Effects of night surgery on postoperative mortality and morbidity: a multicentre cohort study

Friederike C Althoff,[1] Luca J Wachtendorf ,[1] Paul Rostin,[1,2] Peter Santer ,[1] Maximilian S Schaefer,[1] Xinling Xu,[1] Stephanie D Grabitz,[1] Hovig Chitilian,[2] Timothy T Houle,[2] Gabriel A Brat,[3] Oluwaseun Akeju,[2] Matthias Eikermann [1]

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjqs-2020-011684).

[1]Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA
[2]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA
[3]Surgery, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA

Correspondence to
Professor Matthias Eikermann, Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA 02215, USA; meikerma@bidmc.harvard.edu

FCA, LJW and PR contributed equally.

Received 3 June 2020
Revised 4 September 2020
Accepted 9 September 2020
Published Online First 7 October 2020

To cite: Althoff FC, Wachtendorf LJ, Rostin P, *et al*. *BMJ Qual Saf* 2021;**30**:678–688.

ABSTRACT

Background Surgery at night (incision time 17:00 to 07:00 hours) may lead to increased postoperative mortality and morbidity. Mechanisms explaining this association remain unclear.

Methods We conducted a multicentre retrospective cohort study of adult patients undergoing non-cardiac surgery with general anaesthesia at two major, competing tertiary care hospital networks. In primary analysis, we imputed missing data and determined whether exposure to night surgery affects 30-day mortality using a mixed-effects model with individual anaesthesia and surgical providers as random effects. Secondary outcomes were 30-day morbidity and the mediating effect of blood transfusion rates and provider handovers on the effect of night surgery on outcomes. We further tested for effect modification by surgical setting.

Results Among 350 235 participants in the primary imputed cohort, the mortality rate was 0.9% (n=2804/322 327) after day and 3.4% (n=940/27 908) after night surgery. Night surgery was associated with an increased risk of mortality (OR_{adj} 1.26, 95% CI 1.15 to 1.38, p<0.001). In secondary analyses, night surgery was associated with increased morbidity (OR_{adj} 1.41, 95% CI 1.33 to 1.48, p<0.001). The proportion of patients receiving intraoperative blood transfusion and anaesthesia handovers were higher during night-time, mediating 9.4% (95% CI 4.7% to 14.2%, p<0.001) of the effect of night surgery on 30-day mortality and 8.4% (95% CI 6.7% to 10.1%, p<0.001) of its effect on morbidity. The primary association was modified by the surgical setting (p-for-interaction<0.001), towards a greater effect in patients undergoing ambulatory/same-day surgery (OR_{adj} 1.81, 95% CI 1.39 to 2.35) compared with inpatients (OR_{adj} 1.17, 95% CI 1.02 to 1.34).

Conclusions Night surgery was associated with an increased risk of postoperative mortality and morbidity. The effect was independent of case acuity and was mediated by potentially preventable factors: higher blood transfusion rates and more frequent provider handovers.

INTRODUCTION

More than 5% of surgeries are performed outside of standard operating room hours and up to 74% of procedures performed at night are planned as elective cases.[1] Although unavoidable in urgent circumstances, night surgery itself may be an independent risk factor of perioperative mortality and morbidity.

Previous studies analysing the effect of night surgery on mortality and morbidity provided equivocal findings: while higher mortality rates were suggested in patients undergoing night surgery across surgical specialties,[2] other studies only found surgery during the early (13:00 to 17:00 hours)[3] or late afternoon and evening (16:00 to 23:00 hours)[4] to be associated with higher mortality or morbidity in non-emergency cases. It remains unclear whether surgery at night affects patient survival, and whether the effect varies by acuity and condition of the patient.

It is important to identify potentially preventable elements of night surgery that contribute to its potential risk. Discussions aiming at understanding mechanisms that may drive a higher risk of night surgery have only focused on providers' sleep deprivation. Studies on healthcare providers suggested that night shift work and variation in daylight exposure disrupt circadian rhythms, leading to increased medical errors.[5–8] Contributing factors may be sleep-deprived fatigue, prolonged reaction time, impaired situational awareness and a natural circadian variability in technical performance.[5 6 9] However, it has not yet been defined whether there are intraoperative factors that notably differ between day and night surgeries and may be modified to improve outcomes.

In this multicentre cohort study, we hypothesised that exposure to surgery at night affects patient survival and postoperative complications. We then tested whether intraoperative blood transfusions and anaesthesia handovers during

night-time were potential mediators of the effect of night surgery on adverse outcomes. We further assessed whether the effect of night surgery was driven by a higher case acuity of patients undergoing surgery at night.

METHODS

Study design

Data were obtained for surgical patients at institution A between October 2005 and September 2017 and at institution B and one affiliated community hospital between January 2007 and December 2015. The study was approved by the institutional review boards at each institution (protocol numbers 2018P000786 and 2019P000825). The requirement for written informed consent was waived. Data were collected from hospital-registry databases (online supplemental file 1, section 1). This manuscript adheres to the STROBE guidelines online supplemental file 2.[10]

Study population

We included patients aged 18 years or older who had an American Society of Anaesthesiologists' (ASA) status below 6 and underwent non-cardiac surgery with general anaesthesia. Missing data required for the primary analysis were imputed using multiple imputation with chained equations (online supplemental file 1, section 3). For secondary, sensitivity, and exploratory analyses, the complete-case method was used.

Study exposure and outcomes

Night surgery was defined as a surgical incision time between 17:00 and 07:00 hours. Surgical times were based on timestamps in electronic anaesthesia records. The primary outcome was mortality within 30 days of surgery. Secondary outcomes were 30-day morbidity, defined as a composite outcome including renal, cardiovascular, bleeding, infection, intestinal/digestive, and pulmonary complications within 30 days of surgery, as defined by the International Classification of Diseases, Ninth and Tenth Revision (online supplemental eTable 1)[11] and the mediating effect of blood transfusion rates and provider handovers on the effect of night surgery on outcomes.

Primary analysis and covariates

We used multivariable-adjusted mixed-effects logistic regression to investigate the effect of night surgery on 30-day mortality. We included individual anaesthesia and surgical providers as random effects in the primary model. Analyses were adjusted for confounding variables based on literature review and clinical plausibility (online supplemental eTable 2). Patient factors included age, sex, body mass index, ASA physical status classification, surgical care setting (ambulatory care setting and same-day discharge versus inpatient surgery), Charlson Comorbidity Index, a 1-year history of cancer, home oxygen or respirator dependency, chronic pulmonary disease, coronary artery disease, congestive heart failure and ischaemic stroke. Procedure-related confounding variables included emergency surgery, surgical specialty, duration of surgery, date of surgery and work relative value units. Anaesthesia-related factors were vasopressor dose, intraoperative hypotension (defined as mean arterial pressure <55 mm Hg), SpO_2/FiO_2-ratio, transfusion of packed red blood cell units (PRBC) and handover between anaesthesiologists. Finally, we included the institution (A versus B) in the model. To address potential bias due to missing data, we performed multiple imputation with chained equations for the primary analysis.

Secondary analyses

In secondary analyses, we investigated whether night surgery was associated with 30-day morbidity by using multivariable-adjusted logistic regression. Further, we used path mediation analysis to evaluate the role of intraoperative factors as potential mediators of the effect of night surgery on 30-day mortality and morbidity. The two mediator candidates analysed were the intraoperative transfusion rate (proportion of patients transfused with PRBC) and the proportion of cases with an intraoperative handover between anaesthesiologists. To define complete handovers between anaesthesiologists, we used unique provider identification numbers as well as sign-in and sign-out times.

First, we tested the hypothesis that intraoperative transfusion rates were higher during night cases than day cases. We used a multivariable-adjusted logistic regression model on the association between night surgery and transfusion rate that included all confounding variables of the primary analysis. To verify this observation, we additionally adjusted for intraoperative estimated blood loss (mL) as well as mild and moderate to severe anaemia within 30 days prior to surgery. Preoperative haemoglobin values of ≥11 to ≤12.9 g/dL in men and ≥11 to ≤11.9 g/dL in women were used to define mild anaemia, and values of ≤10.9 g/dL were used to define moderate to severe anaemia in both men and women.[12] In addition, we tested whether variability across individual surgeons and anaesthesiologists had an impact on the association between night surgery and transfusion rate by including provider-related confounding variables and random effects for individual providers into the model (online supplemental file 1, section 5.1). Similarly, we tested the hypothesis that handovers between anaesthesiologists occur more frequently during night-time.

Second, we used adjusted analyses to examine whether transfusion rates and handovers were associated with the outcomes of 30-day mortality and morbidity, indicating potential effect mediation. We additionally tested for a potential interaction between the effects of the two mediators on the outcomes including the interaction term 'transfusion rate*handover' in the model.

Conditional on an association between the mediators and the study outcomes, we performed adjusted formal mediation analysis based on the method by Buis.[13] We estimated ORs of the indirect (mediated) effect of transfusion rate and handovers, respectively, and the total (unmediated) effect of night surgery on mortality and morbidity, using bootstrapping with 1000 replications.[13–15] Percentage mediation by the mediators was calculated using the following form: (ln (indirect effect)/ln (total effect)) × 100.[15] Finally, we combined the two mediators into one model to test the mediating effect of both higher proportions of blood transfusion and handovers during night-time on the association between night surgery and outcomes.

Exploratory analyses

With an exploratory intent, we performed interaction analysis to assess whether the association between night surgery and mortality was modified by the surgical care setting (ambulatory and same-day surgery versus inpatient surgery). Subgroup analyses were performed across groups of the interaction term. Patient characteristics in subgroups are provided in online supplemental eTables 6 and 7. To further address potential concerns that the effect may be driven by a higher case acuity of patients operated at night, we tested the primary association in a subgroup of patients undergoing non-emergency surgery, after excluding emergency and acute care services. In this subgroup, we repeated the interaction analysis by surgical care setting. Conversely, we examined the effect of night surgery on mortality in a subgroup of patients undergoing emergency surgery (online supplemental eTable 8).

Sensitivity analyses

We performed several sensitivity analyses to confirm the robustness of the effect of night surgery on mortality. We repeated the primary multivariable-adjusted mixed-effects logistic regression analysis with random effects for anaesthesia and surgical providers in the complete-case cohort after excluding cases with missing confounder data. We performed propensity score matching and provide patient characteristics in the propensity-matched cohort in online supplemental eTable 9. We further provide data on postoperative major adverse events within 30 days, indicating potential causes of death (online supplemental file 1, section 4). In addition, we tested whether the association between night surgery and mortality was modified by a recent diagnosis of cancer by including an interaction term between night surgery and 1 year diagnosis of cancer (online supplemental file 1, section 6.2). We tested for potential effect modification of the association between night surgery and mortality by case delays (ie, difference between scheduled and actual start time in minutes) by including an interaction term between night surgery and case delay. We also investigated the mediating effect of case delays on the association between night surgery and mortality (online supplemental file 1, section 5.2). Finally, we conducted several subgroup analyses to ensure that the impact of night surgery on mortality was not driven by a narrow patient population. Details on all sensitivity analyses are described in section 6 of online supplemental file 1.

Sample size justification

Assuming a two-sided alpha level of 0.05, an observed proportion of night surgeries of 8.0% in the primary cohort, a baseline mortality risk of 0.6%[16] and a clinically significant risk increase of 30% in the group of patients who underwent night surgery, the sample size of this study provided a power of 94.0% to detect a difference between patients undergoing surgery during the night versus day.

Statistical analyses

Confounding variables demonstrating linear associations with the primary outcome were included as continuous, whereas variables with non-linear associations were categorised into quintiles (online supplemental file 1, section 2). A two-sided $p<0.05$ was considered statistically significant. Analyses were performed using Stata (Stata, V.13) and RStudio (RStudio, V.3.2.5).

Patient and public involvement

No patients or the public were involved in the design or conduct of this study. Patients or the public were not invited to contribute to the writing or editing of this document for readability or accuracy.

RESULTS

Study cohort

In this study, 377 163 cases were considered for inclusion. After application of exclusion criteria and imputation of missing data, the final cohort for the primary analysis consisted of 350 235 cases (figure 1). A total of 322 327 (92.0%) patients underwent day surgery (07:00 to 17:00 hours) and 27 908 (8.0%) underwent night surgery (17:01 to 06:59 hours). In the complete-case cohort, 303 892 cases remained after excluding cases with missing data. Patient characteristics and distribution of variables by study groups are detailed in table 1 and online supplemental eTables 3–5.

Primary analysis

30-day mortality

In total, 3744 (1.5%) patients died within 30 days after surgery, 2804 (0.9%) after day surgery and 940 (3.4%) after night surgery. Night surgery was associated with increased mortality within 30 days of surgery in unadjusted (OR 2.45, 95% CI 2.26 to 2.65, $p<0.001$) as well as adjusted analyses (adjusted OR (OR_{adj}) 1.26, 95% CI 1.15 to 1.38, $p<0.001$; table 2).

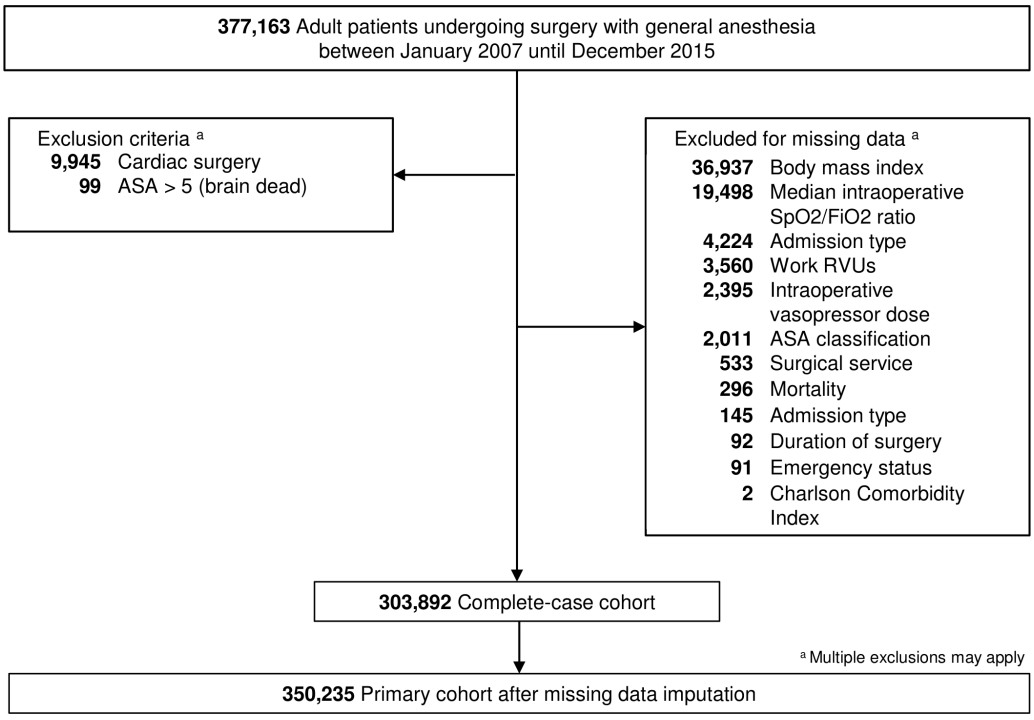


Figure 1 Study flowchart. ASA, American Society of Anesthesiologist's Physical Status Classification System; RVU, relative value unit.

Secondary analyses

30-day morbidity

In total, 2234 (0.7%) patients had complications within 30 days after surgery, 1769 (0.6%) after day surgery and 465 (2.3%) after night surgery. We found a significant association between night surgery and morbidity (OR_{adj} 1.41, 95% CI 1.33 to 1.48, p<0.001; table 2).

