.953	(0.684 - 1.330)	1.476***	(1.241 - 1.755)	1.607***	(1.349 - 1.915)	1.570***	(1.333 - 1.849)
other neurological disorders	2.294***	(1.562 - 3.369)	2.146***	(1.634 - 2.818)	1.198	(0.885 - 1.621)	1.598***	(1.207 - 2.116)
paralysis	1.418	(0.866 - 2.321)	1.422*	(1.014 - 1.993)	1.249	(0.878 - 1.776)	1.130	(0.799 - 1.600)
peripheral vascular disorders	1.561**	(1.190 - 2.047)	1.151	(0.970 - 1.367)	1.259*	(1.055 - 1.503)	1.423***	(1.214 - 1.669)
psychoses	0.417	(0.045 - 3.841)	0.477	(0.147 - 1.541)	1.904	(0.756 - 4.792)	1.012	(0.413 - 2.481)
pulmonary circulation disorders	3.547***	(2.491 - 5.049)	2.146***	(1.633 - 2.819)	1.567**	(1.179 - 2.082)	1.234	(0.923 - 1.650)
renal failure	0.942	(0.721 - 1.231)	1.125	(0.949 - 1.334)	1.750***	(1.489 - 2.056)	1.233*	(1.039 - 1.462)
rheumatoid arthritis/collagen vascular diseases	1.041	(0.443 - 2.445)	0.825	(0.462 - 1.476)	0.962	(0.544 - 1.701)	0.600	(0.312 - 1.154)
solid tumor without metastasis	0.105***	(0.039 - 0.282)	0.960	(0.353 - 2.613)	1.074	(0.327 - 3.534)	1.648	(0.542 - 5.013)
valvular disease	0.808	(0.550 - 1.185)	1.099	(0.855 - 1.413)	0.922	(0.712 - 1.193)	0.969	(0.743 - 1.265)
weight loss	0.967	(0.745 - 1.255)	1.761***	(1.517 - 2.045)	1.333***	(1.142 - 1.558)	1.557***	(1.345 - 1.803)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	1.937***	(1.526 - 2.460)	1.199*	(1.018 - 1.413)	1.257*	(1.055 - 1.498)	1.468***	(1.255 - 1.718)
transfer from other hospital	2.503***	(1.487 - 4.213)	2.160***	(1.497 - 3.118)	1.731**	(1.180 - 2.540)	1.805***	(1.263 - 2.578)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.137***	(1.417 - 3.224)	1.384*	(1.024 - 1.870)	1.267	(0.940 - 1.708)	1.148	(0.845 - 1.560)

colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.422***	(1.940 - 3.024)	2.065***	(1.806 - 2.408)	1.711***	(1.470 - 1.991)	1.627***	(1.415 - 1.871)
HOSPITAL COVARIATES								
case volume	0.678***	(0.577 - 0.796)	0.907	(0.764 - 1.075)	0.835**	(0.730 - 0.955)	0.988	(0.851 - 1.147)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	1.164	(0.862 - 1.572)	0.951	(0.661 - 1.369)	0.808	(0.632 - 1.033)	0.843	(0.638 - 1.113)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.512	(0.889 - 2.571)	0.807	(0.355 - 1.837)	1.374	(0.840 - 2.246)	2.195*	(1.267 - 3.801)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	1.034	(0.725 - 1.473)	1.089	(0.682 - 1.740)	0.797	(0.580 - 1.095)	0.733	(0.518 - 1.037)
private	0.900	(0.635 - 1.276)	1.238	(0.828 - 1.850)	1.807***	(1.375 - 2.376)	0.853	(0.629 - 1.158)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers

*** p<0.001

** p <0.01

* p<0.05

S13: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including 28.363 non-cancer colon resections in 208 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref		Ref		Ref	
female	0.988	(0.896 - 1.090)	0.746***	(0.691 - 0.807)	0.748***	(0.689 - 0.811)	0.872**	(0.804 - 0.946)
age	1.056***	(1.051 - 1.060)	1.016***	(1.014 - 1.019)	1.026***	(1.023 - 1.030)	0.997	(0.995 - 1.000)
alcohol abuse	1.483***	(1.190 - 1.847)	2.400***	(1.985 - 2.902)	1.745***	(1.435 - 2.121)	1.350**	(1.099 - 1.657)
blood loss anemia	0.388***	(0.246 - 0.612)	1.296	(0.945 - 1.777)	1.140	(0.831 - 1.565)	1.150	(0.828 - 1.597)
cardiac arrhythmias	1.666***	(1.499 - 1.851)	1.627***	(1.487 - 1.781)	1.605***	(1.464 - 1.760)	1.166***	(1.053 - 1.291)
chronic pulmonary disease	1.405***	(1.231 - 1.603)	1.463***	(1.310 - 1.633)	1.154*	(1.028 - 1.296)	1.264***	(1.123 - 1.422)
coagulopathy	4.166***	(3.747 - 4.632)	2.920***	(2.665 - 3.198)	3.515***	(3.209 - 3.851)	1.602***	(1.451 - 1.769)
congestive heart failure	1.764***	(1.562 - 1.993)	1.972***	(1.770 - 2.197)	1.733***	(1.555 - 1.932)	1.282***	(1.135 - 1.448)
deficiency anemia	0.943	(0.732 - 1.214)	1.219	(0.995 - 1.493)	1.428***	(1.166 - 1.749)	1.188	(0.967 - 1.459)
depression	0.582***	(0.472 - 0.717)	1.488***	(1.288 - 1.719)	1.071	(0.918 - 1.249)	1.564***	(1.354 - 1.807)
diabetes, complicated	1.332*	(1.105 - 1.606)	1.430***	(1.211 - 1.688)	1.187*	(1.005 - 1.404)	1.326***	(1.104 - 1.593)
diabetes, uncomplicated	1.170*	(1.026 - 1.334)	1.304***	(1.172 - 1.450)	1.226***	(1.098 - 1.368)	1.172***	(1.046 - 1.314)
fluid and electrolyte disorders	1.828***	(1.641 - 2.037)	2.715***	(2.495 - 2.955)	2.930***	(2.681 - 3.202)	1.929***	(1.764 - 2.110)
hypertension, complicated	0.527***	(0.430 - 0.645)	0.680***	(0.570 - 0.812)	0.847*	(0.712 - 1.008)	0.965	(0.794 - 1.172)
hypertension, uncomplicated	0.489***	(0.440 - 0.543)	0.933	(0.858 - 1.015)	0.861***	(0.789 - 0.940)	1.107*	(1.011 - 1.210)
hypothyroidism	0.729***	(0.631 - 0.842)	1.152*	(1.034 - 1.283)	1.064	(0.949 - 1.192)	1.210***	(1.081 - 1.354)
liver disease	5.708***	(4.967 - 6.559)	1.408***	(1.238 - 1.601)	2.827***	(2.491 - 3.207)	0.802**	(0.694 - 0.925)
lymphoma	1.016	(0.683 - 1.513)	0.858	(0.602 - 1.223)	0.895	(0.624 - 1.284)	0.978	(0.668 - 1.433)
metastatic cancer	-		-		-		-	
obesity	0.768***	(0.657 - 0.897)	1.180***	(1.055 - 1.321)	1.557***	(1.390 - 1.745)	1.737***	(1.557 - 1.938)
other neurological disorders	1.612***	(1.360 - 1.912)	1.949***	(1.686 - 2.253)	1.498***	(1.289 - 1.740)	1.313***	(1.123 - 1.536)
paralysis	1.284*	(1.039 - 1.587)	1.482***	(1.237 - 1.777)	1.124	(0.930 - 1.356)	1.238*	(1.021 - 1.500)
peripheral vascular disorders	2.129***	(1.898 - 2.405)	1.626***	(1.458 - 1.813)	1.675***	(1.500 - 1.871)	1.266***	(1.125 - 1.426)
psychoses	0.518*	(0.279 - 0.963)	2.462***	(1.639 - 3.698)	0.660	(0.405 - 1.074)	1.516	(0.994 - 2.313)
pulmonary circulation disorders	1.348**	(1.094 - 1.662)	1.737***	(1.445 - 2.088)	1.296***	(1.070 - 1.570)	1.040	(0.849 - 1.274)
renal failure	1.381***	(1.228 - 1.553)	1.073	(0.969 - 1.189)	1.494***	(1.351 - 1.653)	0.996	(0.889 - 1.117)
rheumatoid arthritis/collagen vascular diseases	1.046	(0.791 - 1.384)	1.120	(0.885 - 1.416)	0.981	(0.770 - 1.250)	1.143	(0.893 - 1.462)
solid tumor without metastasis	-		-		-		-	
valvular disease	0.954	(0.803 - 1.133)	0.861	(0.738 - 1.004)	0.944	(0.810 - 1.102)	0.942	(0.795 - 1.116)
weight loss	0.799**	(0.696 - 0.917)	1.717***	(1.543 - 1.910)	1.520***	(1.365 - 1.693)	2.013***	(1.803 - 2.248)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	1.936***	(1.706 - 2.197)	1.727***	(1.564 - 1.906)	1.479***	(1.330 - 1.645)	1.197***	(1.086 - 1.320)
transfer from other hospital	2.610***	(2.169 - 3.140)	2.299***	(1.959 - 2.698)	2.027***	(1.718 - 2.391)	1.202*	(1.015 - 1.423)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.577***	(1.397 - 1.780)	1.436***	(1.296 - 1.590)	1.443***	(1.299 - 1.604)	1.095	(0.978 - 1.225)

total colon resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	3.173***	(2.705 - 3.723)	1.604***	(1.395 - 1.843)	2.545***	(2.213 - 2.927)	0.958	(0.830 - 1.107)
colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.159	(0.936 - 1.436)	1.320**	(1.116 - 1.562)	1.404***	(1.183 - 1.667)	1.314***	(1.107 - 1.560)
HOSPITAL COVARIATES								
case volume	0.961	(0.844 - 1.094)	0.876	(0.753 - 1.018)	0.950	(0.841 - 1.073)	1.135	(0.987 - 1.304)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	1.091	(0.886 - 1.345)	0.918	(0.682 - 1.235)	0.775*	(0.631 - 0.953)	1.058	(0.837 - 1.336)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.336	(0.855 - 2.087)	0.712	(0.347 - 1.461)	1.586	(0.999 - 2.520)	1.802*	(1.070 - 3.034)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	0.900	(0.688 - 1.177)	1.028	(0.696 - 1.519)	0.836	(0.638 - 1.096)	0.736**	(0.543 - 0.996)
private	1.284*	(1.015 - 1.626)	1.433*	(1.035 - 1.986)	1.893***	(1.505 - 2.380)	0.775	(0.601 - 1.001)

Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers
*** p<0.001
** p <0.01
* p<0.05

S14: Multivariate analysis of case-, care- and hospital-related covariates of patient safety including 6.692 non-cancer rectum resections in 195 hospitals