Transfusion rate

The proportion of patients receiving intraoperative blood transfusions was 5.5% (n=1149) during night surgeries and 2.8% (n=7882) during day surgeries. Night surgery was significantly associated with a higher transfusion rate in adjusted analysis (OR_{adj} 1.25, 95% CI 1.15 to 1.35, p<0.001). The effect remained robust in a subgroup of cases where data on intraoperative estimated blood loss and preoperative haemoglobin levels were available, after additional adjustment for blood loss, mild anaemia, and moderate to severe anaemia within 30 days prior to surgery (OR_{adj} 1.17, 95% CI 1.04 to 1.31, p=0.009; n=1 31 371), as well as when additionally accounting for a potential variability in transfusion practice across individual anaesthesia providers (OR_{adj} 1.19, 95% CI 1.10 to 1.30, p=0.005; n=1 28 691) and across individual surgeons (OR_{adj} 1.35, 95% CI 1.21 to 1.51, p<0.001, n=1 62 907; online supplemental file 1, section 5).

Higher transfusion rate was significantly associated with an increased risk of 30-day mortality (OR_{adj} 1.72, 95% CI 1.50 to 1.98, p<0.001) and morbidity (OR_{adj} 1.68, 95% CI 1.59 to 1.78, p<0.001). Higher transfusion rates during night surgery mediated 5.9% (95% CI 2.4% to 9.3%; p=0.001) of the effect of night surgery on mortality, and 4.9% (95% CI 3.8% to 6.1%; p<0.001) of its effect on morbidity (table 3 and figure 2).

Handover of anaesthesia care

Anaesthesia handovers occurred in 22.6% (n=4686) of night surgeries and 8.8% (n=24 949) of day surgeries. Night surgery was significantly associated with a higher proportion of handovers in adjusted analysis (OR_{adj} 4.12, 95% CI 3.94 to 4.30, p<0.001). Anaesthesia handovers were significantly associated with an increased risk of morbidity (OR_{adj} 1.10, 95% CI 1.05 to 1.14, p<0.001) and mediated 4.1% (95% CI 2.3% to 5.9%, p<0.001) of the effect of night surgery on morbidity in formal mediation analysis (table 3).

There were no interaction effects between the two mediators on 30-day mortality (p-for-interaction: 0.395) and morbidity (p-for-interaction: 0.125). When combining both mediators into one mediation model, higher transfusion rates together with more handovers during night-time mediated 9.4% (95% CI 2.4% to 16.4%, p<0.001) of the effect of night surgery on 30-day mortality and 8.4% (95% CI 6.3% to 10.4%, p<0.001) of its effect on morbidity (table 3 and figure 2).

Exploratory analyses

Ambulatory and same-day surgery versus inpatient surgery

The effect of night surgery was modified by the surgical care setting (p-for-interaction<0.001) towards a greater effect among patients who underwent ambulatory or same-day surgery (OR_{adj} 1.81, 95% CI 1.39

Table 1 Characteristics and distribution of variables by day versus night surgery in primary cohort

Patient characteristics	Day surgery (n=3 22 327)	Night surgery (n=27 908)	Standardised difference
Sex, male, n (%)	141 869 (44.0%)	14 213 (49.0%)	0.139
Age (years), mean±SD	54.08±16.47	52.77±18.77	0.074
BMI (kg/m^2), mean±SD*	28.35±6.85	27.79±6.91	0.081
ASA status, median (IQR)*	2 (2 to 3)	2 (2 to 3)	−0.241
ASA ≥3, n (%)*	108 366 (33.8%)	113 029 (46.9%)	−0.269
Admission type, n (%)*			−0.703
Ambulatory	119 881 (37.6%)	3536 (12.9%)	
Same day admission	143 328 (45.0%)	12 407 (45.3%)	
Inpatient	55 680 (17.4%)	11 469 (41.8%)	
Institution			0.146
A	186 593 (57.9%)	18 127 (64.9%)	
B	135 734 (42.1%)	9781 (35.1%)	
Intraoperative data			
Duration of surgery (min), median (IQR)*	132.00 (85.00 to 205.00)	113.00 (80.00 to 165.00)	0.234
Handover of anaesthesia care, n (%)	28 827 (8.9%)	6093 (21.8%)	−0.363
Emergency surgery, n (%)*	9464 (2.9%)	10 868 (39.0%)	−0.987
Work RVUs, median (IQR)*	12.75 (7.03 to 19.61)	10.93 (7.07 to 17.80)	0.159
Packed red blood cell units transfused intraoperatively, n (%)			−0.191
0 units	311 914 (96.8%)	25 785 (92.4%)	
1 unit	4475 (1.4%)	819 (2.9%)	
2 units	3745 (1.2%)	666 (2.4%)	
≥3 units	2193 (0.7%)	638 (2.3%)	
Intraoperative hypotensive minutes of MAP <55 mm Hg, median (IQR)	0.00 (0.00 to 2.00)	0.00 (0.00 to 3.00)	−0.036
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.01 (0.00 to 0.10)	0.01 (0.00 to 0.12)	−0.016
Median SpO_2/FiO_2 ratio, median (IQR) *	184.21 (161.29 to 222.27)	178.57 (147.06 to 206.25)	0.190

Frequency distributions of patient comorbidities and surgical services by day versus night surgery are provided in the online supplemental eTables 3 and 4. Characteristics and distribution of variables by day versus night surgery for the complete-case cohort are provided in the online supplemental eTable 5. Normally distributed continuous variables were expressed as mean (±SD), non-normally distributed variables as median (IQR), and categorical variables as frequency (percentages).

*Variables with missing data; Characteristics and distribution of variables by day versus night surgery are presented for cases with observed data.

ASA, American Society of Anesthesiologist's Physical Status Classification System; BMI, body mass index; CCI, Charlson Comorbidity Index; MAP, mean arterial pressure; RVUs, relative value units.

to 2.35, p<0.001) compared with inpatient surgery (OR_{adj} 1.17, 95% CI 1.02 to 1.34, p=0.026; table 4).

Non-emergency surgery

Among 282 526 patients undergoing non-emergency surgery, night surgery was associated with 1.35-fold higher adjusted odds for 30-day mortality compared with day surgery, respectively (95% CI 1.16 to 1.56, p<0.001; table 4). Analysis of this subgroup demonstrated robust results when including an interaction term by the surgical care setting (p-for-interaction=0.001; ambulatory/same-day surgery: OR_{adj} 2.22, 95% CI 1.60 to 3.07, p<0.001; inpatient surgery: OR_{adj} 1.20, 95% CI 1.01 to 1.43, p=0.036) (table 4).

Emergency surgery

Characteristics of emergency cases by night versus day surgery are provided in online supplemental eTable 8. Of 13 566 emergency surgeries, 52.8% (n=7162) were performed at night and 47.2% (n=6404) were performed during the day. Distributions of emergency and non-emergency cases throughout the day are shown in online supplemental eFigure 1. Risks of adverse outcomes were similar between emergency surgeries performed during the night versus day (mortality: OR_{adj} 1.13, 95% CI 0.91 to 1.40, p=0.27; morbidity: OR_{adj} 1.04, 95% CI 0.94 to 1.16, p=0.427).

Sensitivity analyses

Propensity score matching and mixed-effects logistic regression analysis in the complete-case cohort confirmed our primary finding (OR_{adj} 1.21, 95% CI 1.06 to 1.39, p=0.005, n=41 414; OR_{adj} 1.34, 95% CI 1.18 to 1.52, n=2 89 480 cases with provider data available). The case delay time was longer in patients who underwent night surgery compared with day surgery (78 (SD 150) vs 17 (SD 50) min,

Table 2 Results of 30-day mortality (primary outcome) and 30-day morbidity (secondary outcome) associated with night surgery

			Unadjusted analysis			Adjusted analysis		
Primary outcome	**Day surgery (n=322 327)**	**Night surgery (n=27 908)**	**Absolute difference (95% CI)***	**OR (95% CI)**	**P value**	**Adjusted absolute difference (95% CI)†**	**OR_{adj} (95% CI)**	**P value**
30 day mortality	2804 (0.9%)	940 (3.4%)	–	2.45 (2.26 to 2.65)	<0.001	–	1.26 (1.15 to 1.38)	<0.001
			Unadjusted analysis			**Adjusted analysis**		
Secondary outcome	**Day surgery (n=283 185)**	**Night surgery (n=20 707)**	**Absolute difference (95% CI)***	**OR (95% CI)**	**P value**	**Adjusted absolute difference (95% CI)†**	**OR_{adj} (95% CI)**	**P value**
30-day morbidity	22 919 (8.1%)	2723 (13.2%)	5.1% (4.6% to 5.5%)	1.72 (1.65 to 1.79)	<0.001	2.1% (1.7% to 2.4%)	1.41 (1.33 to 1.48)	<0.001
Cardiovascular	6875 (2.4%)	599 (2.9%)	0.5% (0.2 to 0.7)	1.2 (1.10 to 1.30)	<0.001	0.2% (0.0% to 0.3%)	1.14 (1.03 to 1.27)	0.011
Pulmonary	1533 (0.5%)	203 (1.0%)	0.4% (0.3% to 0.6%)	1.82 (1.57 to 2.11)	<0.001	0.1% (0.1% to 0.2%)	1.46 (1.22 to 1.74)	<0.001
Renal	2565 (0.9%)	409 (2.0%)	1.1% (0.9% to 1.3%)	2.20 (1.98 to 2.45)	<0.001	0.2% (0.1% to 0.3%)	1.42 (1.25 to 1.61)	<0.001
Intestinal/ Digestive	1712 (0.6%)	113 (0.5%)	0.1% (0.2% to 0.1%)	0.90 (0.75 to 1.09)	0.29	0.0% (0.0% to 0.0%)	0.79 (0.62 to 1.0)	0.051
Haemorrhage	9342 (3.3%)	1232 (5.9%)	2.7% (2.3% to 3.5%)	1.85 (1.74 to 1.97)	<0.001	1.2% (0.9 to 1.45)	1.50 (1.39 to 1.62)	<0.001
Infections	6454 (2.3%)	1032 (5.0%)	2.7% (2.4% to 3.0%)	2.25 (2.10 to 2.41)	<0.001	0.9% (0.7% to 1.1%)	1.59 (1.46 to 1.72)	<0.001

Data are expressed as frequency (prevalence in %). Statistical analyses were performed using multivariable logistic regression. OR, absolute differences and adjusted absolute differences are reported.
*Absolute difference indicates the difference in risk between compared groups, as estimated following unadjusted regression analysis.
†Adjusted absolute difference indicates the difference in risk attributable to use of night surgery, as estimated following adjusted regression analysis.

p<0.001). The interaction term between night surgery and case delay in minutes was marginally significant (p=0.055), and the association between night surgery and mortality remained significant in this analysis (OR_{adj} 1.26, 95% CI 1.06 to 1.50, p=0.009, n=1 59 591). Case delay did not mediate the effect of night surgery on mortality. Details of sensitivity analyses are provided in the online supplemental file 1.

DISCUSSION

In this large multicentre study of non-cardiac surgical patients, we made the following observations: first, risks of postoperative mortality and morbidity at 30 days were higher among patients who underwent night surgery compared with day surgery. Second, a higher blood transfusion rate and more frequent anaesthesia handovers during night-time partly mediated

Table 3 Adjusted ORs with 95% CIs and p values obtained from path mediation analysis of intraoperative blood transfusion rates and handovers of anaesthesia care as potential mediators in the association between night surgery and 30-day mortality and morbidity

Mediator	**Direct effect* (95% CI)**	**Indirect effect† (95% CI)**	**Total effect‡ (95% CI)**	**Mediated in %§ (95% CI)**
Primary outcome: 30-day mortality				
Transfusion rate	1.36 (1.21 to 1.54) P<0.001	1.02 (1.01 to 1.03) P<0.001	1.39 (1.23 to 1.57) P<0.001	5.9% (2.4% to 9.3%) P=0.001
Handover	1.36 (1.21 to 1.54) P<0.001	1.01 (0.99 to 1.03) P=0.175	1.39 (1.23 to 1.56) P<0.001	4.2% (-2.5% to 11.0%) P=0.217
Both mediators combined	1.36 (1.20 to 1.55) P<0.001	1.03 (1.01 to 1.05) P=0.006	1.41 (1.24 to 1.60) P=0.002	9.4% (2.4% to 16.4%) P=0.008
Secondary outcome: 30-day morbidity				
Transfusion rate	1.41 (1.33 to 1.48) P<0.001	1.02 (1.01 to 1.02) P<0.001	1.43 (1.36 to 1.51) P<0.001	4.9% (3.8% to 6.1%) P<0.001
Handover	1.41 (1.34 to 1.49) P<0.001	1.01 (1.01 to 1.02) P<0.001	1.43 (1.36 to 1.51) P<0.001	4.1% (2.3% to 5.9%) P<0.001
Both mediators combined	1.41 (1.34 to 1.48) P<0.001	1.03 (1.02 to 1.04) P<0.001	1.45 (1.38 to 1.53) P<0.001	8.4% (6.3 to 10.4%) P<0.001

Results were justified using bootstrapping analysis with 1000 samples.[13 14]
*Direct effect comparing odds for mortality/morbidity if everyone had undergone night surgery versus odds for mortality/morbidity if everyone had undergone day surgery, thereby fixing rates of blood transfusion/handovers to the value they would have had during day surgery.
†Indirect effect assuming that every patient underwent night surgery. We compare odds for mortality/morbidity when rates of blood transfusion/handovers change from the value during night surgery to the one during day surgery.
‡Total effect comparing odds for mortality/morbidity if everyone had undergone night surgery versus odds for mortality/morbidity if everyone had undergone day surgery.
§Percentage mediation by blood transfusion/handovers was calculated using the following form: (ln (indirect effect)/ln (total effect)) × 100.

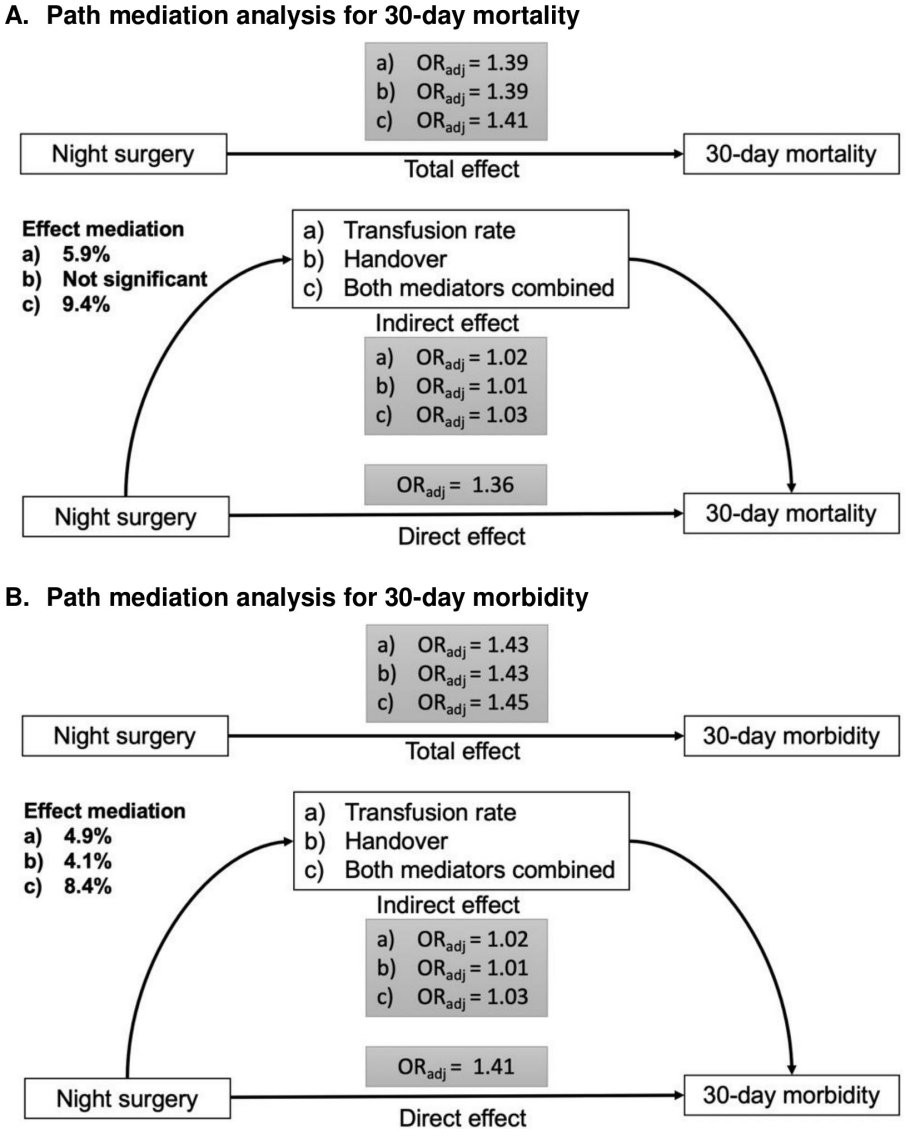


Figure 2 Path mediation analyses for 30-day mortality and morbidity. Mediation effects of (a) intraoperative blood transfusion rates, (b) handovers of anaesthesia care as well as (c) a combination of both mediators on the association between night surgery and 30-day mortality (A) and morbidity (B) are shown. Transfusion rates mediated 5.9% and 4.9% of the effect of night surgery on 30-day mortality and morbidity, respectively. Handovers mediated 4.1% of the effect of night surgery on 30-day morbidity. Combination of handovers and transfusion rates mediated 9.4% and 8.4% of the effect of night surgery on 30-day mortality and morbidity, respectively. Adjusted ORs are shown for total, indirect and direct effect.

Table 4 Results of 30-day mortality across exploratory analyses

Analysis	N	OR$_{adj}$ (95% CI)	P value
Interaction analysis			
Surgical setting			P-for-interaction<0.001
Ambulatory/same-day surgery	253 523	1.81 (1.39 to 2.35)	<0.001
Inpatient surgery	50 369	1.17 (1.02 to 1.34)	=0.026
Subgroup analyses			
Non-emergency surgery	282 526	1.35 (1.16 to 1.56)	<0.001
Interaction analysis by surgical setting:			P-for-interaction=0.001
Ambulatory/same-day surgery	242 247	2.22 (1.60 to 3.07)	<0.001
Inpatient surgery	40 279	1.20 (1.01 to 1.43)	=0.036
Emergency surgery	13 566	1.13 (0.91 to 1.40)	0.27

Statistical analyses were performed using multivariable logistic regression. Interaction terms were included in the primary model to test for effect modification. Subgroup analyses were performed across levels of the interaction term. Adjusted ORs (OR$_{adj}$) are reported.

the effect of night surgery. The adverse effects of night surgery were modified by admission status and acuity level: magnified adverse effects were observed in patients who underwent ambulatory or same-day surgery while the effect was not significant in patients undergoing emergency surgery. These findings suggest that the increased risk of mortality and morbidity after night surgery was not driven by a higher case acuity, but could be attributed to differences in the surgical management of patients operated during night-time.

Relation to other studies

Previous studies reported inconclusive results on the effect of operation time on postoperative outcome. More complications after surgery at night were previously described in smaller studies among patients undergoing orthopaedic,[17] neurosurgery,[18] and plastic surgery,[19] laparoscopic cholecystectomy,[20] coronary interventions[21] and general and vascular surgery.[4 22] In the latter study,[22] higher mortality was only detected for patients undergoing elective surgery, a finding which we confirm with our study, and was also reported in other studies with negative results in patients who underwent emergency surgery.[23 24]

Other studies did not identify harmful effects of night surgery. A single-centre investigation in Germany including non-emergency cases across surgical fields suggested an increased in-hospital mortality only when the surgery was conducted during the early afternoon (13:00 to 17:00 hours).[3] In a study that used National Surgical Quality Improvement Program data, night-time surgery in patients undergoing elective surgery was not associated with postoperative morbidity and mortality.[4]

Finally, a recent meta-analysis summarised 40 observational studies on the association between night surgery and mortality. The largest study included in this meta-analysis used the National Anesthesia Clinical Outcomes Registry to analyse three patient (age, sex, ASA status) and procedure-related (emergency, surgery type, operation time between 16:00 to 06:59 hours) factors associated with 48-hour mortality after surgery.[2] Our study adds the important information that the association between night surgery and increased mortality is robust even when adjusting for important confounders such as case delays and intraoperative risk factors. In addition, we present potentially preventable mediators of the increased risk of mortality and morbidity observed in patients undergoing night surgery: frequent anaesthesia provider handovers and higher rates of intraoperative blood transfusion.

Meaning of this study

We present a hypothesis driven study from two major tertiary care hospital networks. In our cohort, patients who underwent night surgery were more often hospitalised and underwent more emergency procedures than those undergoing day surgery. The effect of night surgery on mortality was more pronounced in ambulatory and same-day admitted cases compared with inpatients. This novel observation supports the hypothesis that night surgery itself was associated with adverse outcomes and that its effect was not driven by a higher case acuity or a more severe condition of patients undergoing night surgery. This further suggests that patients who were just admitted to the hospital and who may not have received the appropriate preoperative workup may represent a risk group where it would be clinically meaningful to avoid night surgery. Among emergency patients, we did not find a difference in mortality between day and night cases. The effect of night surgery on adverse outcome may be weaker in emergency patients because other factors such as severity of the condition may be more important, while the emergency surgery has to be performed immediately regardless of the time of day or night.

The novelty of this study relates to the identification of preventable mediators of the adverse effects of night surgery. Mediation analysis is a tool for providing explanation of an observed association within observational studies.[25–27] We identified that the risk of receiving intraoperative blood transfusion was higher among patients undergoing night surgery. The effect was robust when accounting for preoperative anaemia, intraoperative blood loss and an individual provider-related variability in transfusion practice. Mediation analysis revealed that the higher transfusion rate observed during night-time explained 5.9% of the increased mortality and 4.9% of the increased complication risk after night surgery. We speculate that higher transfusion rates independent of patient and procedural risk factors may indicate an early and more liberal treatment of conditions that may occur within the postoperative period, such as a decrease in haemoglobin levels, thereby aiming to prevent the need for further therapy during night-time. Multiple studies have shown that a restrictive rather than liberal transfusion strategy with respect to WHO recommended transfusion thresholds and clinical symptoms of anaemia (transfusion triggers) is associated with improved outcomes after surgery.[28–33] Various interventions have been recommended to reduce transfusion rates, such as enhancing a patient's physiological tolerance of anaemia by optimising oxygenation, decreasing oxygen consumption and ensuring normovolaemia.[34 35]

We observed that handovers from one anaesthesia provider to another occurred 2.5 times more often during night surgeries compared with surgeries during day-time. In a recent study published in JAMA, anaesthesia handovers have been identified as a risk factor of increased postoperative mortality and major complications.[11] We were able to confirm in our mediation analysis that the higher proportion of handovers contributed to an increased complication risk

after night surgery. This may be explained by the fact that during night-time, circulating teams of surgeons, anaesthesia providers and nurses are stretched and less specialised than day teams. It has been shown that liver and thoracic organ transplants do not have adverse outcomes following night surgery which may be due to the typically permanent and highly specialised composition of transplant teams.[36–38] Based on our findings, we speculate that low acuity cases such as ambulatory surgeries are particularly prone to errors due to reduced attention and improper communication within changing teams. For the high acuity patients, there may be a higher level of communication and rechecking that prevents failures.

We also observed significantly longer case delays among patients who underwent night surgery, which could be related to a longer fasting period in patients undergoing surgery at night-time. Fasting prior to surgery leads to a catabolic metabolism that affects a patient's stress response to surgery and postoperative insulin resistance and increases patient discomfort,[39 40] which might add to the negative effects of night surgery on postoperative outcome. Implementation of case-specific fasting guidelines may help decrease the harmful effects of long fasting periods on postoperative outcomes.

Implications for clinicians and policymakers

The observed higher proportion of blood transfusions and handovers may reflect differences in the surgical management of patients operated during night-time. Different behaviour patterns of providers during night-time may in some cases rather promote self-interest than patient-centred and individualised care. The observed key factors contributing to a higher risk of night surgery should be modified and adapted to practice patterns during the day to improve outcomes after night surgery.

In our study, almost 60% of cases performed at night were non-emergency procedures. Of those, 60% were ambulatory or same-day surgeries, which carried the highest risk of mortality attributable to night surgery. In these cases, postponing a surgical procedure should be considered to allow time for both the patient and provider to prepare for surgery. In a recent study, efforts to implement standardised protocols for patient urgency classification and operating room booking aimed at a more selective out-of-hours use of operation rooms for emergency services.[41] First results demonstrated higher operating room efficiency during standard hours (increased case time during the day), while operation time at night decreased by 26%.[41] Adapted to the local conditions, further hospitals should evaluate the implementation of standardised scheduling tools for non-emergency patients. In addition, if night surgery has to be conducted, we suggest that blood transfusion protocols should be rigorously implemented, and handovers be minimised.

There are several limitations to our study. Patients who underwent night surgery were more often inpatients and emergency cases and may be generally sicker than patients undergoing surgery during standard hours. To address confounding related to these differences, we used an interaction analysis which demonstrated a greater effect of night surgery on mortality among patients undergoing ambulatory/same-day surgery compared with inpatients, while no association between night surgery and mortality was found in a subgroup of emergency patients. We used several sensitivity analyses such as propensity score matching and repeating the primary analysis in the complete-case cohort, and the similar results were confirmatory. In addition, path mediation models have been described as a more complex form of multiple regression models, which still cannot establish causality of an effect (as compared with experimental studies) but can be used to determine whether hypotheses from observational data are plausible.[25 42] However, potential unmeasured confounders may have affected results of this observational study.

Conclusion

We demonstrate that surgery at night was associated with an increased risk of mortality and morbidity in a large multicentre cohort. Patients who underwent ambulatory or same-day surgery were particularly vulnerable to the adverse effect of night surgery. Higher exposures to blood transfusions and anaesthesia handovers during night-time partly explained the increased complication risk. Based on our findings, the risk of night surgery did not appear to be driven by a higher case acuity but could partly be attributed to a different surgical management of patients operated during night-time.

Contributors Study concept and design: FCA, PR, PS, SDG, MSS, XX, HC, OA, GAB, TTH, ME. Acquisition, analysis or interpretation of data: All authors. Drafting of the manuscript: FCA, PR, LJW, ME. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: XX, TTH, FCA, PR, LJW, PS, GAB, MSS, ME. Obtained funding: ME. Administrative, technical or material support: All authors. Study supervision: XX, TTH, GAB, ME. All authors had full access to the data in the study and can take responsibility for the integrity of the data and the accuracy of analyses.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests ME has received unrestricted funds from philanthropic donors Jeffrey and Judith Buzen during the study period and has received grants for investigator-initiated trials not related to this manuscript from Merck & Co and serves as a consultant on the advisory board of Merck & Co. ME holds equity of Calabash Bioscience Inc. and is an Associate Editor of the British Journal of Anaesthesia.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Due to the sensitive nature of the data collected

for this study, requests to access the dataset from qualified researchers trained in human subjects research and confidentiality may be sent to Matthias Eikermann at meikerma@bidmc.harvard.edu.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Luca J Wachtendorf http://orcid.org/0000-0002-9966-2092
Peter Santer http://orcid.org/0000-0002-1735-0774
Matthias Eikermann http://orcid.org/0000-0002-7893-0596

REFERENCES

1 Cortegiani A, Gregoretti C, Neto AS, *et al*. Association between night-time surgery and occurrence of intraoperative adverse events and postoperative pulmonary complications. *Br J Anaesth* 2019;122:361–9.
2 Whitlock EL, Feiner JR, Chen L-L. Perioperative mortality, 2010 to 2014: a retrospective cohort study using the National anesthesia clinical outcomes registry. *Anesthesiology* 2015;123:1312–21.
3 Kork F, Spies C, Conrad T, *et al*. Associations of postoperative mortality with the time of day, week and year. *Anaesthesia* 2018;73:711–8.
4 Kelz RR, Freeman KM, Hosokawa PW, *et al*. Time of day is associated with postoperative morbidity: an analysis of the National surgical quality improvement program data. *Ann Surg* 2008;247:544–52.
5 Anderson C, Sullivan JP, Flynn-Evans EE, *et al*. Deterioration of neurobehavioral performance in resident physicians during repeated exposure to extended duration work shifts. *Sleep* 2012;35:1137–46.
6 Barger LK, Ayas NT, Cade BE, *et al*. Impact of extended-duration shifts on medical errors, adverse events, and attentional failures. *PLoS Med* 2006;3:e487.
7 Landrigan CP, Rothschild JM, Cronin JW, *et al*. Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med* 2004;351:1838–48.
8 Gold DR, Rogacz S, Bock N, *et al*. Rotating shift work, sleep, and accidents related to sleepiness in hospital nurses. *Am J Public Health* 1992;82:1011–4.
9 Howard SK, Rosekind MR, Katz JD, *et al*. Fatigue in anesthesia: implications and strategies for patient and provider safety. *Anesthesiology* 2002;97:1281–94.
10 von Elm E, Altman DG, Egger M, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453–7.
11 Jones PM, Cherry RA, Allen BN, *et al*. Association between handover of anesthesia care and adverse postoperative outcomes among patients undergoing major surgery. *JAMA* 2018;319:143–53.
12 Chan DXH, Sim YE, Chan YH, *et al*. Development of the combined assessment of risk encountered in surgery (cares) surgical risk calculator for prediction of postsurgical mortality and need for intensive care unit admission risk: a single-center retrospective study. *BMJ Open* 2018;8:e019427.
13 Buis ML. Direct and indirect effects in a logit model. *Stata J* 2010;10:11–29.
14 Grotta A, Bellocco R. A review of mediation analysis in Stata: principles, methods and applications 2013. Available: https://www.stata.com/meeting/italy13/abstracts/materials/it13_grotta.pdf
15 Hadland SE, Rivera-Aguirre A, Marshall BDL, *et al*. Association of pharmaceutical industry marketing of opioid products with mortality from Opioid-Related overdoses. *JAMA Netw Open* 2019;2:e186007–e07.
16 Ng PY, Ng AK-Y, Subramaniam B, *et al*. Association of preoperatively diagnosed patent foramen ovale with perioperative ischemic stroke. *JAMA* 2018;319:452–62.
17 Ricci WM, Gallagher B, Brandt A, *et al*. Is after-hours orthopaedic surgery associated with adverse outcomes? A prospective comparative study. *J Bone Joint Surg Am* 2009;91:2067–72.
18 Linzey JR, Burke JF, Sabbagh MA, *et al*. The effect of surgical start time on complications associated with neurological surgeries. *Neurosurgery* 2018;83:501–7.
19 Lee K-T, Mun G-H. Is after-hours free-flap surgery associated with adverse outcomes? *J Plast Reconstr Aesthet Surg* 2013;66:460–6.
20 Phatak UR, Chan WM, Lew DF, *et al*. Is nighttime the right time? risk of complications after laparoscopic cholecystectomy at night. *J Am Coll Surg* 2014;219:718–24.
21 Glaser R, Naidu SS, Selzer F, *et al*. Factors associated with poorer prognosis for patients undergoing primary percutaneous coronary intervention during off-hours: biology or systems failure? *JACC Cardiovasc Interv* 2008;1:681–8.
22 Kelz RR, Tran TT, Hosokawa P, *et al*. Time-of-day effects on surgical outcomes in the private sector: a retrospective cohort study. *J Am Coll Surg* 2009;209:434–45.
23 van Zaane B, van Klei WA, Buhre WF, *et al*. Nonelective surgery at night and in-hospital mortality: prospective observational data from the European surgical outcomes study. *Eur J Anaesthesiol* 2015;32:477–85.
24 Zafar SN, Libuit L, Hashmi ZG, *et al*. The sleepy surgeon: does night-time surgery for trauma affect mortality outcomes? *Am J Surg* 2015;209:633–9.
25 Rudolph KE, Goin DE, Paksarian D, *et al*. Causal mediation analysis with observational data: considerations and illustration examining mechanisms linking neighborhood poverty to adolescent substance use. *Am J Epidemiol* 2019;188:598–608.
26 Camacho-Soto A, Warden MN, Searles Nielsen S, *et al*. Traumatic brain injury in the prodromal period of Parkinson's disease: a large epidemiological study using Medicare data. *Ann Neurol* 2017;82:744–54.
27 Atlantis E, Shi Z, Penninx BJWH, *et al*. Chronic medical conditions mediate the association between depression and cardiovascular disease mortality. *Soc Psychiatry Psychiatr Epidemiol* 2012;47:615–25.
28 Hébert PC, Wells G, Blajchman MA, *et al*. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. transfusion requirements in critical care Investigators, Canadian critical care Trials Group. *N Engl J Med* 1999;340:409–17.
29 Hajjar LA, Vincent J-L, Galas FRBG, *et al*. Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. *JAMA* 2010;304:1559–67.