	IN-HOSPITAL DEATH		POST-OPERATIVE RESPIRATORY FAILURE		RENAL FAILURE		POST-OPERATIVE WOUND INFECTION	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CASE COVARIATES								
sex								
male	Ref.		Ref		Ref		Ref	
female	0.733*	(0.542 - 0.992)	0.739**	(0.601 - 0.908)	0.746**	(0.607 - 0.917)	0.651***	(0.539 - 0.786)
age	1.074***	(1.058 - 1.089)	1.013***	(1.006 - 1.021)	1.023***	(1.016 - 1.031)	1.000	(0.994 - 1.006)
alcohol abuse	0.809	(0.348 - 1.882)	1.801*	(1.008 - 3.219)	1.355	(0.754 - 2.434)	1.080	(0.601 - 1.941)
blood loss anemia	0.797	(0.305 - 2.082)	1.735	(0.877 - 3.432)	1.886	(0.970 - 3.668)	1.927*	(1.014 - 3.663)
cardiac arrhythmias	2.130***	(1.569 - 2.892)	1.573***	(1.243 - 1.990)	1.608***	(1.281 - 2.017)	1.015	(0.795 - 1.295)
chronic pulmonary disease	0.908	(0.601 - 1.371)	1.570**	(1.180 - 2.088)	0.977	(0.726 - 1.315)	1.402*	(1.066 - 1.845)
coagulopathy	5.767***	(4.191 - 7.937)	3.713***	(2.934 - 4.697)	3.703***	(2.949 - 4.650)	1.947***	(1.550 - 2.447)
congestive heart failure	1.851***	(1.309 - 2.617)	1.887***	(1.426 - 2.497)	1.543**	(1.180 - 2.017)	1.269	(0.943 - 1.708)
deficiency anemia	0.765	(0.362 - 1.616)	1.008	(0.606 - 1.675)	1.039	(0.640 - 1.689)	1.430	(0.911 - 2.244)
depression	0.591	(0.326 - 1.073)	1.043	(0.723 - 1.505)	1.220	(0.859 - 1.732)	1.208	(0.869 - 1.679)
diabetes, complicated	2.158**	(1.267 - 3.674)	0.990	(0.627 - 1.564)	2.155***	(1.423 - 3.265)	1.292	(0.821 - 2.032)
diabetes, uncomplicated	1.233	(0.838 - 1.815)	1.133	(0.849 - 1.513)	1.549**	(1.176 - 2.038)	0.950	(0.709 - 1.272)
fluid and electrolyte disorders	1.619**	(1.185 - 2.213)	3.048***	(2.458 - 3.779)	3.006***	(2.430 - 3.719)	1.944***	(1.594 - 2.370)
hypertension, complicated	0.345***	(0.189 - 0.628)	0.657*	(0.419 - 1.031)	0.910	(0.596 - 1.390)	1.042	(0.663 - 1.638)
hypertension, uncomplicated	0.511***	(0.377 - 0.694)	0.928	(0.751 - 1.147)	0.813	(0.658 - 1.003)	1.041	(0.851 - 1.273)
hypothyroidism	0.742	(0.491 - 1.121)	0.919	(0.695 - 1.214)	1.051	(0.803 - 1.376)	1.093	(0.845 - 1.416)
liver disease	5.966***	(3.793 - 9.384)	1.550*	(1.068 - 2.252)	2.060***	(1.451 - 2.925)	0.795	(0.540 - 1.172)
lymphoma	0.685	(0.151 - 3.108)	0.930	(0.309 - 2.800)	0.656	(0.221 - 1.944)	0.884	(0.308 - 2.539)
metastatic cancer	-		-		-		-	
obesity	0.853	(0.538 - 1.352)	1.534**	(1.152 - 2.043)	1.400*	(1.054 - 1.861)	1.871***	(1.460 - 2.396)
other neurological disorders	2.558***	(1.586 - 4.126)	1.428	(0.968 - 2.106)	1.117	(0.755 - 1.652)	1.113	(0.754 - 1.642)
paralysis	0.798	(0.421 - 1.514)	1.276	(0.780 - 2.088)	1.508	(0.940 - 2.421)	1.158	(0.714 - 1.881)
peripheral vascular disorders	2.505***	(1.743 - 3.599)	1.502**	(1.119 - 2.018)	1.629***	(1.227 - 2.163)	1.048	(0.774 - 1.419)
psychoses	1.703	(0.166 - 17.483)	1.385	(0.317 - 6.052)	3.384	(0.925 - 12.382)	1.386	(0.359 - 5.356)
pulmonary circulation disorders	1.770	(0.965 - 3.246)	1.636	(0.983 - 2.725)	1.114	(0.667 - 1.859)	1.203	(0.725 - 1.997)
renal failure	1.472*	(1.047 - 2.068)	1.633***	(1.252 - 2.129)	1.755***	(1.368 - 2.250)	1.395**	(1.071 - 1.818)
rheumatoid arthritis/collagen vascular diseases	0.864	(0.358 - 2.087)	1.948*	(1.171 - 3.242)	1.083	(0.609 - 1.925)	1.001	(0.571 - 1.754)
solid tumor without metastasis	-		-		-		-	
valvular disease	1.236	(0.771 - 1.982)	0.999	(0.671 - 1.488)	1.300	(0.888 - 1.903)	0.719	(0.469 - 1.104)
weight loss	0.761	(0.507 - 1.143)	1.969***	(1.503 - 2.580)	1.944***	(1.504 - 2.513)	2.204***	(1.709 - 2.843)
HEALTHCARE COVARIATES								
admission reason								
referral	Ref.		Ref.		Ref.		Ref.	
emergency case	2.060***	(1.470 - 2.885)	1.590***	(1.253 - 2.018)	1.382**	(1.094 - 1.746)	0.992	(0.797 - 1.234)
transfer from other hospital	2.583***	(1.468 - 4.487)	1.510	(0.962 - 2.369)	1.949**	(1.269 - 2.993)	1.102	(0.713 - 1.704)
weekend surgery								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.770**	(1.179 - 2.658)	1.391*	(1.012 - 1.912)	1.499*	(1.101 - 2.042)	0.870	(0.613 - 1.235)

colon and rectum resection								
no	Ref.		Ref.		Ref.		Ref.	
yes	2.967***	(2.184 - 4.030)	2.183***	(1.750 - 2.725)	2.190***	(1.771 - 2.709)	1.318*	(1.066 - 1.630)
HOSPITAL COVARIATES								
case volume	0.777*	(0.614 - 0.983)	0.793*	(0.642 - 0.978)	0.863	(0.733 - 1.015)	0.956	(0.795 - 1.150)
area								
urban	Ref.		Ref.		Ref.		Ref.	
rural	0.851	(0.536 - 1.351)	0.881	(0.580 - 1.337)	0.872	(0.646 - 1.176)	0.865	(0.613 - 1.220)
university hospital								
no	Ref.		Ref.		Ref.		Ref.	
yes	1.529	(0.712 - 3.283)	0.849	(0.354 - 2.034)	1.176	(0.701 - 1.972)	2.375**	(1.316 - 4.287)
ownership								
public	Ref.		Ref.		Ref.		Ref.	
non-profit	0.556*	(0.323 - 0.959)	1.098	(0.652 - 1.849)	0.702	(0.489 - 1.008)	0.775	(0.516 - 1.166)
private	0.981	(0.594 - 1.621)	1.614*	(1.020 - 2.556)	1.331	(0.960 - 1.846)	0.791	(0.546 - 1.147)

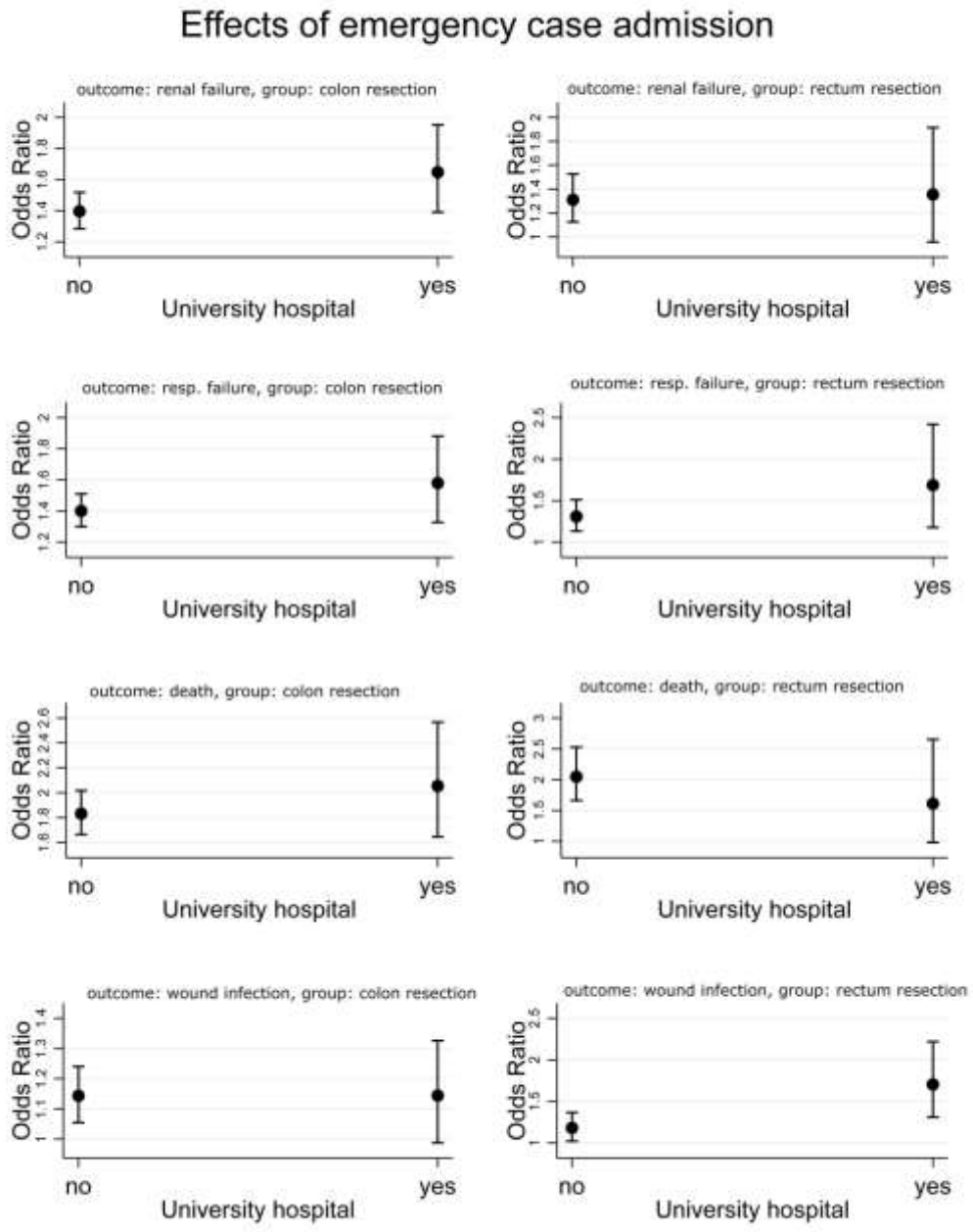
Note: Elixhauser Groups drug abuse, peptic ulcer disease and AIDS/ HIV were not included into the regression due to a low case numbers

*** p<0.001

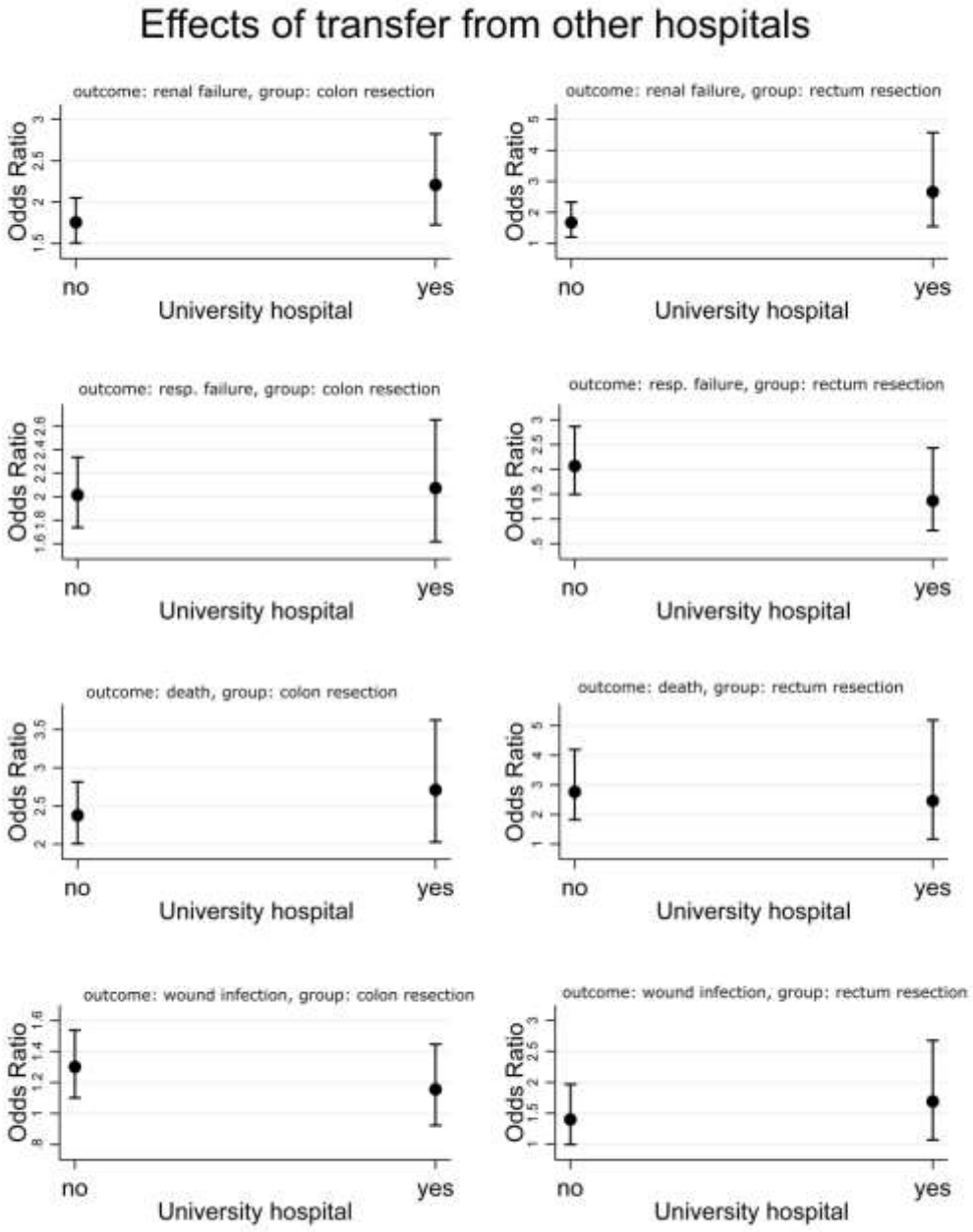
** p <0.01

* p<0.05

S15 – Figure: Interactions between emergency admission and university hospital status


Effects of emergency case admission
outcome: renal failure, group: colon resection
outcome: renal failure, group: rectum resection
outcome: resp. failure, group: colon resection
outcome: resp. failure, group: rectum resection
outcome: death, group: colon resection
outcome: death, group: rectum resection
outcome: wound infection, group: colon resection
outcome: wound infection, group: rectum resection
Odds Ratio
no
yes
University hospital

S16 – Figure: Interactions between transfer from other hospital admission and university hospital status


Effects of transfer from other hospitals
outcome: renal failure, group: colon resection
outcome: renal failure, group: rectum resection
outcome: resp. failure, group: colon resection
outcome: resp. failure, group: rectum resection
outcome: death, group: colon resection
outcome: death, group: rectum resection
outcome: wound infection, group: colon resection
outcome: wound infection, group: rectum resection
Odds Ratio
no
yes
University hospital

4.3 Publikation (3): Prediction of Inpatient Pressure Ulcers Based on Routine Healthcare Data Using Machine Learning Methodology

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Prediction of inpatient pressure ulcers based on routine healthcare data using machine learning methodology

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Despite the relevance of pressure ulcers (PU) in inpatient care, the predictive power and role of care-related risk factors (e.g. anesthesia) remain unclear. We investigated the predictability of PU incidence and its association with multiple care variables. We included all somatic cases between 2014 and 2018 with length of stay ≥ 2d in a German university hospital. For regression analyses and prediction we used Bayesian Additive Regression Trees (BART) as nonparametric modeling approach. To assess predictive accuracy, we compared BART, random forest, logistic regression (LR) and least absolute shrinkage and selection operator (LASSO) using area under the curve (AUC), confusion matrices and multiple indicators of predictive performance (e.g. sensitivity, specificity, F1, positive/ negative predictive value) in the full dataset and subgroups. Analysing 149,006 cases revealed high predictive variable importance and associations between incident PU and ventilation, age, anesthesia (≥1 h) and number of care-involved wards. Despite high AUCs (range 0.89–0.90), many false negative predictions led to low sensitivity (range 0.04–0.10). Ventilation, age, anesthesia and number of care-involved wards were associated with incident PU. Using anesthesia as a proxy for immobility, an hourly repositioning is indicated. The low sensitivity indicates major challenges for correctly predicting PU based on routine data.