30 Carson JL, Terrin ML, Noveck H, *et al*. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011;365:2453–62.
31 Althoff FC, Neb H, Herrmann E, *et al*. Multimodal patient blood management program based on a Three-pillar strategy: a systematic review and meta-analysis. *Ann Surg* 2019;269:794–804.
32 WH A. Availability, safety and quality of blood products, 2010. Available: http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R12-en.pdf
33 Farmer SL, Towler SC, Leahy MF, *et al*. Drivers for change: Western Australia patient blood management program (WA PBMP), world health assembly (WHA) and Advisory Committee on blood safety and availability (ACBSA). *Best Pract Res Clin Anaesthesiol* 2013;27:43–58.
34 Meybohm P, Richards T, Isbister J, *et al*. Patient blood management bundles to facilitate implementation. *Transfus Med Rev* 2017;31:62–71.
35 Leahy MF, Roberts H, Mukhtar SA, *et al*. A pragmatic approach to embedding patient blood management in a tertiary hospital. *Transfusion* 2014;54:1133–45.
36 Thuluvath PJ, Amjad W, Savva Y, *et al*. Survival outcomes are not affected when liver transplant surgery is done at night, during weekends, or summer months. *Transplant Direct* 2019;5:e449.
37 Halliday N, Martin K, Collett D, *et al*. Is liver transplantation 'out-of-hours' non-inferior to 'in-hours' transplantation? A retrospective analysis of the UK Transplant Registry. *BMJ Open* 2019;9:e024917.
38 George TJ, Arnaoutakis GJ, Merlo CA, *et al*. Association of operative time of day with outcomes after thoracic organ transplant. *JAMA* 2011;305:2193–9.
39 Gustafsson UO, Scott MJ, Schwenk W, *et al*. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. *World J Surg* 2013;37:259–84.
40 Longchamp A, Harputlugil E, Corpataux J-M, *et al*. Is overnight fasting before surgery too much or not enough? how basic aging research can guide preoperative nutritional recommendations to improve surgical outcomes: a mini-review. *Gerontology* 2017;63:228–37.
41 Sandbaek BE, Helgheim BI, Larsen OI, *et al*. Impact of changed management policies on operating room efficiency. *BMC Health Serv Res* 2014;14:224–24.
42 Streiner DL. Finding our way: an introduction to path analysis. *Can J Psychiatry* 2005;50:115–22.

Effects of Night Surgery on Postoperative Mortality and Morbidity

A Multicentre Cohort Study

Supplement 1

1 Data sources

Several data management systems were used to compile the final database: Perioperative data (anaesthesia record data, monitored patient parameters) were retrieved from the Anaesthesia Information Management System (AIMS). Clinical variables (electronic health record data including International Classification of Diseases 9thand 10th revision [ICD-9/10] diagnostic codes) were obtained through the Research Patient Data Registry (RPDR). The financial tracking database, Enterprise Performance Systems Inc. (EPSi), was used to obtain information regarding hospital admission and discharge. Demographics and discharge disposition data were available in a Research Patient Data Registry (RPDR) and Enterprise Performance Systems Inc. (EPSi) and allowed extraction of mortality data.

The Anaesthesia Information Management System (AIMS) as well as the Perioperative Information Management System (PIMS) were utilised for patient data. Anaesthesia-related data were collected from AIMS and surgical data, such as the surgical specialty and duration of the procedure were provided by PIMS. Current Procedural Terminology (CPT) codes to define work relative value units were obtained from the Center for Clinical Computing (CCC) anaesthesia billing database.

International Classification of Diseases (ICD) codes regarding comorbidities and encounter dates were collected from the Admission Discharge Transfer (ADT) and Casemix databases. Data on mortality were retrieved from the Miscellaneous (MISC) database. Data were de-identified and subsequently combined across institutions.

2 Categorisation of confounding variables

Confounding variables of the primary model were included according to the linearity assumption. Variables demonstrating non-linear associations with the primary outcome were categorised into quintiles (age, duration of surgery, work relative value units, date of surgery, vasopressor equivalent dose, and SpO_2/FiO_2-ratio) or clinically relevant groups (BMI, ASA

status, Charlson Comorbidity Index, intraoperative hypotension (defined as mean arterial pressure < 55 mmHg), and packed red blood cell (PRBC) units transfused.

3 Multiple Imputation

For the primary analysis, we imputed missing data by utilising multiple imputation. We conducted five imputations of five iterations each. The variable with the highest number of missing values prior to imputation was BMI (36,937 missing values), followed by SpO2/FiO2 ratio (19,498 missing values), and admission type (4,224 missing values). The variables anaesthesia and surgical provider which were included into the multivariable-adjusted mixed effects model were not imputed. Cases with missing data for the random effects were excluded before imputation.

4 Potential causes of 30-day mortality

We additionally analysed the following postoperative complication data that have been validated by our team in previous studies. Details on the definition of complications are provided below. We made comparisons between patients undergoing day versus night surgery: Acute kidney injury (AKI), major adverse cardiac events (MACE), stroke after surgery, and reintubation. There were significantly increased risks of AKI, MACE, acute heart failure, and reintubation among patients who underwent night surgery (eTable 10.a).

We then assessed whether these major postoperative adverse events associated with night surgery occurred more often among patients who died within 30 days after surgery (eTable 10.b). Particularly acute kidney failure (24.3% vs. 3.4%), major adverse cardiac events (13.1% vs 1.9%), and reintubation (16.9% vs. 0.6%) occurred much more frequently in patients who died within 30 days, and occurred more frequently after night surgeries. Both renal and cardiac complications have also been shown to be associated with higher transfusion rates,[1-4] as well as higher frequency of anaesthesia handovers.[5] Information on the data sources and variable creation of the postoperative complication data is given below.

4.1 Postoperative acute kidney injury

Institution A

Postoperative AKI was identified according to the following protocol: the most recent creatinine lab values prior to surgery, within a 30-day window, and creatinine values within 48 hours after surgery were extracted and the differences between creatinine values were calculated. Patients with an increase of 0.3 mg/dl or 50% or more from baseline in the first 48 hours after surgery were considered to AKI, according to the Kidney Disease Improving Global Outcomes (KDIGO) Guidelines.[6 7] Cases without creatinine values but with an ICD-9 diagnostic code of AKI (eTable 16) within seven days of surgery, but not thirty days prior, were also considered to have this outcome. Finally, cases without data on serum creatinine or AKI administrative codes following surgery were considered free of this outcome on the premise that there was no clinically meaningful concern for kidney injury in such patients. Our definition of AKI was validated by chart review and studies have been published previously using this definition.[8]

Institution B

Postoperative AKI was identified according to the following protocol: the creatinine lab values prior to surgery, within a 6-month window, and creatinine values within 48 hours after surgery were extracted and the difference between creatinine values was calculated. Those patients with an increase of 0.3 mg/dl or 50% or more from baseline in the first 48 hours after surgery were considered to AKI, according to the Kidney Disease Improving Global Outcomes (KDIGO) Guidelines.[6 7] Cases without creatinine values but with an ICD-9/10 diagnostic code of AKI within seven days of surgery, but not thirty days prior, were also considered to have this outcome (eTable16). Finally, cases without data on serum creatinine or AKI administrative codes following surgery were considered free of this outcome on the premise that there was no clinically meaningful concern for kidney injury in such patients.

4.2 Postoperative major adverse cardiovascular events (MACE)

Postoperative major adverse cardiovascular events were identified using ICD-9/10 diagnostic codes at both institutions, including myocardial infarction, cardiac arrest, and acute heart failure within 30 days after surgery, but not seven days prior to surgery. Cases without the described diagnostic codes were considered free of this outcome on the premise that there was no clinically meaningful concern for major adverse cardiovascular events in such patients.

4.3 Postoperative stroke

Postoperative stroke was identified using ICD-9/10 diagnostic codes at both institutions, including stroke within thirty days after surgery, but not seven days prior to surgery. Cases without the described diagnostic codes were considered free of this outcome on the premise that there was no clinically meaningful concern for stroke in such patients.

4.4 Postoperative reintubation

Institution A

Postoperative reintubation was identified using CPT codes of intubation events (CPT 31500, CPT 94002) within 7 days after the day of surgery.

Institution B

Postoperative reintubation was identified using data from the respiratory therapist database, while any ventilated patient in the hospital was recorded by this database. This variable definition has been used in previous studies and is therefore highly-validated.[9]

5 Mediation analysis

5.1 Potential impact of provider variability on the association between night surgery and transfusion rate

We tested whether variability across individual providers had an impact on the association between night surgery and the mediator transfusion rate. Therefore, we used a mixed-effects logistic regression analysis having individual anaesthesiologists as random effects and adding anaesthesia provider-related variables to the primary confounder model to account for the individual provider's experience level:

- overall number of anaesthesia cases (median number 423 [IQR 296 to 563]),
- number of anaesthesia cases per trimester (median number 54 [IQR 32 to 75])
- number of anaesthesia cases up to index surgery at the respective hospital (median number 189 [IQR 81 to 339])
- and the anaesthesia provider type (residents, certified registered nurse anaesthetists (CRNA), or attendings).

To designate the primary anaesthesia provider responsible for each case, we used the following definitions: The primary anaesthesia provider was the resident in resident plus attending-cases and the CRNA in CRNA plus attending-cases. In cases where two attendings delivered anaesthesia care, the primary provider was the attending who stayed the longest. If more than two providers were responsible for a case, the primary provider was the one who stayed longest, and if different provider types stayed equally long, the resident or CRNA was defined as primary provider. For this analysis, only providers who performed both day and night surgeries during the study period were included.

Similarly, we repeated this sensitivity analysis having individual surgeons as random effects and including indicators of the individual surgeon's experience level in the primary confounder model:

- overall number of surgeries (median number 1,130 [IQR 526 to 1,932])
- number of surgeries per trimester (median number 47 [IQR 27 to 69])
- and number of surgeries up to the index surgery (median number 427 [IQR 142 to 946])

Further important transfusion-associated factors such as estimated intraoperative blood loss and preoperative mild and moderate to severe anaemia within 30 days prior to surgery, respectively, were also added to the primary confounder model to analyse the association between transfusion rate and night surgery.

Results

The observation of a higher risk of blood transfusion associated with night surgery remained robust when accounting for a potential variability in transfusion practice across individual anaesthesia providers (OR_{adj} 1.19, 95% CI 1.10 to 1.30, p=0.005; n=128,691) and across individual surgeons (OR_{adj} 1.35, 95% CI 1.21 to 1.51, p<0.001, n=162,907).

5.2 Case delay as potential mediator

To evaluate the role of case delay as potential mediator in the association between night surgery and 30-day mortality, we used path mediation analysis in a subgroup of sufficient data for case delays. Case delay was defined as difference between scheduled and actual start time in minutes in a subgroup with available data. First, we tested the hypothesis that case delays were higher during night cases than day cases. We used a multivariable-adjusted linear regression model on the association between night surgery and case delays that included all confounding variables of the primary analysis. Second, we used adjusted logistic regression analyses to examine whether case delay was associated with 30-day

mortality, indicating potential effect mediation. Conditional on an association between the mediator and 30-day mortality, we performed adjusted formal mediation analysis. We estimated odds ratios of the indirect (mediated) effect of case delay, and the total (unmediated) effect of night surgery on mortality, using bootstrapping with 1,000 replications. Percentage mediation by the mediators was calculated using the following equation: [ln (indirect effect)/ln (total effect)] x 100.

Results

Data on case delay was available for 159,666 cases. The case delay time was longer in patients who underwent night surgery compared with day surgery (78 [SD 150] vs. 17 [SD 50] minutes, p<0.001). Night surgery was significantly associated with an increased case delay in adjusted linear regression analysis (Coef. 54.86, 95 % CI 53.35 to 56.37, p<0.001). Case delay was significantly associated with an increased risk of 30-day mortality (OR_{adj} 1.001, 95% CI 1.000 to 1.001, p=0.001). Case delay was found to not mediate the effect of night surgery on mortality (p=0.548).

6 Sensitivity analyses

6.1 Robustness of the primary analysis to analytic approach

To account for potential bias originating from systematic differences between patients operated during the day versus night, we tested the robustness of the association between night surgery and 30-day mortality and morbidity in several analytic approaches. We performed propensity score-matched analysis based on the probability of 30-day mortality conditional on all confounding variables included in the primary model. Night versus day cases were matched on a 1:1 basis using a calliper of 0.1 without replacement. To determine the impact of provider variability on the association between night surgery and 30-day mortality, we used a multivariable-adjusted mixed-effects logistic regression model that included individual anaesthesia and surgical providers as random effects (eTable 2).

Results

Propensity score matching and multivariable-adjusted mixed-effects logistic regression analysis confirmed our primary finding (OR_{adj} 1.21, 95% CI 1.06 to 1.39, p=0.005, n=41,414; OR_{adj} 1.34, 95% CI 1.18 to 1.52, n=289,480 cases with anaesthesia provider and surgical provider data available).

6.2 Potential modification of the primary analysis by a one-year diagnosis of cancer

We tested whether the association between night surgery and 30-day mortality was modified by a recent diagnosis of cancer, including the interaction term "night surgery * one-year diagnosis of cancer" in the multivariable-adjusted logistic regression model. We included both types of solid and non-solid cancer, which were defined by ICD-9/10 diagnostic codes (eTable 11).[10]

Results

The primary association between 30-day mortality and night surgery was not modified by a recent diagnosis of cancer (p-for-interaction=0.2). Using linear combinations of the association between night surgery and 30-day mortality, and the interaction term, we confirmed the association of night surgery and 30-day mortality in subgroups of patients with or without a diagnosis of cancer (without cancer: OR_{adj}1.26, 95% CI 1.06 to 1.49, p=0.007; with cancer: OR_{adj}1.46, 95% CI 1.24 to 1.71, p<0.001).

6.3 Subgroup analyses

In subgroup analyses, we assessed whether the association between night surgery and 30-day mortality varied by patient population to ensure that the impact of night surgery on mortality was not driven by a narrow patient population. First, we excluded patients with an ASA status of more than 3 to further address that the effect may be driven by a more severe condition of patients undergoing night surgery. In addition, we performed analyses within

subgroups based on age (quartiles), work RVUs (quartiles), hospital networks (institution A versus B), cases managed by different anaesthesia provider types (residents, CRNAs, attendings), among general surgery patients and finally, in a subgroup including only the 50 most frequently performed surgeries (≥1,000 cases within our cohort; CPT codes are provided in eTable 13), to have a more generalisable sample.

Results

Results remained robust across subgroup analyses after excluding patients with an ASA status of more than 3 (OR_{adj} 1.43, 95% CI 1.13 to 1.79, p=0.003), in patients undergoing one of the 50 most frequently performed surgeries (OR_{adj} 1.44, 95% CI 1.07 to 1.92, p=0.015, n= 119,796), and across subgroups by age, surgical complexity, hospital networks, and the provider type that performed primary anaesthesia care (eTable 14). Among 54,615 patients undergoing general surgery, we found a 1.86 times higher adjusted odds ratio for 30-day mortality associated with night surgery (95% CI 1.31 to 2.65, p=0.001).

6.4 Sample size justification in a subgroup of emergency patients

As described in the main manuscript, we examined the effect of night surgery in a subgroup of patients undergoing emergency surgery. Characteristics of emergency patients were compared between night and day surgeries (eTable 8). In order to ensure sufficient power for this subgroup analysis, we performed a power analysis based on the observed rates of night surgery and mortality within that cohort, assuming a two-sided alpha level of 0.05. In this subgroup, we achieved a power of 80 % to detect a clinically significant difference of 27 % between the groups.

6.5 Effect of specific time windows

Based on a recent study that investigated the effect of operation time on postoperative mortality and morbidity among non-emergency patients,[11] we performed analyses in specific time windows in this subgroup. 30-day mortality and morbidity were categorised by the time surgery started (eTable 12).

Results

The risk of 30-day mortality was significantly higher for surgery start times between 3:00 and 10:59 pm than baseline risk during routine operating hours (7:00 to 11:59 am) (eFigure 2a). Similarly, the risk of 30-day morbidity increased when surgeries started between 4:00 pm and 6:59 am compared with baseline risk (eFigure 2b).

6.6 Effect of weekend surgery

To address that the effect of night surgery on mortality may partly be due to logistic processes and staffing, we investigated the effect of weekend surgery on mortality in the full cohort as well as in a subgroup of patients undergoing day surgery.

Results

In this analysis, exposure to weekend surgery was not associated with 30-day mortality in the full cohort (p=0.867) and in a subgroup of 283,260 patients undergoing day surgery (p=0.766).

6.7 Analysis by year of surgery

We used a Poisson regression analysis correlating the number of patients who underwent night surgery with the respective year of surgery, while accounting for the logarithm of the total number of patients who underwent surgery during that year. To further examine

whether the effect changed over the study period, we included an interaction term between night surgery and the year of surgery in the primary model.

Results

In the Poisson regression analysis, we found an incidence rate ratio of 1.01 (95% CI 1.01 to 1.02, p<0.001) per year. The analysis was performed in the years 2006 to 2017. Year of surgery did not modify the effect of night surgery on 30-day mortality (p-for-interaction=0.415).

6.8 Mortality starting three months after surgery

We compared mortality risk after excluding the first three months after surgery from the logistic regression analysis.

Results

Evaluation of mortality starting three months after surgery revealed no difference in mortality between patients undergoing day and night surgery (OR_{adj} 0.98, 95% CI 0.91 to 1.05, p=0.501).

6.9 Additional confounding variables

We added several confounding variables individually to the association between night surgery and 30-day mortality to evaluate the robustness of the effect with respect to variables not included in the primary analysis (eTable 15).

6.10 Varying definitions of night surgery

We applied varying definitions of night surgery (5 pm to 9 pm and 9 pm to 6:59 am) to test the robustness of the effect on 30-day mortality varying by exposure classification.

Night surgery was associated with a higher risk of 30-day mortality across varying definitions of the exposure variable (5 pm to 9 pm: OR_{adj} 1.33 95% CI 1.17 to 1.51 p<0.001; 9 pm to 6:59 am: OR_{adj} 1.32 95% CI 1.09 to 1.60, p=0.005).

7 Supplemental tables

eTable 1. Definition of the secondary outcome

The definition of the secondary outcome 30-day morbidity was based on the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10 codes).

Types of complications	**ICD-10 diagnostic and procedure codes**	**ICD-9 diagnostic and procedure codes**
Atrial fibrillation or flutter	I4800 I4801 I481 I483 I484 I4890 I4891	427.31 427.32
Acute renal failure	N170 N171 N172 N178 N179	583.6 583.7 584.5 584.6 584.7 584.8 584.9
Bleeding	T810 R58	998.1 459.0 99.07 99.03

Cardiac arrest or life-threatening incident	R092 I460 I461 I469	799.1 V12.53 427.5
Coma	R4020 R4029	780.01
Deep venous thrombosis	I801 I802 I803 I808 I809	410.11 451.11 451.19 451.2 451.89 451.9
Major disruption of wound	T813	998.30

Myocardial infarction & associated complications	I210	410
	I211	429.5
	I212	429.6
	I213	429.71
	I214	429.79
	I2140	
	I2141	
	I2142	
	I2149	
	I219	
	I220	
	I221	
	I228	
	I229	
	I230	
	I231	
	I232	
	I233	
	I234	
	I235	
	I236	
	I2380	
	I2381	
	I2382	
	I2388	
	I2389	

New-onset haemodialysis	3E1M39Z	38.95 39.27 39.95 54.98 **Additional CPT codes:** 90935 90937 90945 90947 90966 90970 90999
Pneumonia	J120 J121 J122 J123 J128 J129 J13 J14 J150 J151 J152 J153 J154	480 481 482 483 484 485 486 507 507.1 507.8 517.1

	J155 J156 J157 J158 J159 J160 J168 J170 J171 J172 J173 J178 J180 J181 J182 J188 J189 J690 J691 J698	
Pulmonary embolism	I260 I269	415

Sepsis	A410	38.10
	A411	38.11
	A412	38.12
	A413	38.19
	A414	38.3
	A4150	38.40
	A4151	38.41
	A4152	38.42
	A4158	38.43
	A4159	38.49
	A4180	995.91
	A4188	
	A419	
Shock	R570	785.5
	R571	
	R572	
	R578	
	R579	
Stroke		362.31
	H341	362.34
	I630	430
	I631	431
	I632	433.91
	I634	434.01
	I635	434.11
	I636	434.91
		435

	I638	435.2
	I639	435.9
	I64	437.7
	I610	V17.1
	I611	
	I612	
	I613	
	I614	
	I615	
	I616	
	I618	
	I619	
	I600	
	I601	
	I602	
	I603	
	I604	
	I605	
	I606	
	I607	
	I608	
	I609	
	G450	
	G451	
	G452	
	G453	

	G454 G458 G459	
Ventilator use for 48 hours or more	V46.11	Z99.11
Additional cardiac complications	I97.0 I97.11 I97.130 I97.190	429.4
Functional digestive disorders	K91.1 K91.0 K91.89	564.2 564.3 564.4
Haemorrhage, haematoma or inflammation complicating a procedure not elsewhere classified	D78.01 D78.02 D78.21 D78.22 D78.31 D78.32 D78.33 E36.01 E36.02 E89.821 E89.820 E89.810 E89.811	998.1 998.11 998.12 998.13 998.5 998.51 998.59

	E89.822 E89.823 G97.31 G97.32 G97.51 G97.52 G97.61 G97.62 G97.63 G97.64 H59.111 H59.112 H59.113 H59.119 H59.121 H59.122 H59.123 H59.129 H59.311 H59.312 H59.313 H59.319 H59.321 H59.322 H59.323 H59.329	

	H59.331	
	H59.332	
	H59.333	
	H59.339	
	H59.341	
	H59.342	
	H59.343	
	H59.349	
	H59.351	
	H59.352	
	H59.353	
	H59.359	
	H59.361	
	H59.362	
	H59.363	
	H59.369	
	H95.21	
	H95.22	
	H95.51	
	H95.52	
	H95.53	
	H95.54	
	H95.41	
	H95.42	
	I97.410	
	I97.411	

	I97.418	
	I97.42	
	I97.610	
	I97.611	
	I97.618	
	I97.620	
	I97.621	
	I97.622	
	I97.630	
	I97.631	
	I97.638	
	I97.640	
	I97.641	
	I97.648	
	J95.61	
	J95.62	
	J95.830	
	J95.831	
	J95.860	
	J95.861	
	J95.863	
	K91.61	
	K91.62	
	K91.840	
	K91.841	
	K91.870	

	K91.871 K91.872 K91.873 L76.01 L76.02 L76.31 L76.32 L76.33 L76.34 L76.21 L76.22 M96.810 M96.811 M96.830 M96.840 M96.841 M99.842 M99.843 M96.831 N99.61 N99.62 N99.820 N99.821 N99.840 N99.841 T88.8XXA	

	K68.11	
Hypotension	I95.3 I95.2 I95.81	458.21 458.29
Infection of tracheostomy	J95.02	519.01
Infection of gastrostomy	K94.22	536.41
Infection of oesophagostomy	K94.32	530.86
Intestinal complications	K91.850 K91.858 K62.5	569.6 569.71 569.79 579.3
Other cardiac, urinary, respiratory or digestive complications not elsewhere specified	I97.710 I97.790 I97.88 I97.89 J95.851 J95.859 J95.88 J95.89 N99.89 T87.40	997.1 997.3 997.31 997.39 997.4 997.5 997.62
Other infection due to medical care not elsewhere classified	T80.219A	999.3

eTable 2. Confounding variables

The primary confounder model included a large number of variables (fixed effects). As sensitivity analysis, we used mixed-effects logistic regression by including the random effects of 1,478 anaesthesia and 1,190 surgical providers in the model.

Fixed effects		**Random effects**
Patient-related characteristics		**Individual provider**
Age [y], quintiles Sex BMI [kg/m^2], categorical ASA physical status, categorical CCI, categorical History of chronic obstructive pulmonary disease, binary History of chronic heart failure, binary History of coronary artery disease, binary History of malignant disease, binary Stroke 1 year prior to surgery, binary Home oxygen therapy		Anaesthesia provider Surgeon
Procedure-related characteristics		
Duration of surgery [min], quintiles Date of surgery, quintiles Surgery type, categorical Surgical setting, categorical Emergency surgery, binary Work RVUs, quintiles Hospital network (institution A versus B)	+	
Anaesthesia-related characteristics		
Intraoperative hypotensive minutes [MAP <55 mmHg], quintiles Units of packed red blood cells (0, 1, 2, ≥3 units) Intraoperative dose of vasopressors [mg], quintiles SpO2/FiO2 ratio, quintiles Handover of anaesthesia care, binary		

Abbreviations: ASA, American Society of Anaesthesiologists Physical Status Classification System; BMI, body mass index; CCI, Charlson Comorbidity Index; MAP, mean arterial pressure; RVUs, relative value units.

eTable 3. Comorbidities within one year prior to surgery among patients undergoing day surgery versus night surgery in the primary imputed cohort

Patient comorbidities, n (%)	Day surgery n = 322,327	Night surgery n = 27,908	Standardised difference
Coronary artery disease	33,938 (10.5%)	3,724 (13.3%)	-0.087
Myocardial infarction	13,732 (4.3%)	1,657 (5.9%)	-0.076
Heart failure	20,662 (6.4%)	2,960 (10.6%)	-0.151
Ischemic stroke	5,585 (1.73%)	816 (2.92%)	-0.079
Cerebrovascular disease	21,195 (6.6%)	2,702 (9.7%)	-0.114
Peripheral vascular disease	25,549 (7.9%)	3,173 (11.4%)	-0.117
Diabetes mellitus with chronic complications	14,306 (4.4%)	1,789 (6.4%)	-0.087
Diabetes mellitus without chronic complications	46,742 (14.5%)	4,739 (17.0%)	-0.068
Renal disease	22,454 (7.0%)	3,016 (10.8%)	-0.135
Moderate to severe liver disease	3,076 (1.0%)	666 (2.4%)	-0.112
Chronic obstructive pulmonary disease	56,249 (17.5%)	5,081 (18.2%)	-0.020
Malignant disease (with or without metastasis)	92,546 (28.7%)	5,644 (20.2%)	0.198
Peptic ulcer disease	3,864 (1.2%)	649 (2.3%)	-0.086
Dementia	2,181 (0.7%)	384 (1.4%)	-0.069
Hemiplegia	5,515 (1.7%)	1,012 (3.6%)	-0.119
HIV infection	2,855 (0.9%)	299 (1.1%)	-0.019

CCI, median (IQR)	1 (0, 3)	1 (0, 3)	-0.071
Home oxygen therapy	2,287 (0.7%)	260 (0.9%)	-0.025

eTable 4. Surgical services among patients undergoing day surgery versus night surgery in the primary imputed cohort

The surgical service was included as a categorical variable in the primary confounder model with a standardised difference of 0.168 between patients undergoing day versus night surgery. Characteristics and distribution of variables by day versus night surgery are presented for cases with observed data.

Surgical service, n (%)	**Day surgery** **n = 322,327**	**Night surgery** **n = 27,908**
Non-operating room anaesthesia	5,952 (1.9%)	276 (1.0%)
Burn surgery	1,942 (0.6%)	65 (0.2%)
Acute care surgery	8,606 (2.7%)	3,819 (13.7%)
General surgery	54,667 (17.0%)	5,092 (18.3%)
Gynaecology	31,607 (9.8%)	2,040 (7.3%)
Neurosurgery	21,177 (6.6%)	2,521 (9.0%)
Oral/Maxillofacial surgery/Otolaryngology	3,488 (1.1%)	90 (0.3%)
Orthopedic surgery	76,262 (23.7%)	5,492 (19.7%)
Other	3,800 (1.2%)	416 (1.5%)
Plastic surgery	8,963 (2.8%)	525 (1.9%)
Radiology	730 (0.2%)	92 (0.3%)
Surgical oncology	21,354 (6.6%)	1,424 (5.1%)
Thoracic surgery	1,413 (0.4%)	147 (0.5%)
Transplant surgery	14,674 (4.6%)	391 (1.4%)
Urology	21,412 (6.6%)	1,467 (5.3%)

Vascular surgery	6,161 (1.9%)	1,089 (3.9%)

eTable 5. Characteristics and distribution of variables by day versus night surgery in the complete-case cohort

Patient characteristics	**Day surgery n = 283,185**	**Night surgery n = 20,707**
Sex, male, n (%)	123,530 (43.6%)	10,270 (49.6%)
Age (years), mean ± SD	53.98 ± 16.38	51.96 ± 18.65
BMI (kg/m^2), mean ± SD	28.36 ± 6.86	27.79 ± 6.89
ASA status, median (IQR)	2 (2, 3)	2 (2, 3)
ASA ≥ 3, n (%)	90,415 (31.9%)	8,676 (41.9%)
Admission type, n (%)		
Ambulatory	107,409 (37.9%)	3,002 (14.5%)
Same day admission	133,359 (47.1%)	9,753 (47.1%)
Inpatient	42,417 (15.0%)	7,952 (38.4%)
Comorbidities within 1 year prior to surgery, n (%)		
Coronary artery disease	28,579 (10.1%)	2,505 (12.1%)
Myocardial infarction	11,202 (4.0%)	1,099 (5.3%)
Heart failure	16,894 (6.0%)	2,018 (9.7%)
Ischemic stroke	4,719 (1.7%)	531 (2.6%)
Cerebrovascular disease	18,124 (6.4%)	1,854 (9.0%)
Peripheral vascular disease	21,012 (7.4%)	2,210 (10.7%)
Diabetes mellitus with chronic complications	11,465 (4.0%)	1,228 (5.9%)
Diabetes mellitus without chronic complications	39,427 (13.9%)	3,270 (15.8%)
Renal disease	18,671 (6.6%)	2,117 (10.2%)