Pressure ulcers (PU) are serious adverse events in inpatient care. Constant pressure caused by limited mobility due to e.g. ventilation, anesthesia or other severe physical or mental impairments leads to reduced blood perfusion of tissues. The ischemia leads to hypoxia of the tissue. The arising toxic metabolites lead to irreversible damage of nerve cells and, in most severe cases, to necrosis. In addition, age and age-related comorbidities like type 2 diabetes, dementia, obesity or incontinence, severely increase the risk of PU[1]. Due to the fact that this adverse event can be prevented in the majority of cases PUs are a well-established patient safety outcome and content of inpatient quality assurance in multiple countries[2]. Depending on the legislation, inpatient care providers need to report this patient safety outcome on the basis of uniformly defined and standardized data sets. Consequently, large routine data sets are evaluated by the responsible authority using statistical methods like logistic regression. For benchmarking purposes, results are usually expressed as indicators statistically adjusting for patient age, comorbidities (e.g., type 2 diabetes, infections, immobility) or intensive care with ventilation[2]. In the event of outliers corrective measures are triggered by the responsible authority. Previous works suggested that care-related risk factors like reason for admission (e.g. emergency vs. referral), (length of) performed surgery, intensive care or wards involved in care play an important role[3–7]. These risk factors also serve as possible proxies for the acuity of a medical case. As the high prevalence of different comorbidities like diabetes mellitus leads to a relatively large high-risk population an early identification of patients at risk is crucial for an early prevention of PU[8]. Furthermore, risk factors can interact and thus significantly increase a patient's risk of developing a PU. In this case, simple approaches to statistical adjustment are inappropriate, particularly regarding prospective prediction of PU.

One approach of handling complex interactions is stratification into small and homogeneous patient groups, which has the disadvantage of low statistical power and precision[9]. An another approach is the use of non-parametric statistical methods that facilitate data-driven detection of complex interactions between risk factors

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and flexible investigation of relationships with the outcome. One of these approaches is the machine learning method Bayesian Additive Regression Trees (BART). Similar to all nonparametric machine learning methods, BART has the advantage that the researcher does not have to specify the functional form of the predictive relationship between outcome and risk factors. Instead, these relationships are learned from the data and may include complex interactions between risk factors and highly nonlinear and non-monotonic relationships between risk factors and outcome. At the same time, BART is a fully Bayesian approach and allows for statistical inference, e.g. in terms of derivation of credible intervals[10].

Based on an appropriate risk identification, repositioning is a widely established and guideline-recommended pressure ulcer prevention strategy[11,12]. Despite widespread acceptance in clinical practice the determination of an evidence based time interval for repositioning is still missing. A recent Cochrane review systematically reviewed, critically appraised and summarized the randomized evidence concerning this question. The review showed no differences between the widely practiced two hour- or longer repositioning frequencies. However, the included RCTs had small sample sizes and were of poor study quality[13,14].

BART as a non-parametric statistical method is able to handle continuous variables without assuming linearity in the predictor term as is inherent to logistic regression[10,15]. Therefore BART affords the user the opportunity to model the incidence of pressure ulcers related to the continuous length of anesthesia appropriately—without assuming linearity.

In summary, two aims have been identified for the analysis of PU using BART as a machine learning approach in a large routine data set of a tertiary care provider:

1. To explore *relationships* between incidence of PU and
   - (length of) anesthesia,
   - wards involved in care and
   - admission reasons (emergency, transfer from another hospital)
   - intensive care treatment (with/ without ventilation),
   - adjusting for age, sex and comorbidities.

2. To examine *predictability* of pressure ulcers using BART based on routine data

Results

Overall, 149,006 cases were included for analysis (51.5% male, median age 64 years, interquartile range 48–76 years). Incident pressure ulcers were documented in 4,663 cases (3.1%). With respect to the test year 2018, 901 incident pressure ulcers (3.0%) in 29,338 hospital cases were documented (Table 1). Referring to admission context, around one third (35.8%) of the included cases were admitted as emergency case and 3.5% were transferred from other hospitals. Around the half of the cases (49.7%) included surgery and full anesthesia. More than 50% of the analyzed cases were treated on one ward. One fifth (19.6%) of the cases analyzed received intensive care with (4.1%) or without (15.5%) ventilation.

Variable importance derived from BART model. According to the results of a tenfold cross validation, a BART model with 50 trees yielded the best predictive performance and, thus, was chosen for analysis. Variable importances (Fig. 1) derived from the fitted BART model were highest for.

- ICU with ventilation (0.109)
- Age (0.107)
- length of anesthesia (0.105)
- the number of wards involved in care of the patient (0.101)

The prognosis of incident PU is particularly influenced by these 4 variables. If a higher age or ICU with ventilation is given, then the model tends to predict an incidental PU. The most important comorbidity variables were mobility (0.067) and incontinence (0.063).

Regression analysis of care-related risk factors on the predicted probability of pressure ulcers. According to the estimated partial dependence, the average predicted probability of pressure ulcers for intensive care with ventilation was about 8 times (7.5 percentage points) higher than for cases with neither intensive care nor ventilation. Comparing intensive care with and without ventilation, the average predicted probability of incident PU was 4 times higher (6.8 percentage points) in cases treated with ventilation (Fig. 2).

Anesthesia in general was associated with an increased risk of PU (Fig. 3). A monotonous increase was observed between 50 and 120 min of anesthesia. In this timeframe, the average predicted probability of incident pressure ulcer doubled. Between 120 and 240 min of anesthesia, the average predicted probability remained stable and increased after 240 min of anesthesia with a broadening credible interval.

The average predicted probability of incident pressure ulcer was higher, when more than one hospital ward was involved in care (Fig. 4).

The remaining care variables such as admission as emergency case or transfer from another hospital were related to a higher average predicted probability of incident PU compared to referral admissions (Fig. 5).

The average predicted probability for incident PU was 1.5 times higher (1.45 percentage points) in cases transferred from other hospitals than in referral admissions.

Outcome/variable	Overall		Training data (2014–2017)		Test data (2018)	
	n/median	%/Q1; Q3	n/median	%/Q1; Q3	n/median	%/Q1; Q3
Incident pressure ulcer						
Yes	4,663	(3.1%)	3,757	(3.1%)	906	(3.1%)
No	144,343	(96.9%)	115,911	(96.9%)	28,432	(96.9%)
Age						
Median	64	(48;76)	64	(47;75)	64	(49;77)
Male sex						
Yes	76,774	(51.5%)	61,540	(51.4%)	15,234	(51.9%)
No	72,232	(48.5%)	58,128	(48.6%)	14,104	(48.1%)
Diabetes mellitus type 2						
Yes	26,893	(18%)	21,402	(17.9%)	5,491	(18.7%)
No	122,113	(82%)	98,266	(82.1%)	23,847	(81.3%)
BMI ≥ 40						
Yes	1,603	(1.1%)	1,200	(1.0%)	403	(1.4%)
No	147,403	(98.9%)	118,468	(99.0%)	28,935	(98.6%)
Underweight and/or malnutrition						
Yes	1,069	(0.7%)	813	(0.7%)	256	(0.9%)
No	147,937	(99.3%)	118,855	(99.3%)	29,082	(99.1%)
Dementia and/or vigilance disturbance						
Yes	4,167	(2.8%)	3,200	(2.7%)	967	(3.3%)
No	144,839	(97.2%)	116,468	(97.3%)	28,371	(96.7%)
Infections						
Yes	8,866	(6%)	6,914	(5.8%)	1,952	(6.7%)
No	140,140	(94%)	112,754	(94.2%)	27,386	(93.3%)
Other severe diseases*						
Yes	32,988	(22.1%)	25,795	(21.6%)	7,193	(24.5%)
No	116,018	(77.9%)	93,873	(78.4%)	22,145	(75.5%)
Mobility						
Yes	10,016	(6.7%)	7,716	(6.4%)	2,300	(7.8%)
No	138,990	(93.3%)	111,952	(93.6%)	27,038	(92.2%)
Incontinence						
Yes	13,287	(8.9%)	10,558	(8.8%)	2,729	(9.3%)
No	135,719	(91.1%)	109,110	(91.2%)	26,609	(90.7%)
Admission: emergency case						
Yes	53,418	(35.8%)	42,593	(35.6%)	10,825	(36.9%)
No	95,588	(64.2%)	77,075	(64.4%)	18,513	(63.1%)
Admission: transfer from another hospital						
Yes	5,275	(3.5%)	4,195	(3.5%)	1,080	(3.7%)
No	143,731	(96.5%)	115,473	(96.5%)	28,258	(96.3%)
Anesthesia						
Yes	74,037	(49.7%)	59,049	(49.3%)	14,988	(51.1%)
No	74,969	(50.3%)	60,619	(50.7%)	14,350	(48.9%)
Length of anesthesia (minutes)						
Median	142	(87;214)	0	(0;140)	37	(0;150)
Wards involved in care						
Median	1	(1;2)	1	(1;2)	1	(1;2)
Intensive care with ventilation						
Yes	6,106	(4.1%)	4,854	(4.1%)	1,252	(4.3%)
No	142,900	(95.9%)	114,814	(95.9%)	28,086	(95.7%)
Intensive care without ventilation						
Yes	23,041	(15.5%)	18,636	(15.6%)	4,405	(15%)
No	125,965	(84.5%)	101,032	(84.4%)	24,933	(85%)

Table 1. Patient and care characteristics of 149,006 analyzed cases between 2014 and 2018. *Candidiasis (B37.1, B37.7) anemia (D50-D53, D61-D64, D72.8), liver diseases (K70, K72, K74), renal diseases (N17, N18.4, N18.5, N99.0, Z99.2), ascites (R18), anuria (R34), diabetic polyneuropathy (G63.2), oedema (R60), abnormality of albumin (R77), hospital acquired pneumonia (U69.00!).

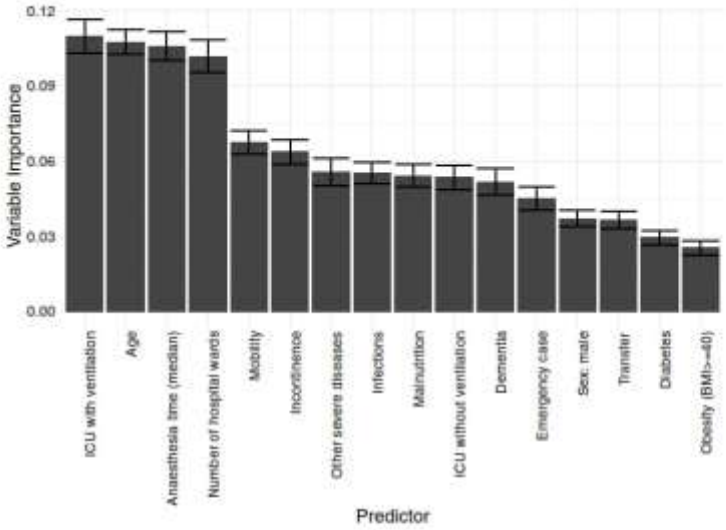

Figure 1. Variable importance. The variable importance shows which variable (predictor) was most predictive for incident pressure ulcer from the highest (ICU with ventilation) to the lowest (BMI ≥ 40) predictive power.

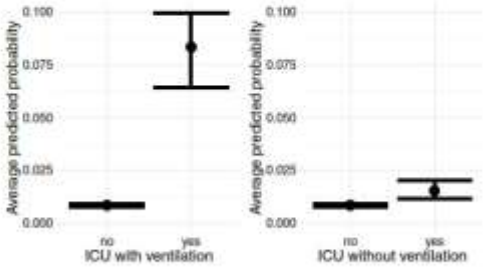

Figure 2. Associations between intensive care and incident pressure ulcer. Average predicted probability between non-intensive care, intensive care with ventilation, intensive care without ventilation and the incidence of pressure ulcers at a 95% credibility interval.