Moderate to severe liver disease	2,460 (0.9%)	441 (2.1%)
Chronic obstructive pulmonary disease	48,581 (17.2%)	3,644 (17.6%)
Malignant disease (with or without metastasis)	84,716 (29.9%)	4,485 (21.7%)
Peptic ulcer disease	3,279 (1.2%)	446 (2.2%)
Dementia	1,699 (0.6%)	246 (1.2%)
Hemiplegia	4,657 (1.6%)	688 (3.3%)
HIV infection	2,382 (0.8%)	222 (1.1%)
CCI, median (IQR)	1 (0, 3)	1 (0, 3)
Home oxygen therapy	1,803 (0.6%)	168 (0.8%)
Intraoperative data		
Duration of surgery (min), median (IQR)	133.00 (86.00, 207.00)	113.00 (80.00, 164.00)
Handover of anaesthesia care, n (%)	24,949 (8.8%)	4,686 (22.6%)
Intraoperative hypotensive minutes of MAP <55mmHg, median (IQR)	0.00 (0.00, 2.00)	0.00 (0.00, 1.00)
Emergency surgery, n (%)	6,404 (2.3%)	7,162 (34.6%)
Work RVUs, median (IQR)	13.18 (7.38, 19.91)	10.62 (7.08, 17.63)
Packed red blood cell units transfused intraoperatively, n (%)		
0 units	275,303 (97.2%)	19,558 (94.5%)
1 unit	3,433 (1.2%)	469 (2.3%)
2 units	2,852 (1.0%)	373 (1.8%)
≥ 3 units	1,597 (0.6%)	307 (1.5%)
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.01 (0.00, 0.11)	0.00 (0.00, 0.11)
Median SpO_2/FiO_2 ratio, median (IQR)	183.33 (161.29, 220.22)	178.57 (152.31, 206.56)

Surgical service, n (%)		
Non-operating room anaesthesia	5,549 (2.0%)	244 (1.2%)
Burn surgery	1,754 (0.6%)	59 (0.3%)
Acute care surgery	7,365 (2.6%)	3,069 (14.8%)
General surgery	50,982 (18.0%)	3,633 (17.5%)
Gynaecology	29,245 (10.3%)	1,742 (8.4%)
Neurosurgery	19,338 (6.8%)	1,806 (8.7%)
Oral/Maxillofacial surgery/Otolaryngology	3,085 (1.1%)	83 (0.4%)
Orthopedic surgery	63,206 (22.3%)	3,936 (19.0%)
Other	3,067 (1.1%)	318 (1.5%)
Plastic surgery	7,808 (2.8%)	354 (1.7%)
Radiology	643 (0.2%)	77 (0.4%)
Surgical oncology	18,478 (6.5%)	1,005 (4.9%)
Thoracic surgery	1,297 (0.5%)	145 (0.7%)
Transplant surgery	13,893 (4.9%)	355 (1.7%)
Urology	18,007 (6.4%)	991 (4.8%)
Vascular surgery	4,909 (1.7%)	757 (3.7%)
Hospital network (institution A vs. B), n (%)	148,703 (52.5%)	11,329 (54.7%)
30-day mortality	1,769 (0.6%)	465 (2.3%)
30-day morbidity	22,919 (8.1%)	2,723 (13.2%)

Abbreviations: ASA, American Society of Anesthesiologists Physical Status Classification System; BMI, body mass index; CCI, Charlson Comorbidity Index; IQR, interquartile range; MAP, mean arterial pressure; SD, standard deviation, RVUs, relative value units.

eTable 6. Characteristics and distribution of variables by patients who underwent ambulatory/same-day surgery versus inpatient surgery

Normally distributed continuous variables were expressed as mean (± SD), non-normally distributed variables as median (IQR), and categorical variables as frequency (percentages).

Patient characteristics	Ambulatory/same-day surgery n = 253,523	Inpatient surgery n = 50,369
Night surgery, n (%)	12,755 (5.0%)	7,952 (15.8%)
Sex, male, n (%)	108,163 (42.7%)	25,637 (50.9%)
Age (years), mean ± SD	53.06 ± 16.09	57.80 ± 18.21
BMI (kg/m^2), mean ± SD	28.42 ± 6.81	27.82 ± 7.12
ASA ≥ 3, n (%)	69,447 (27.4%)	29,644 (58.9%)
Comorbidities within 1 year prior to surgery, n (%)		
Coronary artery disease	21,766 (8.6%)	9,318 (18.5%)
Myocardial infarction	8,132 (3.2%)	4,169 (8.3%)
Heart failure	10,770 (4.2%)	8,142 (16.2%)
Ischemic stroke	2,714 (1.1%)	2,536 (5.0%)
Cerebrovascular disease	12,372 (4.9%)	7,606 (15.1%)
Peripheral vascular disease	14,597 (5.8%)	8,625 (17.1%)
Diabetes mellitus with chronic complications	8,159 (3.2%)	4,534 (9.0%)
Diabetes mellitus without chronic complications	31,924 (12.6%)	10,773 (21.4%)
Renal disease	13,125 (5.2%)	7,663 (15.2%)
Moderate to severe liver disease	1,625 (0.6%)	1,276 (2.5%)
Chronic obstructive pulmonary disease	41,008 (16.2%)	11,217 (22.3%)
Malignant disease (with or without metastasis)	76,379 (30.1%)	13,881 (27.6%)
Peptic ulcer disease	2,404 (0.9%)	1,321 (2.6%)
Dementia	920 (0.4%)	1,025 (2.0%)
Hemiplegia	2,651 (1.0%)	2,694 (5.3%)
HIV infection	1,956 (0.8%)	648 (1.3%)
CCI, median (IQR)	1 (0, 2)	2 (0, 5)
Home oxygen therapy	1,307 (0.5%)	664 (1.3%)
Intraoperative data		
Duration of surgery (min), median (IQR)	131 (85, 205)	133 (89, 202)
Handover of anaesthesia care, n (%)	9,936 (8.6%)	3,665 (12.8%)
Intraoperative hypotensive minutes of MAP	0.00 (0.00, 2.00)	1.00 (0.00, 3.00)

<55mmHg, median (IQR)		
Emergency surgery, n (%)	7,723 (3.0%)	5,843 (11.6%)
Work RVUs, median (IQR)	12.80 (7.38, 19.61)	13.22 (7.38, 19.66)
Packed red blood cell units transfused intraoperatively, n (%)		
0 units	249,233 (98.3%)	45,628 (90.6%)
1 unit	1,733 (0.7%)	2,169 (4.3%)
2 units	1,573 (0.6%)	1,652 (3.3%)
≥ 3 units	984 (0.4%)	920 (1.8%)
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.00 (0.00, 0.08)	0.04 (0.00, 0.25)
Median SpO_2/FiO_2 ratio, median (IQR)	183.33 (161.90, 220.00)	180.33 (151.15, 217.07)
Surgical service, n (%)		
Non-operating room anaesthesia	4,740 (1.9%)	1,053 (2.1%)
Burn surgery	667 (0.3%)	1,146 (2.3%)
Emergency surgical service	5,148 (2.0%)	5,286 (10.5%)
General surgery	49,163 (19.4%)	5,452 (10.8%)
Gynaecology	29,526 (11.6%)	1,461 (2.9%)
Neurosurgery	15,232 (6.0%)	5,912 (11.7%)
Oral/Maxillofacial surgery	2,866 (1.1%)	302 (0.6%)
Orthopedic surgery	53,605 (21.1%)	13,537 (26.9%)
Other	2,122 (0.8%)	1,263 (2.5%)
Otolaryngology	7,638 (3.0%)	524 (1.0%)
Paediatric surgery	544 (0.2%)	176 (0.3%)
Plastic surgery	17,783 (7.0%)	1,700 (3.4%)
Radiology	858 (0.3%)	584 (1.2%)
Surgical oncology	13,633 (5.4%)	615 (1.2%)
Thoracic surgery	15,469 (6.1%)	3,529 (7.0%)
Transplant surgery	4,407 (1.7%)	1,259 (2.5%)
Urology	23,586 (9.3%)	2,083 (4.1%)
Vascular surgery	6,536 (2.6%)	4,487 (8.9%)
Hospital network (institution A vs. B), n (%)	115,196 (45.4%)	28,664 (56.9%)
Study outcomes, n (%)		
30-day mortality	632 (0.3%)	1,602 (3.2%)

30-day morbidity	21,612 (8.5%)	4,030 (8.0%)

eTable 7. Characteristics and distribution of variables by day versus night surgery in a sub cohort of patients undergoing ambulatory/same-day surgery.

Normally distributed continuous variables were expressed as mean (± SD), non-normally distributed variables as median (IQR), and categorical variables as frequency (percentages).

Patient characteristics	**Day surgery n = 240,768**	**Night surgery n = 12,755**
Sex, male, n (%)	10,1917 (42.33%)	6,246 (48.97%)
Age (years), mean ± SD	52.24 ± 15.95	49.72 ± 18.17
BMI (kg/m^2), mean ± SD	28.45 ± 6.81	27.86 ± 6.71
ASA ≥ 3, n (%)	65,419 (27.17%)	4,028 (31.58%)
Admission type, n (%)		
Ambulatory	107,409 (44.6%)	3,002 (23.5%)
Same day admission	133,359 (55.4%)	9,753 (76.5%)
Comorbidities within 1 year prior to surgery, n (%)		
Coronary artery disease	20,614 (8.6%)	1,152 (9.0%)
Myocardial infarction	7,645 (3.2%)	487 (3.8%)
Heart failure	10,009 (4.2%)	761 (6.0%)
Ischemic stroke	2,549 (1.1%)	165 (1.3%)
Cerebrovascular disease	11,631 (4.8%)	741 (5.8%)
Peripheral vascular disease	13,644 (5.7%)	953 (7.5%)
Diabetes mellitus with chronic complications	7,634 (3.2%)	525 (4.1%)
Diabetes mellitus without chronic complications	30,270 (12.6%)	1,654 (13.0%)
Renal disease	12,195 (5.1%)	930 (7.3%)

Moderate to severe liver disease	1,435 (0.6%)	190 (1.5%)
Chronic obstructive pulmonary disease	39,078 (16.2%)	1,930 (15.1%)
Malignant disease (with or without metastasis)	19,589 (8.1%)	841 (6.6%)
Peptic ulcer disease	2,183 (0.9%)	221 (1.7%)
Dementia	828 (0.3%)	92 (0.7%)
Hemiplegia	2,390 (1.0%)	261 (2.1%)
HIV infection	1,821 (0.8%)	135 (1.1%)
CCI median, (IQR)	1 (0, 2)	1 (0, 2)
Home oxygen therapy	1,231 (0.5%)	76 (0.6%)
Intraoperative data		
Duration of surgery (min), median (IQR)	133.00 (85.00, 207.00)	110.00 (78.00, 159.00)
Handover of anaesthesia care, n (%)	19,911 (8.3%)	2,953 (23.2%)
Intraoperative hypotensive minutes of MAP <55mmHg, median (IQR)	0.00 (0.00, 2.00)	0.00 (0.00, 2.00)
Emergency surgery, n (%)	2,966 (1.2%)	4,757 (37.3%)
Work RVUs, median (IQR)	13.18 (7.38, 19.94)	10.47 (7.07, 16.47)
Packed red blood cell units transfused intraoperatively, n (%)		
0 units	236,926 (98.4%)	12,307 (96.5%)
1 unit	1,556 (0.6%)	177 (1.4%)
2 units	1,426 (0.6%)	147 (1.1%)
≥ 3 units	860 (0.4%)	124 (1.0%)
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.00 (0.00, 0.08)	0.00 (0.00, 0.08
Median SpO_2/FiO_2 ratio, median (IQR)	183.49 (161.30, 220.45)	180.00 (156.35, 208.33)

Surgical service, n (%)		
Non-operating room anaesthesia	4,600 (1.9%)	140 (1.1%)
Burn surgery	650 (0.3%)	17 (0.1%)
Acute care surgery	1,371 (0.6%)	785 (6.2%)
General surgery	46,817 (19.4%)	2,346 (18.4%)
Gynaecology	28,116 (11.7%)	1410 (11.1%)
Neurosurgery	14,378 (6.0%)	854 (6.7%)
Oral/Maxillofacial surgery/Otolaryngology	3,716 (1.5%)	66 (0.5%)
Orthopedic surgery	51,105 (21.2%)	2,500 (19.6%)
Other	10,940 (4.5%)	1,440 (11.3%)
Plastic surgery	17,105 (7.1%)	678 (5.3%)
Radiology	805 (0.3%)	53 (0.4%)
Surgical oncology	13,361 (5.6%)	272 (2.1%)
Thoracic surgery	14,976 (6.2%)	493 (3.9%)
Transplant surgery	3,951 (1.6%)	456 (3.6%)
Urology	22,737 (9.4%)	849 (6.7%)
Vascular surgery	6140 (2.6%)	396 (3.1%)
Hospital network (institution A vs. B), n (%)	109,621 (45.5%)	5,575 (43.7%)
Study outcomes, n (%)		
30-day mortality	497 (0.2%)	135 (1.1%)
30-day morbidity	19,535 (8.1%)	2,077 (16.3%)

Abbreviations: ASA, American Society of Anesthesiologists Physical Status Classification System; BMI, body mass index; CCI, Charlson Comorbidity Index; IQR, interquartile range; MAP, mean arterial pressure; SD, standard deviation, RVUs, relative value units.

eTable 8. Characteristics and distribution of variables among emergency cases

Normally distributed continuous variables were expressed as mean (± SD), non-normally distributed variables as median (IQR), and categorical variables as frequency (percentages).

Patient characteristics	**Day surgery n = 6,404**	**Night surgery n = 7,162**
Sex, male, n (%)	3,217 (50.2%)	3,676 (51.3%)
Age (years), mean ± SD	52.82 ± 20.07	49.32 ± 19.79
BMI (kg/m^2), mean ± SD	27.59 ± 6.81	27.41 ± 6.78
ASA ≥ 3, n (%)	3,024 (47.2%)	2,808 (39.2%)
Admission type, n (%)		
Ambulatory	440 (6.9%)	531 (7.4%)
Same day admission	2,526 (39.4%)	4,226 (59.0%)
Inpatient	3,438 (53.7%)	2,405 (33.6%)
Comorbidities within 1 year prior to surgery, n (%)		
Coronary artery disease	914 (14.3%)	798 (11.1%)
Myocardial infarction	399 (6.2%)	363 (5.1%)
Heart failure	734 (11.5%)	686 (9.6%)
Ischemic stroke	223 (3.5%)	143 (2.0%)
Cerebrovascular disease	764 (11.9%)	587 (8.2%)
Peripheral vascular disease	820 (12.8%)	764 (10.7%)
Diabetes mellitus with chronic complications	368 (5.7%)	335 (4.7%)
Diabetes mellitus without chronic complications	1,064 (16.6%)	998 (13.9%)
Renal disease	731 (11.4%)	628 (8.8%)
Moderate to severe liver disease	172 (2.7%)	205 (2.9%)
Chronic obstructive pulmonary disease	1,148 (17.9%)	1,162 (16.2%)
Malignant disease (with or without metastasis)	1,118 (17.5%)	1,040 (14.5%)
Peptic ulcer disease	172 (2.7%)	202 (2.8%)
Dementia	115 (1.8%)	84 (1.2%)
Hemiplegia	245 (3.8%)	214 (3.0%)
HIV infection	64 (1.0%)	74 (1.0%)
CCI median, (IQR)	1 (0, 3)	1 (0, 3)

Home oxygen therapy	70 (1.1%)	67 (1.0%)
Intraoperative data		
Duration of surgery (min), median (IQR)	124.00 (87.00, 184.00)	112.00 (83.00, 163.00)
Handover of anaesthesia care, n (%)	879 (13.7%)	1,162 (16.2)
Intraoperative hypotensive minutes of MAP <55mmHg, median (IQR)	1.00 (0.00, 3.00)	1.00 (0.00, 3.00)
Work RVUs, median (IQR)	12.15 (8.07, 18.46)	10.62 (8.78, 17.82)
Packed red blood cell units transfused intraoperatively, n (%)		
0 units	5,707 (89.1%)	6,565 (91.7%)
1 unit	299 (4.7%)	186 (2.6%)
2 units	240 (3.8%)	200 (2.8%)
≥ 3 units	158 (2.4%)	211 (2.9%)
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.02 (0.00, 0.21)	0.01 (0.00, 0.14)
Median SpO_2/FiO_2 ratio, median (IQR)	178.57 (149.25, 208.33)	178.57 (153.08, 202.02)
Surgical service, n (%)		
Non-operating room anaesthesia	43 (0.7%)	19 (0.3%)
Burn surgery	29 (0.5%)	8 (0.1%)
Acute care surgery	1,002 (15.6%)	1,632 (22.8%)
General surgery	1,093 (17.1%)	1,621 (22.6%)
Gynaecology	442 (6.9%)	642 (9.0%)
Neurosurgery	560 (8.7%)	490 (6.8%)
Oral/Maxillofacial surgery/Otolaryngology	46 (0.7%)	21 (0.3%)
Orthopedic surgery	1,465 (22.9%)	997 (13.9%)
Other	98 (1.5%)	85 (1.2%)
Plastic surgery	98 (1.5%)	167 (2.3%)
Radiology	32 (0.5%)	36 (0.5%)
Surgical oncology	160 (2.5%)	237 (3.3%)
Thoracic surgery	60 (0.9%)	25 (0.3%)
Transplant surgery	55 (0.9%)	82 (1.1%)
Urology	190 (3.0%)	128 (1.8%)
Vascular surgery	221 (3.5%)	280 (3.9%)

Hospital network (institution A vs. B), n (%)	131,544 (47.5%)	6,554 (48.4%)
Study outcomes, n (%)		
30-day mortality	226 (3.5 %)	219 (3.1%)
30-day morbidity	691 (10.8%)	863 (12.0%)

Abbreviations: ASA, American Society of Anaesthesiologists Physical Status Classification System

eTable 9. Characteristics and distribution of variables after propensity score matching

Normally distributed continuous variables were expressed as mean (± SD), non-normally distributed variables as median (IQR), and categorical variables as frequency (percentages).