While the average predicted probability of incident PU remained constant for patients aged 19–35, the average predicted risk of incident PU monotonously increased for patients aged 35–86 (Supplement S1). Reviewing age in more detail, the predicted probability of incident PU increased constantly by a total of 0.10 percentage points between the age of 35 and 50. Between the age of about 50 and 90, the average predicted probability triples (1.9 percentage points) with a broadening credible interval. Please refer to Supplement S2 and Supplement S3 for the partial dependence plots of male sex and comorbidities.

To illustrate potential patient-specific differences in the predicted risk of pressure ulcers, we considered five examples (Table 2). As most possible risk factors were absent, examples 1 and 2 showed a predicted probability of almost 0%. With longer anesthesia, more comorbidities and intensive care without ventilation, examples 3 and 4 showed increased risks of 6% and 11%, respectively. Due to the presence of multiple risk factors like higher age (70 years), long anesthesia (150 min) and intensive care with ventilation, example 5 showed a high predicted risk of 42% for incident pressure ulcer.

Predictive performance measures. The area under the curve was 0.9 for BART and 0.89 for LASSO, LR and random forest (Supplement S4).

Applied to the whole dataset, between 40 (4.4%) and 80 (8.8%) true positive PU cases in 2018 could be predicted with the models trained on data from 2014 to 2017 (Supplement S5). Between 28,294 (96.4%) and 28,369 (99.8%) cases were correctly predicted as true negative. False negative PU predictions ranged between

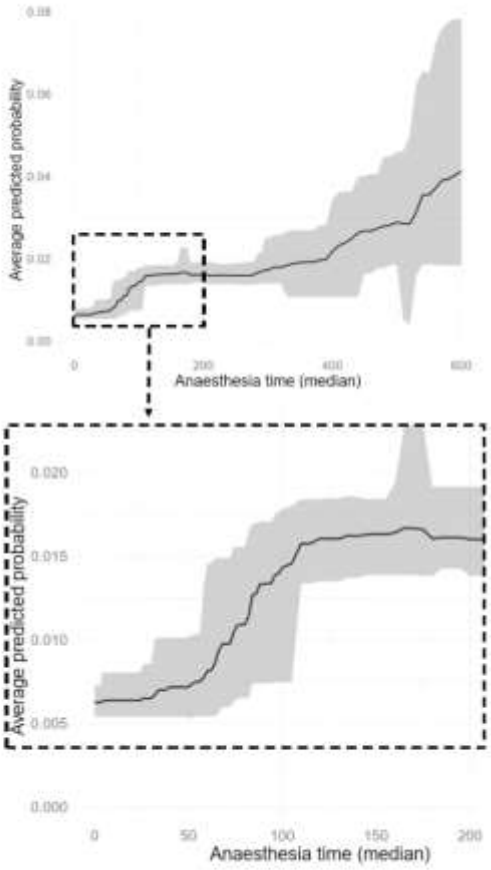

Figure 3. Associations between length of anesthesia and incident pressure ulcer. Average predicted probability between length of anesthesia and the incidence of pressure ulcers at a 95% credibility interval.

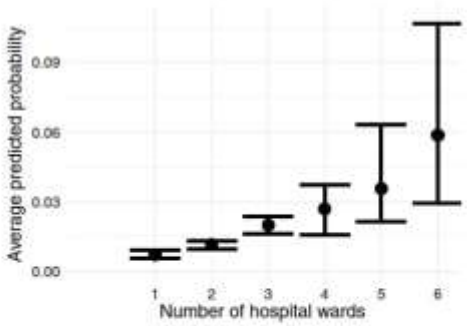

Figure 4. Associations between number of wards involved into care and incident pressure ulcer. Average predicted probability between the number of wards involved in care and the incidence of pressure ulcers at a 95% credibility interval.

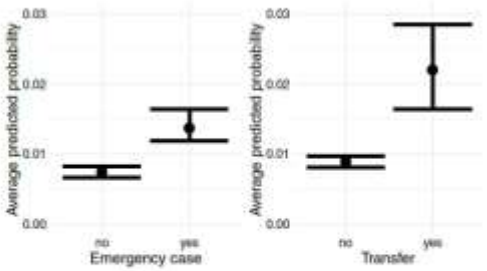

Figure 5. Associations between emergency admissions, transfers from another hospital and incident pressure ulcer. Average predicted probability between non-urgent admissions, emergency admissions, transfers from another hospital and the incidence of pressure ulcers at a 95% credibility interval.

	Example 1	Example 2	Example 3	Example 4	Example 5
Age	20	35	45	50	70
Male sex	Yes	No	Yes	No	Yes
Diabetes	No	No	Yes	Yes	No
BMI ≥ 40	No	No	No	No	No
Underweight and malnutrition	No	No	No	No	Yes
Dementia and vigilance disturbance	No	No	No	No	Yes
Infections	No	No	No	Yes	No
Other severe diseases	No	No	Yes	Yes	No
Mobility	No	No	Yes	No	Yes
Incontinence	No	No	No	No	Yes
Admission: emergency case	No	No	No	Yes	No
Admission: transfer from another hospital	No	No	No	No	Yes
Length of anesthesia	0	60	100	120	150
Wards involved in care	2	1	1	2	4
Intensive care with ventilation	No	No	No	No	Yes
Intensive care without ventilation	No	No	Yes	Yes	No
Predicted probability					
(Low CI-High CI)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.06 (0.02–0.1)	0.11 (0.05–0.2)	0.42 (0.15–0.72)

Table 2. Predicting incident pressure ulcer based on 5 examples of different risk factors and age. *CI* credible interval.

816 (logistic regression) and 866 (LASSO) and false positive PU predictions between 39 (LASSO) and 138 (LR). Evaluation metrics like F1-score (range 0.08–0.16), balanced accuracy (range 0.52–0.55) and positive predictive value (range 0.39–0.58) varied between the different models (Supplement S6). The sensitivity of the prediction for the full dataset ranged between 0.04 (LASSO) and 0.10 (LR). When predicting for cases receiving intensive care, ventilation and anesthesia, evaluation scores like F1 (range 0.10–0.33), positive predictive value (range 0.40–0.59), balanced accuracy (range 0.53–0.59) and sensitivity (range 0.10–0.24) increased. In case of true negative predictions, negative predictive value (0.97) and specificity (1.00) remained stable in the full dataset for all four models. In low-risk groups (no intensive care, no surgery, no anesthesia) specificity also remained stable (1.00) and negative predictive value varied (0.98–0.99).

The prediction of severity in incident PU revealed the lowest sensitivities for less severe PU grades (Grade 1–2: range 0.02–0.09). Sensitivity increased when predicting more severe PU (Grade 4: range 0.17–0.21, Supplement S7).

Discussion

This large observational study presents several important new findings that are relevant for inpatient care of pressure ulcers.

First, critical length of anesthesia has not been determined with a visible threshold before. According to our results, the average predicted probability of incident pressure ulcers begins to increase at 50 min of anesthesia. Subsequently, the probability of incident pressure ulcers steeply increases until reaching a plateau between 120 and 240 min before increasing again. Especially the plateau of incident pressure ulcer risk between 120 and

240 min of limited/ not provided repositioning is in line with the RCTs published up to date and may reflect preventive measures[12]. Considering the whole process of anesthesia with induction, excitement stage, surgical anesthesia and awakening, even short surgeries with their steep increase of incident pressure ulcers within one hour and despite the possible use of preventive interventions can be interpreted as a risk factor despite the possible use of preventive interventions. If this situation is applied to the restricted mobility of many inpatients, this would result in an hourly, timely tightened rather than delayed repositioning in general. The recommendation for a tightened repositioning beginning at approximately 50 min of immobility puts our results in contrast to RCTs published up to date which have not even considered such short repositioning intervals[13,14]. Probably due to small sample sizes/ underpowered comparisons[13], some RCTs suggest longer repositioning intervals of three to four hours of immobility compared to a control group of 2-h repositioning intervals[14,16,17]. Repositioning every two hours is common in clinical practice but not based on reliable evidence[13]. However, it is also necessary to consider the burden to the patient (e.g., sleep disturbances) and staff (e.g., back pain due to manual handling activities) which might result from hourly repositioning[18–20]. As we used observational data from a broad inpatient sample we strongly recommend a (randomized) controlled design with a sufficiently large sample size to provide confirmatory evidence on the hourly repositioning intervals indicated by this analysis.

Second, the high AUCs of 0.89 LR, LASSO and random forest and 0.90 for BART suggest a strong predictive performance. However, less than 10% of cases with pressure ulcers in 2018 could be predicted, and lead to very low sensitivity scores in both full dataset and subgroups (low risk, high risk, grades of incident PU). This suboptimal performance of the prediction models could be explained by multiple reasons.

- The high class imbalance between incidental PU (3.1%) and non-PU (96.9%) might weaken the performance of ROC—analyses regardless of the model chosen[21].
- The high class imbalance between incidental and non-PU also might explain the high specificity and negative predictive value in all models and subgroups included.
- The development of PU has multifactorial causes. For example, our regression model also indicates intensive care with ventilation as a risk factor in addition to age, anesthesia time, comorbidities, incontinence and so on. Some relevant risk factors (e.g. state of consciousness, pain perception, body temperature, medication)[1] may not have been included in our data
- Not every risk factor can be coded well in its severity in secondary data and ICD-10- Codes[22]. For example, an infection may be a local infection or it may have already spread to the bloodstream and organs. Limited mobility might range from walking disability, to the need for a wheelchair or to complete bed confinement. These aspects are not captured by our data.
- The heterogeneity of the underlying risk factors also could weaken the predictive performance.

Given our statistical models, higher sensitivity would be possible but would come at the cost of specificity. This generally highlights the importance of further research on additional strong predictors of pressure ulcers. However, despite the modest predictive performance of the model, relationships between risk factors and the predicted probability of incident pressure ulcers could be estimated with relatively high precision due to the large sample size.

Third, identification of age and intensive care with ventilation as crucial risk factors are in line with the literature[1,7]. Comorbidities, male sex or admission reasons on the other hand did neither reveal high variable importance nor high average predicted probabilities for incident pressure ulcers in a broad, medical complex (e.g. intensive care) and older age sample.

This study analyzed a large sample with a broad range of medical indications as is common in tertiary care facilities. Statistically, flexible predictive analysis using BART as a nonparametric machine learning technique allowed us to handle continuous variables like length of anesthesia or age without presuming specific functional forms of their relationships with the risk of pressure ulcers. The use of referenced and predefined risk factors aiming at specific adjustment and the use of a machine learning approach like BART enabled a tailored and literature-based model. Routine data in general often face a lack of granularity with respect to complete coding and missing time references[22]. In addition, routine data do not always include information on which diagnoses were already present on admission and which were not[23,24]. These challenges could be solved due to the use of multiple data sources to acquire a complete and longitudinal data set. Based on our results and the clear visible thresholds, we are able to derive actionable implications. The monocentric setting can be seen as a limitation with respect to the generalizability of provider-specific structures and processes[25]. However, the setting of an university hospital with its organizationally independent and large clinics, the data completeness and variety underlines the (necessary) medical plurality of this analysis. Due to data protection issues, patients admitted more than once could not be identified, which implies that some patients may have entered the analysis as multiple hospital cases. This large routine data set inhibited a detailed analysis of the administered, and often multimodal, preventive interventions. In general, the use of observational data does not support causal interpretation of results. The routine data collected did not include explicit repositioning time protocols which lead us to use the length of anesthesia as a proxy for limited mobility. This definition might be biased by selection and strongly highlights the need for controlled designs to validate our results.

In addition to well-known risk factors like age, comorbidities and intensive care treatment, our analysis indicates anesthesia and repositioning intervals longer than 50 min as relevant predictors of pressure ulcers. As our results are based on observational data and repositioning needs to consider patients and staff burden, a randomized controlled trial in a large sample would be valuable.

Methods

We conducted a mono-centered cross-sectional study at a tertiary care facility. This study has been carried out in accordance to STROBE as general guideline for observational studies[26] and in particular STROSA for studies analyzing secondary data[27].

Population. We included all adult (≥ 19 years) cases admitted and discharged between 2014 and 2018 in the University Hospital Carl Gustav Carus, Dresden. We excluded children/ adolescents, cases with prevalent PU, psychiatric treatment and length of stay < 2 days.

Outcomes and covariates. The outcome/dependent variable was case-specific incident PU. To correctly identify prevalent and incident PU, a consistent assessment beginning at admission is essential. Especially in nursing home residents, it is not always clear whether a pressure ulcer was already present on admission. Our in-house standard requires a pressure ulcer assessment for high risk cases (internistic treatment, intensive care and surgery) within 24 h from admission. Every PU detected within this timeframe has been marked as prevalent and excluded from our analysis.

We grouped the independent variables into case- and care-related characteristics.

Case-related characteristics include age, (male) sex and comorbidities. To define comorbidities (based on ICD-10) appropriately, we followed the German inpatient quality assurance program. The German inpatient quality assurance indicator for PU adjusts for Diabetes mellitus type 2, BMI ≥ 40, underweight and/ or malnutrition, dementia and/ or vigilance disturbance, infections, other severe diseases, mobility and incontinence. The ICD-10-based definitions are provided in Supplement S8[28].

Care-related characteristics include admission reasons (emergency case, transfer from another hospital), (length of) surgical anesthesia, number of wards involved in care and intensive care with or without ventilation.