PSM cohort n = 14,414	**Day surgeries n = 7,207**	**Night surgeries n = 7,207**
Sex, male, n (%)	10,477 (50.6%)	10,270 (49.6%)
Age (years), mean ± SD	53.17 ± 18.27	51.96 ± 18.65
BMI (kg/m^2), mean ± SD	27.88 ± 7.01	27.79 ± 6.89
ASA ≥ 3, n (%)	9,415 (45.5%)	8,676 (41.9%)
Admission type, n (%)		
Ambulatory	3,079 (14.9%)	3,002 (14.5%)
Same day admission	7,587 (36.6%)	9,753 (47.1%)
Inpatient	10,041 (48.5%)	7,952 (38.4%)
Comorbidities within one year prior to surgery n (%)		
Coronary artery disease	2706 (13.1%)	2505 (12.1%)
Myocardial infarction	1,200 (5.8%)	1,099 (5.3%)
Heart failure	2,173 (10.5%)	2,018 (9.7%)
Ischemic stroke	608 (2.9%)	531 (2.6%)
Cerebrovascular disease	2,000 (9.7%)	1,854 (9.0%)
Peripheral vascular disease	2,240 (10.8%)	2,210 (10.7%)
Diabetes mellitus with chronic complications	1,297 (6.3%)	1,228 (5.9%)
Diabetes mellitus without chronic complications	3,528 (17.0%)	3,270 (15.8%)
Renal disease	2,252 (10.9%)	2,117 (10.2%)
Moderate to severe liver disease	419 (2.0%)	441 (2.1%)
Chronic obstructive pulmonary disease	3,664 (17.7%)	3,644 (17.6%)
Malignant disease (with or without metastasis)	4,657 (22.5%)	4,583 (22.1%)
Peptic ulcer disease	451 (2.2%)	446 (2.2%)
Dementia	299 (1.4%)	246 (1.2%)
Hemiplegia	693 (3.3%)	688 (3.3%)
HIV infection	274 (1.3%)	222 (1.1%)
CCI, median (IQR)	1.00 (0.00, 3.00)	1.00 (0.00, 3.00)
Home oxygen therapy	166 (0.8%)	168 (0.8%)
Intraoperative data		
Duration of surgery (min), median (IQR), median (IQR)	117.00 (78.00, 177.00)	113.00 (80.00, 164.00)
Handover of anaesthesia care, n (%)	2,318 (23.7%)	2,168 (23.2%)
Intraoperative hypotensive minutes of MAP <55mmHg, median (IQR)	0.00 (0.00, 2.00)	0.00 (0.00, 2.00)
Emergency surgery, n (%)	6,323 (30.5%)	7,162 (34.6%)
Work RVUs, median (IQR)	11.43 (6.48, 18.00)	10.62 (7.08, 17.63)

Packed red blood cell units transfused intraoperatively, n (%)		
0 units	19,377 (93.6%)	19,558 (94.5%)
1 unit	579 (2.8%)	469 (2.3%)
2 units	462 (2.2%)	373 (1.8%)
≥ 3 units	289 (1.4%)	307 (1.5%)
Total intraoperative vasopressor dose, norepinephrine equivalent (mg), median (IQR)	0.01 (0.00, 0.14)	0.01 (0.00, 0.11)
Median SpO_2/FiO_2 ratio, median (IQR)	178.57 (151.52, 210.53)	178.57 (152.31, 206.56)
Surgical service, n (%)		
Non-operating room anaesthesia	403 (1.9%)	244 (1.2%)
Burn surgery	337 (1.6%)	59 (0.3%)
Emergency surgical service	1,935 (9.3%)	3,069 (14.8%)
General surgery	3,544 (17.1%)	3,633 (17.5%)
Gynaecology	1,563 (7.5%)	1,742 (8.4%)
Neurosurgery	1,591 (7.7%)	1,806 (8.7%)
Oral/Maxillofacial surgery	140 (0.7%)	83 (0.4%)
Orthopedic surgery	5,112 (24.7%)	3,936 (19.0%)
Other	328 (1.6%)	318 (1.5%)
Otolaryngology	399 (1.9%)	354 (1.7%)
Paediatric surgery	71 (0.3%)	77 (0.4%)
Plastic surgery	869 (4.2%)	1,005 (4.9%)
Radiology	160 (0.8%)	145 (0.7%)
Surgical oncology	416 (2.0%)	355 (1.7%)
Thoracic surgery	1,099 (5.3%)	991 (4.8%)
Transplant surgery	470 (2.3%)	757 (3.7%)
Urology	1,288 (6.2%)	1,217 (5.9%)
Vascular surgery	982 (4.7%)	916 (4.4%)
Hospital network (institution A vs. B), n (%)	9,787 (47.3%)	9,378 (45.3%)

eTable 10.a Association between major postoperative adverse events and night surgery compared with day surgery

Major postoperative adverse events	Day surgery (n = 283,185)	Night surgery (n = 20,707)	Unadjusted analysis			Adjusted analysis		
			Adjusted risk difference (95% CI)	Odds ratio (95% CI)	p-value	Adjusted risk difference (95% CI)	Odds ratio (95% CI)	p-value
Acute kidney injury	9,372 (3.31%)	1,406 (6.79%)	3.48% (3.13 to 3.83%)	2.13 (2.01–2.26)	<0.001	0.24% (0.16 to 0.31%)	1.29 (1.20 to 1.39)	<0.001
Stroke	1,694 (0.60%)	211 (1.02%)	0.42% (0.28 to 0.56%)	1.71 (1.48–1.98)	<0.001	0.00% (–0.01 to 0.01%)	1.04 (0.86 to 1.26)	0.665

Major adverse cardiac events (MACE)	5,382 (1.90%)	678 (3.27%)	1.37% (1.13 to 1.62%)	1.75 (1.61–1.89)	<0.001	0.08% (0.03 to 0.12%)	1.22 (1.10 to 1.36)	<0.001
Myocardial infarction	881 (0.31%)	129 (0.62%)	0.31% (0.20 to 0.42%)	2.01 (1.67–2.42)	<0.001	0.01% (–0.01 to 0.02%)	1.14 (0.93 to 1.42)	0.204
Cardiac arrest	255 (0.09%)	43 (0.21%)	0.12% (0.05 to 0.18%)	2.31 (1.67–3.19)	<0.001	0.01% (–0.01 to 0.02%)	1.21 (0.83 to 1.76)	0.328
Acute heart failure	4,545 (1.60%)	564 (2.72%)	1.12% (0.89 to 1.35%)	1.72 (1.57–1.88)	<0.001	0.06% (0.03 to 0.10%)	1.27 (1.13 to 1.43)	<0.001
Reintubation*	1,738 (0.62%)	291 (1.49%)	0.87% (0.69 to 1.04%)	2.41 (2.12–2.73)	<0.001	0.05% (0.02 to 0.07%)	1.35 (1.17 to 1.56)	<0.001
*Reintubation in a subgroup of available data (n=297,778)								

eTable 10.b Postoperative complications stratified by patients who died within 30 days versus patients who survived

Postoperative complications	**Deceased within 30 days n = 2,234**	**Survived within 30 days n = 301,658**	**p-value**
Acute kidney injury	542 (24.26%)	10,236 (3.39%)	<0.001
Major adverse cardiac events (MACE)	292 (13.07%)	5,768 (1.91%)	<0.001
Cardiac arrest	107 (4.79%)	191 (0.06%)	<0.001
Acute heart failure	162 (7.25%)	4,497 (1.64%)	<0.001
Reintubation *	293 (16.92%)	1,736 (0.59%)	<0.001

* *Reintubation in a subgroup of available data (n = 297,778)*

eTable 11. ICD-9 and ICD-10 codes to define a recent history of solid/non-solid cancer

A one-year history of solid/non-solid cancer was based on the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10 codes).[10]

Variable	ICD-9 code	ICD-10 code	Description
Solid cancer	140.X	C00.X	Malignant neoplasm of lip
	141.X	C01.X, C02.X	Malignant neoplasm of tongue
	142.X	C07.X, C08.X	Malignant neoplasm of major salivary glands
	143.X	C03.X	Malignant neoplasm of gum
	144.X	C04.X	Malignant neoplasm of floor of mouth
	145.X	C05.X, C06.X, C09.X, C14.X	Malignant neoplasm of other and unspecified parts of mouth
	146.X	C10.X	Malignant neoplasm of oropharynx
	147.X	C11.X	Malignant neoplasm of nasopharynx
	148.X	C12.X, C13.X	Malignant neoplasm of hypopharynx
	149.X	C14.X	Malignant neoplasm of other and ill-defined sites within the lip
	150.X	C15.X	Malignant neoplasm of oesophagus
	151.X	C16.X	Malignant neoplasm of stomach
	152.X	C17.X	Malignant neoplasm of small intestine, including duodenum
	153.X	C18.X	Malignant neoplasm of colon

154.X	C19.X, C20.X, C21.X	Malignant neoplasm of rectum, rectosigmoid junction, and anus
155.X	C22.X	Malignant neoplasm of liver and intrahepatic bile ducts
156.X	C23.X, C24.X	Malignant neoplasm of gallbladder and extrahepatic bile ducts
157.X	C25.X	Malignant neoplasm of pancreas
158.X	C48.X	Malignant neoplasm of retroperitoneum and peritoneum
159.X	C26.X	Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum
160.X	C30.X, C31.X	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
161.X	C32.X	Malignant neoplasm of larynx
162.X	C33.X, C34.X	Malignant neoplasm of trachea, bronchus, and lung
163.X	C38.X	Malignant neoplasm of pleura
164.X	C37.X, C38.X	Malignant neoplasm of thymus, heart, and mediastinum
165.X	C39.X	Malignant neoplasm of other and ill-defined sites within the respiratory system and intrathoracic organs
170.X	C40.X, C41.X	Malignant neoplasm of bone and articular cartilage

171.X	C45.X, C49.X	Malignant neoplasm of connective and other soft tissue
172.X	C43.X	Malignant melanoma of skin
173.X	C44.X	Other malignant neoplasm of skin
174.X	C50.X	Malignant neoplasm of female breast
175.X	C50.X	Malignant neoplasm of male breast
176.X	C46.X	Kaposi's sarcoma
179.X	C55.X	Malignant neoplasm of uterus, part unspecified
180.X	C53.X	Malignant neoplasm of cervix uteri
181.X	C58.X	Malignant neoplasm of placenta
182.X	C54.X	Malignant neoplasm of body of uterus
183.X	C56.X	Malignant neoplasm of ovary and other uterine adnexa
184.X	C51.X, C52.X, C57.X	Malignant neoplasm of other and unspecified female genital organs
185.X	C61.X	Malignant neoplasm of prostate
186.X	C62.X	Malignant neoplasm of testis
187.X	C60.X, C63.X	Malignant neoplasm of penis and other male genital organs
188.X	C67.X	Malignant neoplasm of bladder
189.X	C64.X, C65.X, C66.X, C68.X	Malignant neoplasm of kidney and other and unspecified urinary organs
190.X	C69.X	Malignant neoplasm of eye

	191.X	C71.X	Malignant neoplasm of brain
	192.X	C47.X, C70.X, C72.X	Malignant neoplasm of other and unspecified parts of nervous system
	193.X	C73.X	Malignant neoplasm of thyroid gland
	194.X	C74.X, C75.X	Malignant neoplasm of other endocrine glands and related structures
Definitions of solid cancer primary sites			
Lung	162.2, 162.3, 162.4, 162.5, 162.8, 162.9	C34.X	Malignant neoplasm of bronchus and lung
Breast	174.X 233.0	C50	Malignant neoplasm of breast
Colorectal	153.X	C18.X	Malignant neoplasm of colon
	154.0, 154.1, 154.2, 154.3, 154.8	C20	Malignant neoplasm of rectum
Prostate	185, 233.4	C61	Malignant neoplasm of prostate

Pancreatic	157.X	C25.X	Malignant neoplasm of pancreas
Brain	191.X	C71.X	Malignant neoplasm of brain
Hepatobiliary	155.X	C22.X	Malignant neoplasm of liver and intrahepatic bile ducts
	156.X	C23	Malignant neoplasm of gallbladder
Cervical	180.X	C53.X	Malignant neoplasm of cervix uteri
Ovarian	183.0	C56.X	Malignant neoplasm of ovary
Kidney	189.0	C64.0	Malignant neoplasm of kidney, except renal pelvis
Thyroid	193.X	C73	Malignant neoplasm of thyroid gland
Oesophageal	150.X	C15.X	Malignant neoplasm of esophagus
Stomach	151.X	C16.0	Malignant neoplasm of stomach
Bladder	188.X	C67.X	Malignant neoplasm of bladder
Uterus	182.X	C54.X	Malignant neoplasm of corpus uteri
	179.X	C55.X	Malignant neoplasm of uterus, part unspecified
Malignant Melanoma	172.X	C43.X	Malignant melanoma of skin
Lip and oral cavity	140.X	C00.X	Malignant neoplasm of lip
	141.X	C01.X	Malignant neoplasm of base of tongue
		C02.X	Malignant neoplasm of other and unspecified parts of tongue
	143.X	C03.X	Malignant neoplasm of gum

	144.X	C04.X	Malignant neoplasm of floor of mouth
	145.X	C05.X	Malignant neoplasm of palate
	149.X	C06.X	Malignant neoplasm of other and unspecified parts of mouth
Metastatic cancer	196.X.	C77.X	Secondary and unspecified malignant neoplasm of lymph nodes
	197.X	C78.XX	Secondary malignant neoplasm of respiratory and digestive organs
	198.X	C79.XX	Secondary malignant neoplasm of other and unspecified sites
	199.X	C80.0	Disseminated malignant neoplasm, unspecified

Non-solid types of cancer	200.X		Lymphosarcoma and reticulosarcoma
	201.X	C81.X	Hodgkin's disease
	202.X	C82.X, C83.X, C84.X, C85X, C86.X, C96.X C88.X, C90.X	Other malignant neoplasms of lymphoid and histiocytic tissue
	203.X	C91.X	Multiple myeloma and immunoproliferative neoplasms
	204.X	C92.X	Lymphoid leukaemia
	205.X	C93.X	Myeloid leukaemia
	206.X	C94.X	Monocytic leukaemia

	207.X	C95.X	Other specified leukaemia
	208.X		Leukaemia of unspecified cell type

eTable 12. Results of 30-day mortality and morbidity categorised by the time surgery started

30-day mortality				
Operation time	**OR_{adj} (95% CI)**	**p-value**	**Total n**	**n of positive outcome**
7:00-11:59 AM	Baseline	Baseline	165,922	804
12 PM	1.13 (0.95-1.35)	0.178	27,140	182
1 PM	1.10 (0.92-1.31)	0.288	29,802	188
2 PM	1.13 (0.95-1.34)	0.176	26,402	211
3 PM	1.25 (1.04-1.49)	0.015	20,687	217
4 PM	1.32 (1.08-1.62)	0.007	13,214	166
5-6 PM	1.45 (1.19-1.78)	<0.001	9,553	194
7-8 PM	1.50 (1.13-1.99)	0.005	4,543	113
9-10 PM	1.91 (1.31-2.80)	0.001	2,688	67
11 PM - 6:59 AM	1.21 (0.70-2.09)	0.488	3,941	92
30-day morbidity				
Operation time	**OR_{adj} (95% CI)**	**p-value**	**Total n**	**n of positive outcome**
7:00-11:59 AM	Baseline	Baseline	165,922	13,681
12 PM	0.98 (0.93-1.04)	0.339	27,140	2,097
1 PM	0.97 (0.92-1.02)	0.170	29,802	2,274
2 PM	0.99 (0.94-1.05)	0.627	26,402	2,061
3 PM	1.06 (0.99-1.12)	0.073	20,687	1,676
4 PM	1.11 (1.03-1.19)	0.008	13,214	1,126
5-6 PM	1.35 (1.24-1.47)	<0.001	9,553	1,041
7-8 PM	1.65 (1.47-1.86)	<0.001	4,543	654
9-10 PM	1.92 (1.64-2.25)	<0.001	2,688	443
11 PM - 6:59 AM	1.54 (1.29-1.84)	<0.001	3,941	589

eTable 13. Subgroup analysis of the 50 most frequently performed procedures

Defined by primary surgery Current Procedural Terminology (CPT) codes. A total of 108,338 participants were included in this subgroup analysis.