We did not include the Braden score as predictor in the models since it was used for preventive PU screening in the hospital. This implies that likely cases of PU indicated by the Braden score may have been prevented and do not occur in our data. Accordingly, estimating relationships between observed PUs and the Braden score would induce misleading results. Some literature also adds length of hospital stay in risk-adjusted analyses for pressure ulcer on the one hand[29,30]. On the other hand, several studies showed that pressure ulcers extend the length of hospital stay[31–33]. This feedback effect causes endogeneity of length of hospital stay as a predictor of pressure ulcer and could seriously bias the results of our risk factor analysis. Therefore, we decided not to consider length of stay as part of the main analysis. However, we included length of stay as a predictor for sensitivity analysis (Supplement S9). In the main analysis, case complexity was captured by a wide set of variables such as comorbidities, anesthesia, reason for admission, intensive care treatment and ventilation.

Data sources. We used four data sources:

I. internally standardized and routinely collected PU screening for the detection of incident PU,
II. legally (§21 Krankenhausentgeltgesetz) required and prespecified accounting data for age, sex, comorbidities, intensive care treatment, ventilation and admission reasons,
III. case-based surgery protocols for length of surgical anesthesia (induction to awakening)
IV. case-based ward stays for the number of involved hospital wards per case

Study participation, privacy, and ethics. We analyzed pseudonymized routine datasets in a mono-centered setting. If reasonably justified, the legislation of the federal state of Saxony (§35(1–3) "Sächsisches Krankenhausgesetz") does not require individual consent for large pseudonymized and mono-centric routine datasets. The legal justification in the federal state of Saxony is based on the principle of in-house research by the specific providers. We have integrated these data privacy relevant conditions and justifications into our study protocol. The Institutional Review Board (IRB00001473 and IORG0001076) of the Medical Faculty of the TU Dresden reviewed and approved the study protocol.

Patient and public involvement. It was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research. This is a non-interventional cross-sectional analysis based on observational data, predefined outcomes and covariates.

Statistical methods. Descriptive statistics in case of categorical variables were provided as absolute and relative frequencies. Continuous variables were described by the median and the 1st and 3rd quartile. We used Bayesian Additive Regression Trees (BART) to predict pressure ulcers and estimate predictive relationships between pressure ulcers and risk factors[10]. Generally, BART is based on regression trees, which may be used when associations between independent and dependent variables cannot be described linearly. The advantage of regression trees over, e.g., logistic regression is the ability to handle non-logistic associations and interactions. Regression trees build homogeneous groups to identify relationships between the outcome and covariates. At a certain degree of heterogeneity in the groups, the groups are separated to achieve higher homogeneity (splitting). BART combines multiple trees in a "sum-of-trees" model, which facilitates more accurate and stable out-of-sample predictions than single regression trees. This ability led us to prospectively predict incidences of PU in addition to associations between dependent and independent variables. In this regard, it is noteworthy that a high/low predictive power of a model does not necessarily imply accurate/inaccurate estimation of relationships between outcome and covariates[34].

We used data from 2014 to 2017 to fit the BART model. The number of trees (50, 75, 100) served as tuning parameter in tenfold cross validation. We assessed the predictive performance of the selected model based on a confusion matrix and area under the curve (AUC) using data from 2018. An AUC of 0.5 suggests no discrimination (i.e., ability to predict cases with and without incident PU), 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding[35]. In addition to confusion matrices, we analysed performance indicators sensitivity, specificity, positive predictive value, negative predictive value, precision, recall, F1, prevalence, detection rate, detection prevalence, balanced accuracy (in case of high class imbalance) and accuracy. Subgroup analyses were performed for the full dataset, intensive care (yes/no) anesthesia (yes/no), ventilation (yes/no) and the different grades of PU. To assess the predictive performance of specific risk factors, we calculated variable importance as the proportion of times each risk factor was chosen for a splitting rule, i.e. to define a node in the sum-of-trees model. We calculated partial dependences to explore the influence of risk factors (e.g. age) on the predicted probability of pressure ulcers. We used 95%-credible intervals to assess the precision of partial dependence estimates. Statistical analysis was conducted using R 3.6.3 and the package bartMachine[36]. With respect to methodological rigor, the accuracy of BART predictions was compared with those based on multiple logistic regression, random forest, and LASSO (see Supplement S10 for a more detailed description).

Ethics approval

The Institutional Review Board (IRB00001473 and IORG0001076) of the Medical Faculty of the TU Dresden reviewed and approved the study protocol.

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Author contributions

FW designed the study, acquisited the data, defined outcomes and covariates, visualized and interpreted the results and wrote the manuscript. MR is responsible for the statistical methodology and formal analysis and revised the manuscript. LH validated and prepared the data, participated in the definition of the outcome and revised the manuscript. JS and MEG contributed to the design and to visualization of results and revised the manuscript.

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Competing interests

The authors declare no competing interests.

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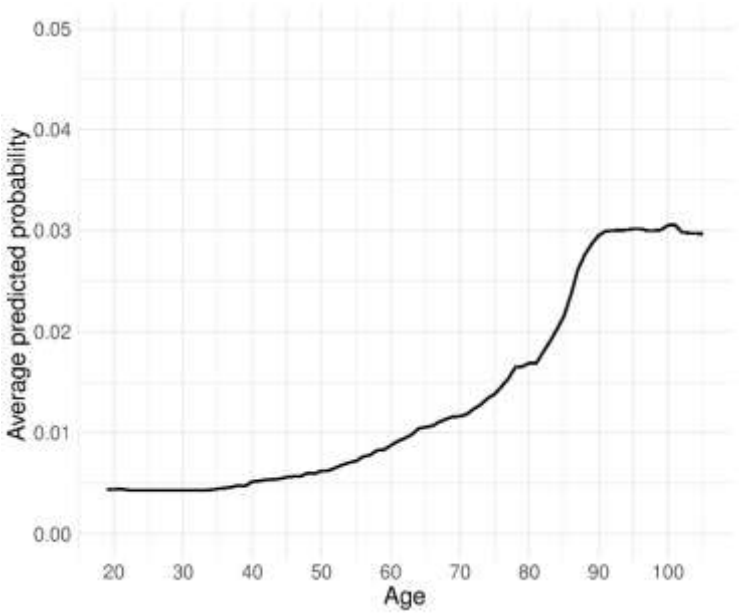
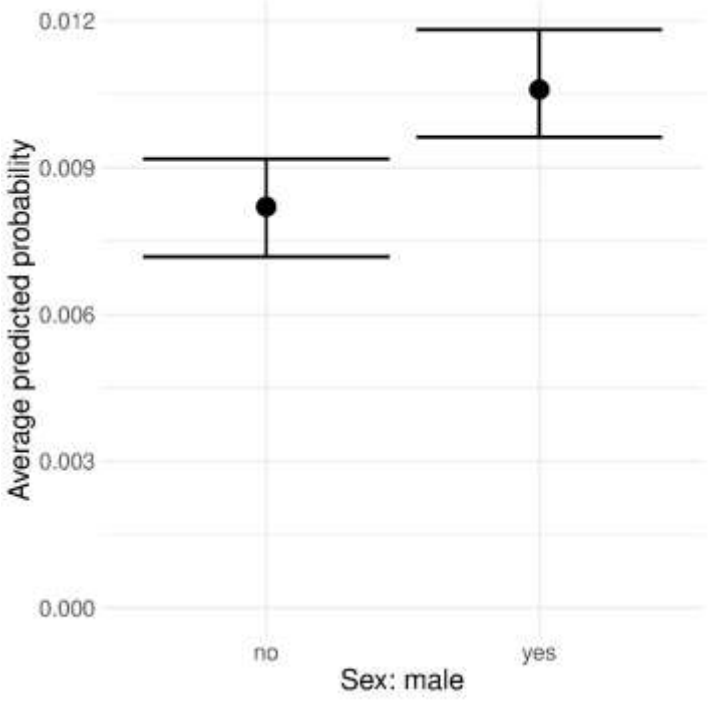
Anlagen Publikation (3) - Supplementary information

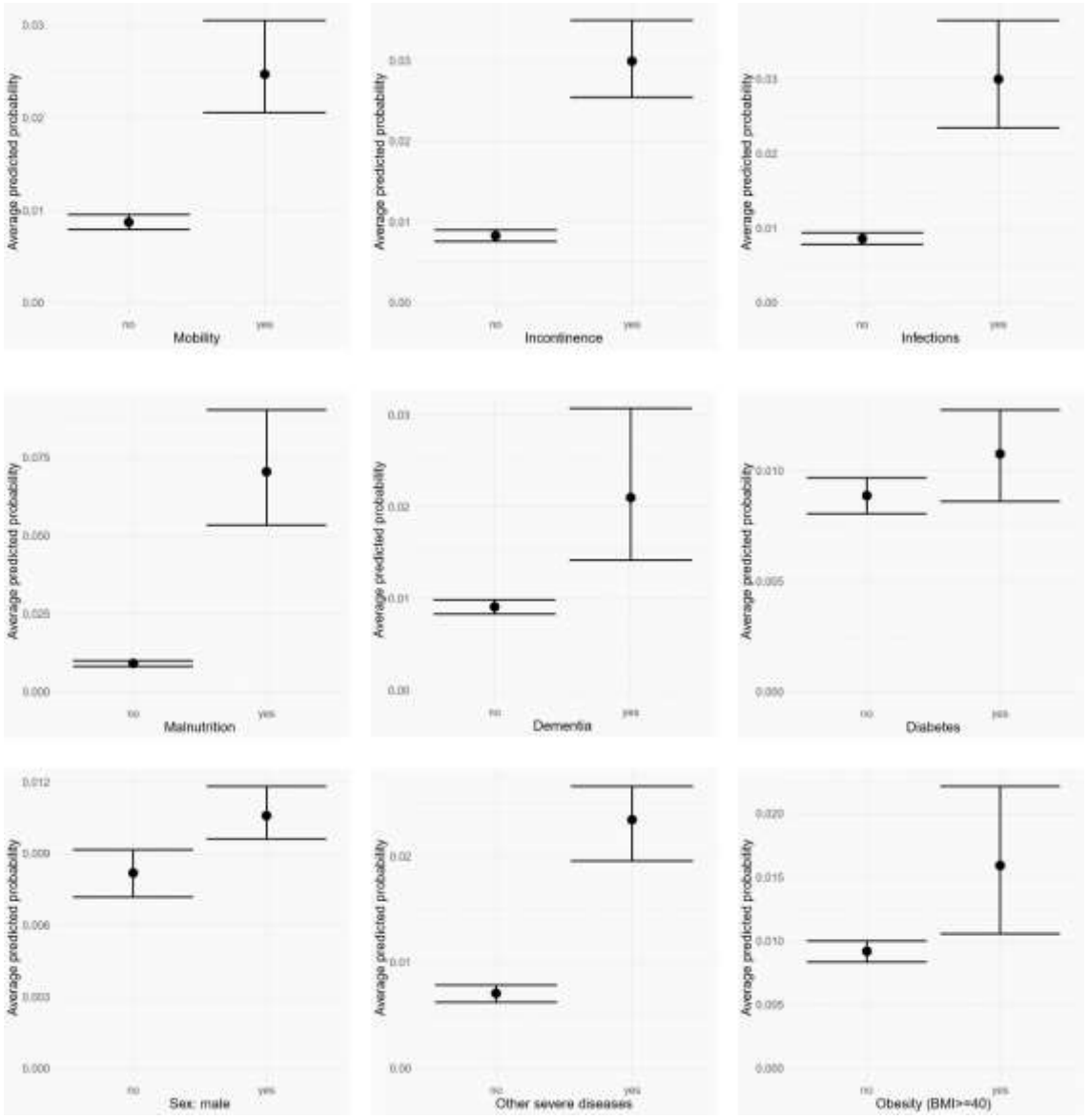
S1 - Average predicted probability of incident pressure ulcers related to age



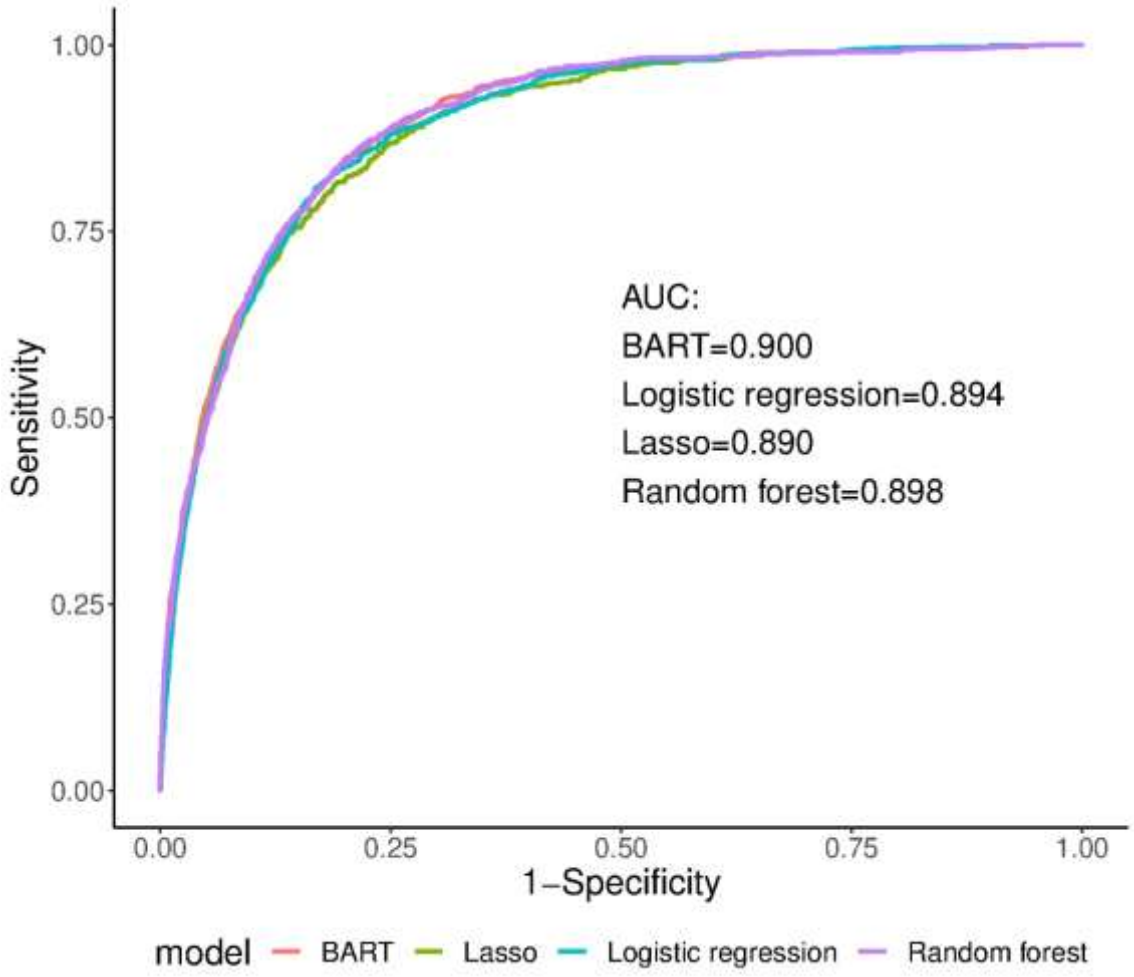
S2 - Average predicted probability of incident pressure ulcers related to male sex



S3 - Average predicted probability of incident pressure ulcers related to comorbidities



S4 - ROC curve of logistic regression, random forest, LASSO and BART



S5 - Confusion Matrix comparing BART, LASSO, logistic regression and random forest in full dataset and subgroups

	Full dataset		Intensive care		No intensive care		Ventilation		No ventilation		Anesthesia		No anesthesia	
	actual yes	actual no	actual yes	actual no	actual yes	actual no	actual yes	actual no	actual yes	actual no	actual yes	actual no	actual yes	actual no
BART														
Predicted yes	80	63	79	62	1	1	74	52	6	11	79	59	1	4
Predicted no	826	28369	512	5004	314	23365	246	880	580	27489	526	14324	300	14045
LASSO														
Predicted yes	40	39	39	39	1	0	39	35	1	4	35	29	5	10
Predicted no	866	28393	552	5027	314	23366	281	897	585	27496	570	14354	296	14039
Logistic regression														
Predicted yes	90	138	89	132	1	6	77	106	13	32	77	91	13	47
Predicted no	816	28294	502	4934	314	23360	243	826	573	27468	528	14292	288	14002
Random forest														
Predicted yes	61	44	61	44	0	0	58	41	3	3	60	41	1	3
Predicted no	845	28388	530	5022	315	23366	262	891	583	27497	545	14342	300	14046

S6 - Predictive performance measures for BART, logistic regression, LASSO and random forest

	full dataset	intensive care		ventilation		anesthesia	
		yes	no	yes	no	yes	no
BART							
Sensitivity	0.09	0.13	0.00	0.23	0.01	0.13	0.00
Specificity	1.00	0.99	1.00	0.94	1.00	1.00	1.00
Positive predictive value	0.56	0.56	0.50	0.59	0.35	0.57	0.20
Negative predictive value	0.97	0.91	0.99	0.78	0.98	0.96	0.98
Precision	0.56	0.56	0.50	0.59	0.35	0.57	0.20
Recall	0.09	0.13	0.00	0.23	0.01	0.13	0.00
F1	0.15	0.22	0.01	0.33	0.02	0.21	0.01
Prevalence	0.03	0.10	0.01	0.26	0.02	0.04	0.02
Detection rate	0.00	0.01	0.00	0.06	0.00	0.01	0.00
Detection prevalence	0.00	0.02	0.00	0.10	0.00	0.01	0.00
Balanced accuracy	0.54	0.56	0.50	0.59	0.50	0.56	0.50
Accuracy	0.97	0.90	0.99	0.76	0.98	0.96	0.98
LASSO							
Sensitivity	0.04	0.07	0.00	0.12	0.00	0.06	0.02
Specificity	1.00	0.99	1.00	0.96	1.00	1.00	1.00
Positive predictive value	0.51	0.50	1.00	0.53	0.20	0.55	0.33
Negative predictive value	0.97	0.90	0.99	0.76	0.98	0.96	0.98
Precision	0.51	0.50	1.00	0.53	0.20	0.55	0.33
Recall	0.04	0.07	0.00	0.12	0.00	0.06	0.02
F1	0.08	0.12	0.01	0.20	0.00	0.10	0.03
Prevalence	0.03	0.10	0.01	0.26	0.02	0.04	0.02
Detection rate	0.00	0.01	0.00	0.03	0.00	0.00	0.00
Detection prevalence	0.00	0.01	0.00	0.06	0.00	0.00	0.00
Balanced accuracy	0.52	0.53	0.50	0.54	0.50	0.53	0.51
Accuracy	0.97	0.90	0.99	0.75	0.98	0.96	0.98

	full dataset	intensive care		ventilation		anesthesia	
		yes	no	yes	no	yes	no
Logistic regression							
Sensitivity	0.10	0.15	0.00	0.24	0.02	0.13	0.04
Specificity	1.00	0.97	1.00	0.89	1.00	0.99	1.00
Positive predictive value	0.39	0.40	0.14	0.42	0.29	0.46	0.22
Negative predictive value	0.97	0.91	0.99	0.77	0.98	0.96	0.98
Precision	0.39	0.40	0.14	0.42	0.29	0.46	0.22
Recall	0.10	0.15	0.00	0.24	0.02	0.13	0.04
F1	0.16	0.22	0.01	0.31	0.04	0.20	0.07
Prevalence	0.03	0.10	0.01	0.26	0.02	0.04	0.02
Detection rate	0.00	0.02	0.00	0.06	0.00	0.01	0.00
Detection prevalence	0.01	0.04	0.00	0.15	0.00	0.01	0.00
Balanced accuracy	0.55	0.56	0.50	0.56	0.51	0.56	0.52
Accuracy	0.97	0.89	0.99	0.72	0.98	0.96	0.98
Random forest							
Sensitivity	0.07	0.10	0.00	0.18	0.01	0.10	0.00
Specificity	1.00	0.99	1.00	0.96	1.00	1.00	1.00
Positive predictive value	0.58	0.58	n/a*	0.59	0.50	0.59	0.25
Negative predictive value	0.97	0.90	0.99	0.77	0.98	0.96	0.98
Precision	0.58	0.58	n/a*	0.59	0.50	0.59	0.25
Recall	0.07	0.10	0.00	0.18	0.01	0.10	0.00
F1	0.12	0.18	n/a*	0.28	0.01	0.17	0.01
Prevalence	0.03	0.10	0.01	0.26	0.02	0.04	0.02
Detection rate	0.00	0.01	0.00	0.05	0.00	0.00	0.00
Detection prevalence	0.00	0.02	0.00	0.08	0.00	0.01	0.00
Balanced accuracy	0.53	0.55	0.50	0.57	0.50	0.55	0.50
Accuracy	0.97	0.90	0.99	0.76	0.98	0.96	0.98

Note: n/a*: Random forest did not predict a pressure ulcer for this group. Therefore, positive predictive value, precision and F1-score cannot be calculated.

S7 - Sensitivity of BART applied for most severe grades of incidental PU

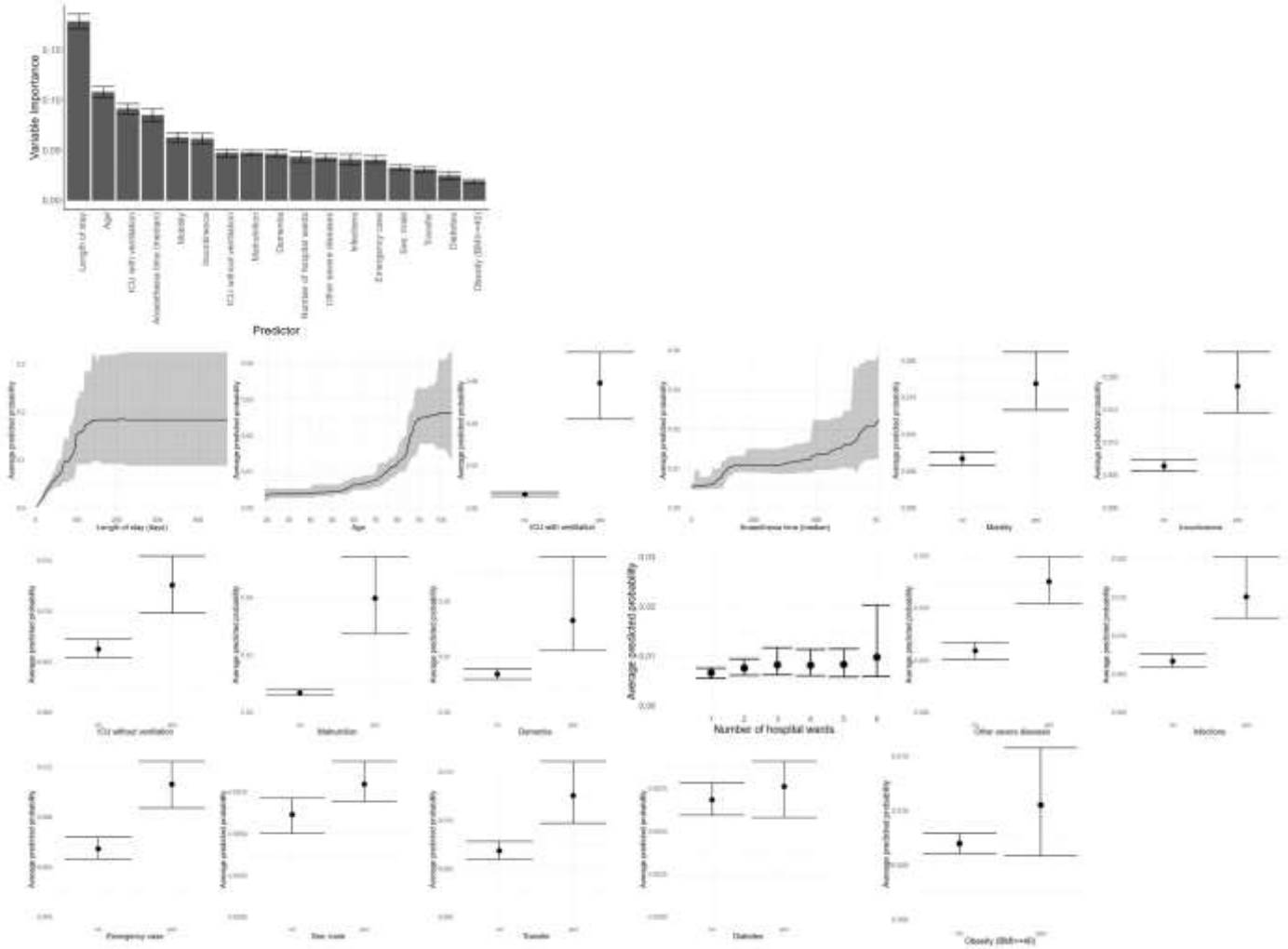
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
BART	0.05	0.07	0.12	0.19
LASSO	0.03	0.03	0.05	0.14
Logistic regression	0.06	0.09	0.12	0.21
Random forest	0.02	0.05	0.11	0.17
n	174	437	217	78

S8 - Definition of comorbidities included based on ICD-10 German Modification

BMI≥40	E66.02* - Obesity due to overconsumption of calories: obesity grade III (WHO) in patients 18 years and older. E66.12* - Drug-induced obesity: obesity grade III (WHO) in patients 18 years and older. E66.22* - Excessive obesity with alveolar hypoventilation: obesity grade III (WHO) in patients 18 years and older. E66.82* - Other obesity: obesity grade III (WHO) in patients 18 years and older. E66.92* - Obesity, unspecified: Obesity grade III (WHO) in patients 18 years and older.
Diabetes	E10 - Type 1 diabetes mellitus E11 - Type 2 diabetes mellitus E13 - Other specified diabetes mellitus
Underweight and malnutrition	E41 - Nutritional marasmus E43 - Unspecified severe protein-energy malnutrition E44 - Protein-energy malnutrition of moderate and mild degree E46 - Unspecified protein-energy malnutrition R64 - Cachexia
Dementia and vigilance disturbance	F00 - Dementia in Alzheimer disease F01 - Vascular dementia F02 - Dementia in other diseases classified elsewhere F03 - Unspecified dementia G30 - Alzheimer disease
Inctontinence	N39 - Other disorders of urinary system R15 - Faecal incontinence R32 - Unspecified urinary incontinence
Infections	A40 - Streptococcal sepsis A41 - Other sepsis J15 - Bacterial pneumonia, not elsewhere classified J16 - Pneumonia due to other infectious organisms, not elsewhere classified J17 - Pneumonia in diseases classified elsewhere J18 - Pneumonia, organism unspecified J69 - Pneumonitis due to solids and liquids M72.6 - Necrotizing fasciitis M86 - Osteomyelitis R57.2 - Septic shock R65 - Systemic Inflammatory Response Syndrome [SIRS]
Other severe diseases	B37.1 - Pulmonary candidiasis B37.7 - Candidal sepsis D50 - Iron deficiency anaemia D51 - Vitamin B12 deficiency anaemia D52 - Folate deficiency anaemia D53 - Other nutritional anaemias D61 - Other aplastic anaemias D62 - Acute posthaemorrhagic anaemia D63 - Anaemia in chronic diseases classified elsewhere D64 - Other anaemias D72.8 - Other specified disorders of white blood cells G63.2 - Diabetic polyneuropathy K70 - Alcoholic liver disease K72 - Hepatic failure, not elsewhere classified K74 - Fibrosis and cirrhosis of liver N17 - Acute renal failure N18.4 - Chronic kidney disease, stage 4 N18.5 - Chronic kidney disease, stage 5 N99.0 - Postprocedural renal failure R18 - Ascites R34 - Anuria and oliguria R60 - Oedema, not elsewhere classified R77.0 - Abnormality of albumin U69.00!* - hospital acquired pneumonia (valid until 2018) Z99.2 - Dependence on renal dialysis
Mobility	G20 - Parkinson disease G81 - Hemiplegia G82 - Paraplegia and tetraplegia G83 - Other paralytic syndromes M24.5 - Contracture of joint M62 - Other disorders of muscle R26.3 - Immobility R40 - Somnolence, stupor and coma R46 - Symptoms and signs involving appearance and behaviour S14 - Injury of nerves and spinal cord at neck level S24 - Injury of nerves and spinal cord at thorax level Z74.0 - Need for assistance due to reduced mobility Z99.3 - Dependence on wheelchair

* only applicable for German Modification

S9 - Variabe Importance and partial dependence plots statistically considering length of stay



S10 – Comparison of BART with alternative predictive models

To assess the relative predictive performance of BART, we considered multiple alternative predictive models. These included logistic regression, random forest, and least absolute shrinkage and selection operator (LASSO). Models were fit using 10-fold cross validation based on data from 2014-2017. The tuning parameters of BART, random forest, and LASSO and their final values are shown in the table below. Based on the best predictive models identified through cross validation, we prospectively predicted PU cases in data from 2018.

Model	Tuning parameter	Tuning parameter after cross validation
BART	Number of trees {25,50,75,100}	50
Random forest	Number of variables to possibly split at in each node {1,2,..,10}	3
LASSO	Regularization parameter {0,0.005,…,1}	0.035

5 Diskussion und Ausblick

5.1 Zusammenfassung der drei Publikationen

Die drei Publikationen zeigen sowohl individuell als auch übergreifend relevante Ergebnisse für die Risikoadjustierung der externen Qualitätssicherung und speziell für Fallmenge-Outcome-Analysen:

(1) Das in *Publikation (1)* durchgeführte **erste systematische Review** zum Einfluss von Fallmengen auf die Mortalität und Komplikationen in der Niedrigrisiko-Geburtshilfe zeigte mit Ausnahme der perinatalen Mortalität studienübergreifend heterogene oder insignfikante Assoziationen im Hinblick auf 28-Tage-Mortalität, Totgeburten, maternale Mortalität, (Not-)Kaiserschnitte oder Komplikationen. Während für Frühgeburten (Lasswell et al., 2010; Walther et al., 2020), neonatalogische Intensivversorgung (Lasswell et al., 2010) oder pädiatrische Herzchirurgie (McAteer et al., 2013) Erfahrungseffekte beschrieben wurden, zeigte das Review zu Niedrigrisiko-Geburten weniger eindeutige Ergebnisse.

Diese studienindividuell gegenläufigen Ergebnisse können unterschiedliche Erklärungsansätze haben. Neben möglichen methodischen Unterschieden, bspw. bei der Berücksichtigung relevanter Variablen wie Geburtszeitpunkt (de Graaf et al., 2010; Restrepo et al., 2018), Personalbesetzung, Infrastruktur (Joyce et al., 2004; Karalis et al., 2016; Restrepo et al., 2018), Arbeitsumgebung (Lake et al., 2016), Qualifikationen (Lake et al., 2012) oder einer vorliegenden Effektmodifikation, kann die in Industriestaaten etablierte perinatale Regionalisierung (Huijts et al., 2018; Kunz et al., 2020; Zeitlin et al., 2004) als risikoadaptierte Versorgung zu einer entsprechenden Risikoselektion und somit zu „nachteiligen“ Effekten von High-Volume-Providern führen. Die in *Publikation (1)* und einer weiteren Publikation (McAteer et al., 2013) identifizierten unterschiedlichen Definitionen von Population, Fallschwellen, Outcomes und statistischer Methodik unterstreichen zudem die Notwendigkeit einheitlicher Definitionen und die Entwicklung und Verwendung von Core Outcome Sets (Duffy et al., 2017; Molloy et al., 2018).

(2) *Publikation (2)* zeigte, dass **Patient:innensicherheit bei kolorektalen Resektionen** auf der Grundlage **multipler Risikofaktorensets** und **Outcomes betrachtet** werden muss. Die Aufnahme als Notfall oder Zuverlegung war - inklusive Adjustierung für fallindividuelle Risiken - sowohl bei Kolon- als auch Rektumresektionen signifikant mit erhöhter Mortalität, postoperativem Lungenversagen, Nierenversagen und

postoperativen Wundinfektionen assoziiert. *Publikation (2)* zeigte zudem auch den Eingriffszeitpunkt (Wochenendchirurgie) als relevanten Einflussfaktor auf die Patient:innensicherheit und bestätigt hierzu die bestehende Literatur in Bezug auf die Relevanz von Notaufnahmen (Anderson et al., 1992; Mullen et al., 2017), Zuverlegungen (Chow et al., 2017; Hernandez-Boussard et al., 2017; Mueller et al., 2019; Sharp et al., 2017; Sharp et al., 2018) und Wochenendchirugie (Chen et al., 2019; Honeyford et al., 2018; Huijts et al., 2018; McCallum et al., 2016; O'Leary et al., 2019; Pauls et al., 2017; Restrepo et al., 2018).

Die Fallmenge war protektiv mit dem Patient:innensicherheitsoutcome von Rektumresektionen assoziiert. In der Gruppe der Kolonresektionen hingegen verblieben Assoziationen zwischen Fallmenge und Patient:innensicherheitsoutcomes mehrheitlich insignifikant. Andere versorgerbezogene Charakteristika, wie der Urbanisierungsgrad oder die Trägerschaft, zeigten ähnlich wie die Fallmenge insignifikante oder uneinheitliche Ergebnisse über die vier betrachteten Outcomes und über beide Gruppen. Bestehende Literatur berichtet ebenfalls unterschiedliche Ergebnisse hinsichtlich Fallmenge (Chioreso et al., 2018; Huo et al., 2017; Link et al., 2017; Malheiro et al., 2021; Roessler et al., 2022), Trägerschaft (Malheiro et al., 2021; Morris et al., 2007) oder Urbanisierungsgrad (Hamidi et al., 2019; Knight, 2013; Malheiro et al., 2021). Diesen heterogenen Ergebnissen liegen, neben allgemeinen Erklärungsansätzen, durch differierende case-mixes, Personalbesetzung, Individualerfahrung oder Krankenhausgröße datensatzbezogene Erklärungsansätze zugrunde (Malheiro et al., 2021; Tserenpuntsag et al., 2014). In Daten nach §21 KHEntgG fehlen Informationen unter anderem zum Personalschlüssel (Etzioni et al., 2014; Yasunaga et al., 2012), der klinischen Expertise (Hall et al., 2016) oder zu Zertifizierungen (Trautmann et al., 2018), die ebenfalls mit dem klinischen Ergebnis und Patient:innensicherheitsoutcomes assoziiert wurden. Zudem legen die unterschiedlichen Ergebnisse zwischen den Gruppen der Kolon- und Rektumresektionen eine Stratifizierung nahe, was in der bestehenden Literatur nicht durchgängig erfolgte (Kolfschoten et al., 2014; Liu et al., 2015).

(3) Die in *Publikation (3)* **erstmalig durchgeführte Analyse zur Rolle des Versorgungssettings** bei inzidentem Dekubitus im Rahmen akutstationärer Versorgung wies auf die Aufnahme als Notfall oder Zuverlegung als relevanten Risikofaktor inklusive Adjustierung für diverse Fallvariablen hin. Zuzüglich waren längere chirurgische Anästhesien (>50 Minuten), eine erhöhte Anzahl behandlungsbeteiligter Stationen und intensivmedizinische Behandlung mit und ohne Beatmung

mit einer erhöhten Dekubitusinzidenz assoziiert. Die steigende Dekubitusinzidenz ab ein- bis mehrstündigen chirurgischen Anästhesien kann bei Annahme eingeschränkter Lagerungsfähigkeit in chirurgischen Eingriffen darauf hindeuten, dass ein Dekubitus schneller auftritt als das gängige, jedoch nicht bewiesene Lagerungsintervall von 120 Minuten suggeriert (European Pressure Ulcer Advisory Panel et al., 2019; Gillespie et al., 2020). Diese Annahme sollte in einer (randomisiert-kontrollierten) Studie überprüft werden. Die erstmalig mit versorgungsnahen Daten durchgeführte Prädiktion gestaltete sich aufgrund einer hohen Zahl von falsch-negativen Ergebnissen und einer folglich geringen Sensitivität sowohl in der Gesamtpopulation als auch Subgruppen als eingeschränkt.

5.2 Stärken und Limitationen der Publikationen

Alle Publikationen haben die Stärke, dass die Analysen auf transparente Art und Weise durchgeführt und publiziert wurden. Das schließt a priori gewählte und in den Publikationen angehangene Definitionen von Kovariaten, Outcomes, Suchstrategien und statistische (Subgruppen-)Analysen mit ein. Die drei Publikationen deckten zudem unterschiedliche dimensionale und methodische Schwerpunkte ab:

(1) Systematisches Review **internationaler** Literatur (Walther et al., 2021),

(2) Querschnittanalyse von 232 **nationalen** Krankenhäusern basierend auf Daten nach §21 KHEntgG (Walther, Schmitt, et al., 2022),

(3) Querschnittanalyse in einem **monozentrischen** Setting basierend auf der Kombination klinischer Daten und Abrechnungsdaten nach §21 KHEntgG - (Walther, Heinrich, et al., 2022).

Diese Herangehensweise ermöglichte, dass die Fragestellungen aus internationaler, nationaler und individualversorgerbezogener Perspektive betrachtet werden konnten. Alle Publikationen haben den Vorteil, dass fünf- (Walther, Schmitt, et al., 2022) oder sechsstellige (Walther, Heinrich, et al., 2022) Populationen und eine hohe (registerdatenbasierte) Studienbreite (Walther et al., 2021) eingeschlossen werden konnten. Das systematische Review zur Niedrigrisiko-Geburtshilfe (Walther et al., 2021) sowie die Querschnittanalysen zur Patient:innensicherheit bei kolorektalen Resektionen (Walther, Schmitt, et al., 2022) und Dekubitusinzidenz (Walther, Heinrich, et al., 2022) basierten auf versorgungsnahen Daten. Die Stärke dieser Datensätze gründet auf großen Populationen und zügige Durchführbarkeit.

Die in den jeweiligen Publikationen (S. 39, Publikation 1; S. 58-59, Publikation 2; S. 97-98, Publikation 3) ausführlich diskutierten Schwächen dieser Daten zeigt sich in einer reduzierten Detailtiefe, wie z.B. der Kodierung detaillierter Risikofaktoren (u.a. Rauchen von Schwangeren), dem eigentlichen Einweisungsgrund oder klinischen Details. Insbesondere der Einweisungsgrund kann im Hinblick auf die Kodierung und ggf. durch die Krankenversicherungen budgetierte Versorgung einen Fehlanreiz darstellen (Busse et al., 2013; Schwierz et al., 2012). Ferner kann auch ein ambulant eingewiesener Fall eine Akutindikation beinhalten (Krämer et al., 2019). Ein weiteres Problem bei der Analyse versorgungsnaher Daten stellt die Present on admission-Problematik dar (Heller, 2008; Maass et al., 2011). In *Publikation (2)* wurde zur Auflösung dieser Limitation ein Set a priori validierter Patient:innensicherheitsoutcomes genutzt, welche mit geringerer Wahrscheinlichkeit bei Aufnahme bereits vorliegen (Maass et al., 2015; Walther, Schmitt, et al., 2022). *Publikation (3)* konnte in der Analyse im Rahmen des monozentrischen Settings die notwendige Information, ob ein Dekubitus bereits bei Aufnahme vorlag, durch die Verknüpfung klinischer Daten und Abrechungsdaten nach §21 KHEntgG lösen (Walther, Heinrich, et al., 2022).

Sowohl die eingeschlossenen Studien des Reviews aus *Publikation (1)* als auch die beiden Analysen der *Publikationen (2)* und *(3)* waren Querschnittdesigns. Querschnittstudien beschreiben keinen zeitlichen Verlauf, sondern eine zeitlich nicht näher ausdifferenzierte Momentaufnahme. Das verhindert den Schluss kausaler Zusammenhänge und erfordert eine tiefgreifendere Forschung im Hinblick auf Ursache und Wirkung zwischen abhängigen und unabhängigen Variablen (Wang & Cheng, 2020). Insbesondere für die Rolle der Fallmenge kann ein Querschnittdesign den angenommenen Lerneffekt durch eine sich erhöhende Fallmenge im Längsschnitt sowie den medizinischen Fortschritt bei langen Beobachtungszeiträumen somit nicht abbilden. Die fehlende Längsschnittbetrachtung, Kontrollgruppe und difference-in-difference-Vergleich über mehrere Zeitpunkte und Gruppen verhindern somit einen ausschließlichen Kausalitätsnachweis in Querschnitt- und beobachtenden Deisgns und zeigen einerseits weiteren Forschungsbedarf auf und unterstreichen die Notwendigkeit einer strukturierten und statistisch anspruchsvollen Planung (Geraedts, 2012).

5.3 Implikationen für externe Qualitätssicherung und Mindestmengen

Externe Qualitätssicherung: Der Aufnahmeanlass ist ein relevanter und zu berücksichtigender Risikofaktor des Versorgungssettings für die Fallakuität und -komplexität (Forschungsziel 1)

Diese Dissertation konnte sowohl anhand der transparent definierten kolorektalen Resektionen als auch anhand einer allgemeinen stationären Versorgungspopulation den Aufnahmeanlass als Risikofaktor für die Patient:innensicherheit - insbesondere in Abhängigkeit der Fallkomplexität und -akuität - hervorheben. Stationäre Versorger unterscheiden sich hinsichtlich ihrer Spezialisierung, Ausstattung, Größe, Fallkomplexität und dem Versorgungsauftrag (Roessler et al., 2019; Roessler et al., 2021; Schoffer et al., 2020). Diese Unterschiede führen zu einer gewollten risikoadaptierten Versorgung von Patienten mit dem Ziel, eine hohe Qualität medizinischer Versorgung unabhängig von der Fallkomplexität zu sichern (Sachverständigenrat zur Begutachtung der Entwicklung im Gesundheitswesen, 2018). Vor dem Hintergrund der Vergleichbarkeit und der gewollten risikoadaptierten Versorgung ist eine angemessene (statistische) Berücksichtigung der Fallkomplexität, welche sich unter anderem durch den Aufnahmeanlass entscheidend ausdrückt, unabdingbar. Wenn in Publikationen angewendet, berücksichtigt die Risikoadjustierung der externen Qualitätssicherung vornehmlich das Alter, Geschlecht und die Komorbiditäten. Die dieser Dissertation zugrundeliegenden Analysen der Patient:innensicherheit bei Dekubitusinzidenz und kolorektalen Resektionen zeigen eindrücklich die Notwendigkeit sowohl von Risikoadjustierung in der externen Qualitätssicherung im Allgemeinen als auch insbesondere die statistische und klinische Relevanz des Aufnahmeanlasses parallel zu Alter, Geschlecht und Komorbiditäten.

Fallmenge: Die Analyse der Fallmenge als Surrogatvariable für Erfahrung erfordert eine sowohl patienten-, versorgungs- und versorgerseitig umfassende als auch methodisch anspruchsvolle Analyse (Forschungsziel 2)

Die signifikante Assoziation des Aufnahmeanlasses mit der Patient:innensicherheit sowie die heterogene Studienevidenz zur Rolle der Fallmenge heben die Bedeutung der Risikoadjustierung sowohl im Hinblick auf indikatorbasierte Vergleiche als auch hinsichtlich wissenschaftlicher Untersuchungen hervor. Sowohl das systematische Review zur Niedrigrisiko-Geburtshilfe (Walther et al., 2021) als auch die mehrere Outcomes und Kovariatensets einschließende Querschnittstudie zur Patient:innensicherheit kolorektaler Resektionen (Walther, Schmitt, et al., 2022) zeigten teilweise heterogene Ergebnisse zum Einfluss der Fallmenge auf das Patient:innensicherheitsoutcome.

Bei der Untersuchung von Fallmenge-Outcome-Vergleichen konnten vor allem die Risikoadjustierung, die Definitionen von Populationen und Outcomes sowie die Detailtiefe des verwendeten Datensatzes als zu berücksichtigende Faktoren exploriert werden. Im Hinblick auf den Versorger und den Einfluss der Fallmenge nimmt die Studienliteratur für verschiedene Indikationen nicht nur die häusliche Gesamtfallmenge, sondern speziell auch die Individualfallmenge eines Operateurs, die Spezialisierung, die Zusammensetzung des Teams und die Arbeitsbelastung in den Fokus (Archampong et al., 2012; Chou et al., 2021; Chowdhury et al., 2007; Hall et al., 2016; Langhorne & Ramachandra, 2020; The UK Neonatal Staffing Study Group, 2002; Turner et al., 2021; Yasunaga et al., 2012). Künftige Untersuchungen sollten in der Analyseplanung die Relevanz der Fallmenge als Surrogatvariable und deren Einflussgrößen berücksichtigen.

5.4 Ausblick - Versorgungssteuerung und Evidenzgrad

Die Erkenntnisse dieser und anderer Arbeiten zu (Mindest-)Fallmengen und Qualitätssicherung beruhen in der Regel auf Beobachtungsdaten. Da Ursache-Wirkungs-Beziehungen nicht ableitbar sind, bleiben Beobachtungs- und Querschnittevidenz inklusive Verzerrungsanfälligkeit (u.a. Selektion, Information) und statistischem Interaktionspotenzial juristisch angreifbar, wie frühere Gerichtsverfahren zu Frühgeburten und Knie-TEP zeigten (Geraedts, 2012; Hammer et al., 2009; Tönnies et al., 2022). Für die verpflichtende eQS führen eine unkontrollierte Evidenz und teilweise gänzlich fehlende Evaluationspläne zu inakzeptabler Studienqualität mit hohen Verzerrungsrisiken (Geraedts & de Cruppé, 2022; Khan & Ollenschläger, 2014). Die Verbesserungsvorschläge zielen insbesondere auf eine prospektive (Evaluations-)Planung oder die Anwendung detaillierter quantitativer und qualitativer Analysen ab (Conry et al., 2012; Farin & Jäckel, 2011; Geraedts & de Cruppé, 2022; Glattacker & Jäckel, 2007; Grol et al., 2002).

Im Sinne Evidenzbasierter Medizin sind versorgungssteuernde globale Interventionen oftmals auf die Beforschung durch Beobachtungsstudien als bestverfügbare Evidenz angewiesen (Sackett et al., 1996). Diese Arbeit zeigt, dass die klare Definition von Population, Risikofaktoren und Outcomes und eine angemessene, der medizinischen Komplexität gerecht werdende statistische Adjustierung ein unabdingbares Schlüsselelement gegenüber Verzerrungs- und Interaktionspotenzialen darstellen. Gemessen an der Relevanz durch die Berichts- und Rechtfertigungspflicht der externen Qualitätssicherung und wettbewerbsverändernden Mindestmengen zeigen die hier

beschriebenen Befunde auf Grundlage einer umfassenden inhaltlichen und statistischen Analyseplanung die Notwendigkeit einer gründlichen (risikoadjustierten) Analyse von Fall-Versorgungs- und Versorgervariablen als relevante Risikofaktoren der Patient:innensicherheit.

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Darstellung des Eigenanteils

Der Autor dieser Dissertation trug maßgeblich zur Entwicklung der zugrundeliegenden Analysen bei, wie auch in den inkludierten Manuskripten beschrieben. Übergeordnet entwickelte der Autor dieser Dissertation nach Vorrecherche und teilweise publizierter Vorarbeiten die Fragestellungen der Publikationen.

Publikation (1) - Das Review wurde durch den Promovenden und die Koautoren a priori geplant. Der Promovend registrierte das Reviewprotokoll. Die Suchstrategie wurde durch den Promovenden entwickelt und in den Fachdatenbanken angewandt. Das Screening, die Daten¬extraktion und Qualitätsbewertung wurde, wie im standardisierten Review-Verfahren üblich, durch den Promovenden in doppelt unabhängiger Form mit den Koautorinnen durchgeführt. Die Ergebnisinterpretation, -synthese und -aufbereitung erfolgte durch den Promovenden im Zusammenhang mit der initialen Erstellung des Manuskripts sowie seiner Finalisierung in Kooperation mit den Koautoren. Der Publikations- und Revisionsprozess sowie die fachliche Korrespondenz wurde durch den Promovenden geführt.

Publikation (2) - Die Untersuchung wurde durch den Promovenden a priori geplant und als Teil der IMPRESS-Studie registriert. Der Promovend definierte die zu analysierenden Daten, Risikofaktoren, Outcomes der Untersuchung und erarbeitete mit dem Letztautor die statistische Methodik. Die Ergebnisinterpretation, -synthese und -aufbereitung erfolgte durch den Promovenden im Zusammenhang mit der initialen Erstellung des Manuskripts sowie seiner Finalisierung in Kooperation mit den Koautoren. Der Publikations- und Revisionsprozess sowie die fachliche Korrespondenz wurde durch den Promovenden geführt.

Publikation (3) - Die Untersuchung wurde durch den Promovenden a priori geplant und das Studienprotokoll bei der Ethikkommission der Technischen Universität Dresden eingereicht. Der Promovend definierte die zu analysierenden Daten, Risikofaktoren, Outcomes der Untersuchung und erarbeitete mit dem Letztautor die statistische Methodik. Die Ergebnisinterpretation, -synthese und -aufbereitung erfolgte durch den Promovenden im Zusammenhang mit der initialen Erstellung des Manuskripts sowie seiner Finalisierung in Kooperation mit den Koautoren. Der Publikations- und Revisions-prozess sowie die fachliche Korrespondenz wurde durch den Promovenden geführt.

Peer-Review-Veröffentlichungen und Vorträge

Themenbereich Patient:innensicherheit & Qualität

Peer-Review Erstautorenschaften und Dissertationsleistung

Walther, F., Schmitt, J., Eberlein-Gonska, M., Kuhlen, R., Scriba, P., Schoffer, O., & Roessler, M. (2022). Relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: cross-sectional evidence from a nationwide sample of 232 German hospitals. *BMJ Open*, 12(7), e058481. https://doi.org/10.1136/bmjopen-2021-058481

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Anlage 1 - Erklärungen zur Eröffnung des Promotionsverfahrens

1. Hiermit versichere ich, dass ich die vorliegende Arbeit ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht.
2. Bei der Auswahl und Auswertung des Materials sowie bei der Herstellung des Manuskripts habe ich Unterstützungsleistungen von folgenden Personen erhalten: entfällt.
3. Weitere Personen waren an der geistigen Herstellung der vorliegenden Arbeit nicht beteiligt. Insbesondere habe ich nicht die Hilfe eines kommerziellen Promotionsberaters in Anspruch genommen. Dritte haben von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen.
4. Die Arbeit wurde bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.
5. Die Inhalte dieser Dissertation wurden in folgender Form veröffentlicht:

   Walther, F., Kuester, D., Bieber, A., Malzahn, J., Rüdiger, M., & Schmitt, J. (2021). Are birth outcomes in low risk birth cohorts related to hospital birth volumes? A systematic review. *BMC Pregnancy and Childbirth*, 21(1), 531. https://doi.org/10.1186/s12884-021-03988-y

   Walther, F., Schmitt, J., Eberlein-Gonska, M., Kuhlen, R., Scriba, P., Schoffer, O., & Roessler, M. (2022). Relationships between multiple patient safety outcomes and healthcare and hospital-related risk factors in colorectal resection cases: cross-sectional evidence from a nationwide sample of 232 German hospitals. *BMJ Open*, 12(7), e058481. https://doi.org/10.1136/bmjopen-2021-058481

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6. Ich bestätige, dass es keine zurückliegenden erfolglosen Promotionsverfahren gab.

7. Ich bestätige, dass ich die Promotionsordnung der Medizinischen Fakultät der Technischen Universität Dresden anerkenne.
8. Ich habe die Zitierrichtlinien für Dissertationen an der Medizinischen Fakultät der Technischen Universität Dresden zur Kenntnis genommen und befolgt.
9. Ich bin mit den "Richtlinien zur Sicherung guter wissenschaftlicher Praxis, zur Vermeidung wissenschaftlichen Fehlverhaltens und für den Umgang mit Verstößen" der Technischen Universität Dresden einverstanden.

Dresden, 28.11.2022

Anlage 2 - Erklärungen über die Einhaltung rechtlicher Bestimmungen

Hiermit bestätige ich die Einhaltung der folgenden aktuellen gesetzlichen Vorgaben im Rahmen meiner Dissertation

☒ das zustimmende Votum der Ethikkommission bei Klinischen Studien, epidemiologischen Untersuchungen mit Personenbezug oder Sachverhalten, die das Medizinproduktegesetz betreffen
Aktenzeichen der zuständigen Ethikkommission:
Publikation (1): entfällt - Systematisches Review
Publikation (2): EK 186052017, IRB00001473, IORG0001076
Publikation (3): BO-EK-520112021, IRB00001473, IORG0001076

☐ die Einhaltung der Bestimmungen des Tierschutzgesetzes Aktenzeichen der Genehmigungsbehörde zum Vorhaben/zur Mitwirkung: entfällt

☐ die Einhaltung des Gentechnikgesetzes: entfällt

☒ die Einhaltung von Datenschutzbestimmungen der Medizinischen Fakultät und des Universitätsklinikums Carl Gustav Carus.

Dresden, 28.11.2022