CPT code description[12 13]	CPT	Frequency	Percent
Laparoscopy, surgical; cholecystectomy	47562	8,545	7.89
Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed	29881	4,841	4.47
Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)	58661	4,547	4.2
Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing (total knee arthroplasty)	27447	3,992	3.68
Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty), with or without autograft or allograft	27130	3,684	3.4
Thyroidectomy, total or complete	60240	3,645	3.36
Hysteroscopy, surgical; with sampling (biopsy) of endometrium and/or polypectomy, with or without D & C	58558	3,460	3.19
Laparoscopy, surgical, appendectomy	44970	3,333	3.08
Laminotomy (hemilaminectomy), with decompression of nerve root(s), including partial facetectomy, foraminotomy and/or excision of herniated intervertebral disc; 1 interspace, lumbar	63030	2,974	2.75
Arthrodesis, posterior or posterolateral technique, single level; lumbar (with lateral transverse technique, when performed)	22612	2,873	2.65
Thromboendarterectomy, including patch graft, if performed;	35301	2,776	2.56

carotid, vertebral, subclavian, by neck incision			
Repair initial inguinal hernia, age 5 years or older; reducible	49505	2,669	2.46
Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)	58571	2,657	2.45
Arthroscopy, shoulder, surgical; with rotator cuff repair	29827	2,626	2.42
Total abdominal hysterectomy (corpus and cervix), with or without removal of tube(s), with or without removal of ovary(s)	58150	2,589	2.39
Reduction mammaplasty	19318	2,555	2.36
Parathyroidectomy or exploration of parathyroid(s)	60500	2,490	2.3
Laparoscopy, surgical prostatectomy, retropubic radical, including nerve sparing, includes robotic assistance, when performed	55866	2,435	2.25
Biopsy or excision of lymph node(s); open, deep axillary node(s)	38525	2,123	1.96
Removal of implant; deep (e.g., buried wire, pin, screw, metal band, nail, rod or plate)	20680	2,099	1.94
Craniectomy, trephination, bone flap craniotomy; for excision of brain tumour, supratentorial, except meningioma	61510	2,088	1.93
Laminectomy, facetectomy and foraminotomy (unilateral or bilateral with decompression of spinal cord, cauda equina and/or nerve root[s], [eg, spinal or lateral recess stenosis]), single vertebral segment; lumbar	63047	2,059	1.9
Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with transbronchial needle aspiration biopsy(s), trachea, main stem and/or lobar bronchus(i)	31629	1,995	1.84
Cystourethroscopy, with ureteroscopy and/or pyeloscopy; with lithotripsy (ureteral catheterization is included)	52353	1,938	1.79

Repair initial incisional or ventral hernia; reducible	49560	1,888	1.74
Gastric restrictive procedure, with gastric bypass for morbid obesity; with short limb (150 cm or less) Roux-en-Y gastroenterostomy	43644	1,684	1.55
Arthrodesis, anterior interbody technique, including minimal discectomy to prepare interspace (other than for decompression); cervical below C2	22554	1,669	1.54
Arthroscopically aided anterior cruciate ligament repair/augmentation or reconstruction	29888	1,616	1.49
Laparoscopy, surgical, gastric restrictive procedure; longitudinal gastrectomy (ie, sleeve gastrectomy)	43775	1,592	1.47
Laparoscopy, surgical; repair initial inguinal hernia	49650	1,486	1.37
Mediastinoscopy - expired code	39400	1,430	1.32
Arthrodesis, anterior interbody technique, including minimal discectomy to prepare interspace (other than for decompression); lumbar	22558	1,419	1.31
Laparoscopy, surgical; colectomy, partial, with anastomosis	44204	1,403	1.3
Arthroplasty, glenohumeral joint; total shoulder (glenoid and proximal humeral replacement (e.g., total shoulder))	23472	1,400	1.29
Revision of reconstructed breast	19380	1,382	1.28
Repair umbilical hernia, age 5 years or older; reducible	49585	1,194	1.1
Pancreatectomy, proximal subtotal with total duodenectomy, partial gastrectomy, choledochoenterostomy and gastrojejunostomy (Whipple-type procedure); with pancreatojejunostomy	48150	1,183	1.09
Enterectomy, resection of small intestine; single resection and anastomosis	44120	1,177	1.09
Nasal/sinus endoscopy, surgical; with biopsy, polypectomy or	31237	1,176	1.09

debridement (separate procedure)			
Treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; with intramedullary implant, with or without interlocking screws and/or cerclage	27245	1,109	1.02
Arthroscopy, knee, surgical; with meniscectomy (medial AND lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed	29880	1,088	1
Total thyroid lobectomy, unilateral; with or without isthmusectomy	60220	1,087	1
Thyroidectomy, including substernal thyroid; cervical approach	60271	1,082	1
Mastectomy, partial	19302	1,076	0.99
Septoplasty or submucous resection, with or without cartilage scoring, contouring or replacement with graft	30520	1,067	0.98
Colectomy, partial; with anastomosis	44140	1,059	0.98
Thoracoscopy, surgical; with lobectomy (single lobe)	32663	1,036	0.96
Renal allotransplantation, implantation of graft; without recipient nephrectomy	50360	1,018	0.94
Cystourethroscopy, with insertion of indwelling ureteral stent (e.g., Gibbons or double-J type)	52332	1,014	0.94
Cholecystectomy	47600	1,010	0.93

eTable 14. Results of additional subgroup analyses

Sensitivity analyses evaluating the robustness of the primary analysis within additional subgroups.

Subgroup analysis by:	**OR_{adj}, p-value**	**Sample size**
Age (quartiles)	1.86 p=0.03 1.44 p=0.028 1.37 p=0.014 1.31 p=0.001	77,179 73,344 73,783 72,242
Work RVUs (quartiles)	1.37 p=0.003 1.41 p=0.029 1.46 p=0.003 1.32 p=0.024	76,508 74,991 68,957 74,975
Hospital network (institution A versus B)	1.52 p<0.001 1.22 p=0.013	143,860 159,957
Anaesthesia provider type (residents, certified registered nurse anaesthetist, or attendings)	1.33 p<0.001 1.47 p=0.018 1.41 p=0.017	178,283 85,517 39,686

eTable 15. Results after adjusting for additional confounding variables

Additional confounding variables were separately added to the logistic regression model.

Additional confounding variable	OR_{adj} [95% CI], p-value	Sample size*
Weekend surgery	1.36 [1.20-1.53], p<0.001	Full cohort
Procedural severity score[14]	1.37 [1.19-1.56], p<0.001	240,855
Community hospital status	1.36 [1.20-1.53], p<0.001	Full cohort
Intraoperative opioid dose	1.37 [1.21-1.54], p<0.001	Full cohort
Score for Prediction of Postoperative Respiratory Complications > 6[15]	1.36 [1.20-1.53], p<0.001	Full cohort
NMBA dose (measured as multiples of NMBA dose needed to reduce twitch height by 95 %)	1.36 [1.20-1.53], p<0.001	303,887
Age-adjusted minimum alveolar concentration of volatiles and nitrous oxide[16]	1.35 [1.19-1.52], p<0.001	Full cohort
Federal insurance status	1.35 [1.20-1.53], p<0.001	303,671
*The number of patients per analysis was determined by the data that were available for the additional confounding variable.		

eTable 16. ICD-9 and ICD-10 codes to define potential causes of death (validated postoperative complications).

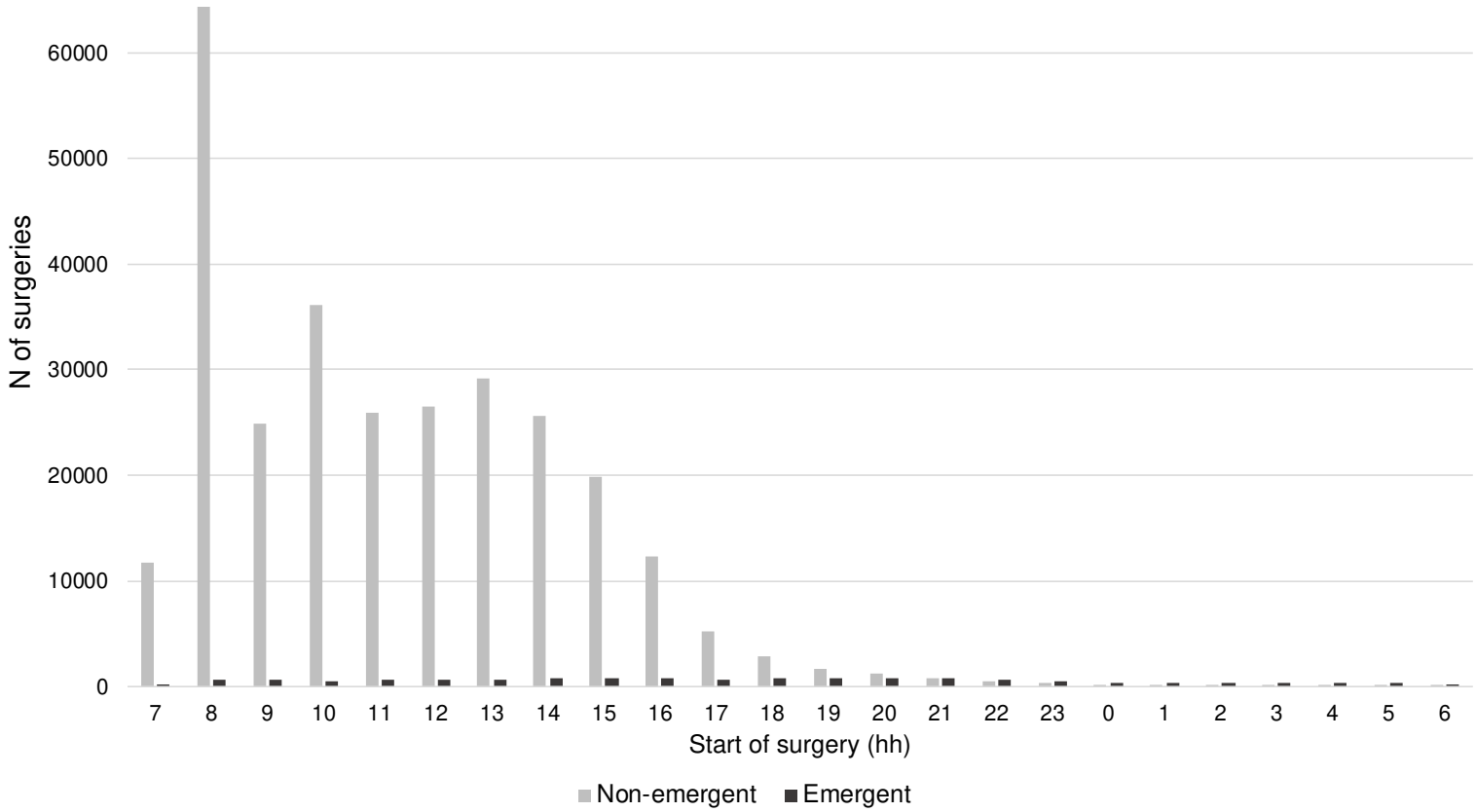
Types of complications	**ICD-9 and ICD-10 diagnostic and procedure codes**
Acute renal failure	584.5 Acute kidney failure with lesion of tubular necrosis 584.6 Acute kidney failure with lesion of renal cortical necrosis 584.7 Acute kidney failure with lesion of renal medullary [papillary] necrosis 584.8 Acute kidney failure with other specified pathological lesion in Kidney N17.0 Acute kidney failure with tubular necrosis N17.1 Acute kidney failure with acute cortical necrosis N17.2 Acute kidney failure with medullary necrosis N17.8 Other acute kidney failure N17.9 Acute kidney failure, unspecified
Myocardial infarction	410 Acute myocardial infarction I21 Acute myocardial infarction I22 Subsequent ST elevation (STEMI) and non-ST elevation (NSTEM) myocardial infarction
Cardiac arrest	427.5 Cardiac arrest I46 Cardiac arrest

Acute heart failure	428.0 Congestive heart failure, unspecified 428.1 Left heart failure 428.20 Systolic heart failure, unspecified 428.21 Acute systolic heart failure 428.23 Acute on chronic systolic heart failure 428.30 Diastolic heart failure, unspecified 428.31 Acute diastolic heart failure 428.33 Acute on chronic diastolic heart failure 428.40 Combined systolic and diastolic heart failure, unspecified 428.41 Acute combined systolic and diastolic heart failure 428.43 Acute on chronic combined systolic and diastolic heart failure 428.9 Heart failure, unspecified I50.1 Left ventricular failure, unspecified I50.20 Unspecified systolic (congestive) heart failure I50.21 Acute systolic (congestive) heart failure I50.23 Acute on chronic systolic (congestive) heart failure I50.30 Unspecified diastolic (congestive) heart failure I50.31 Acute diastolic (congestive) heart failure I50.33 Acute on chronic diastolic (congestive) heart failure I50.40 Unspecified combined systolic (congestive) and diastolic (congestive) heart failure I50.41 Acute combined systolic (congestive) and diastolic (congestive) heart failure

	I50.43 Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure I50.9 Heart failure, unspecified
Stroke	433.01 Occlusion and stenosis of basilar artery with cerebral infarction 433.11 Occlusion and stenosis of carotid artery with cerebral infarction 433.21 Occlusion and stenosis of vertebral artery with cerebral infarction 433.31 Occlusion and stenosis of multiple and bilateral precerebral arteries with cerebral infarction 433.81 Occlusion and stenosis of other specified precerebral artery with cerebral infarction 433.91 Occlusion and stenosis of unspecified precerebral artery with cerebral infarction 434.01 Cerebral thrombosis with cerebral infarction 434.11 Cerebral embolism with cerebral infarction 434.91 Cerebral artery occlusion, unspecified with cerebral infarction 437.1 Other generalized ischemic cerebrovascular disease 437.9 Unspecified cerebrovascular disease I63 Cerebral infarction I67.81 Acute cerebrovascular insufficiency I67.89 Other cerebrovascular disease I67.9 Cerebrovascular disease, unspecified

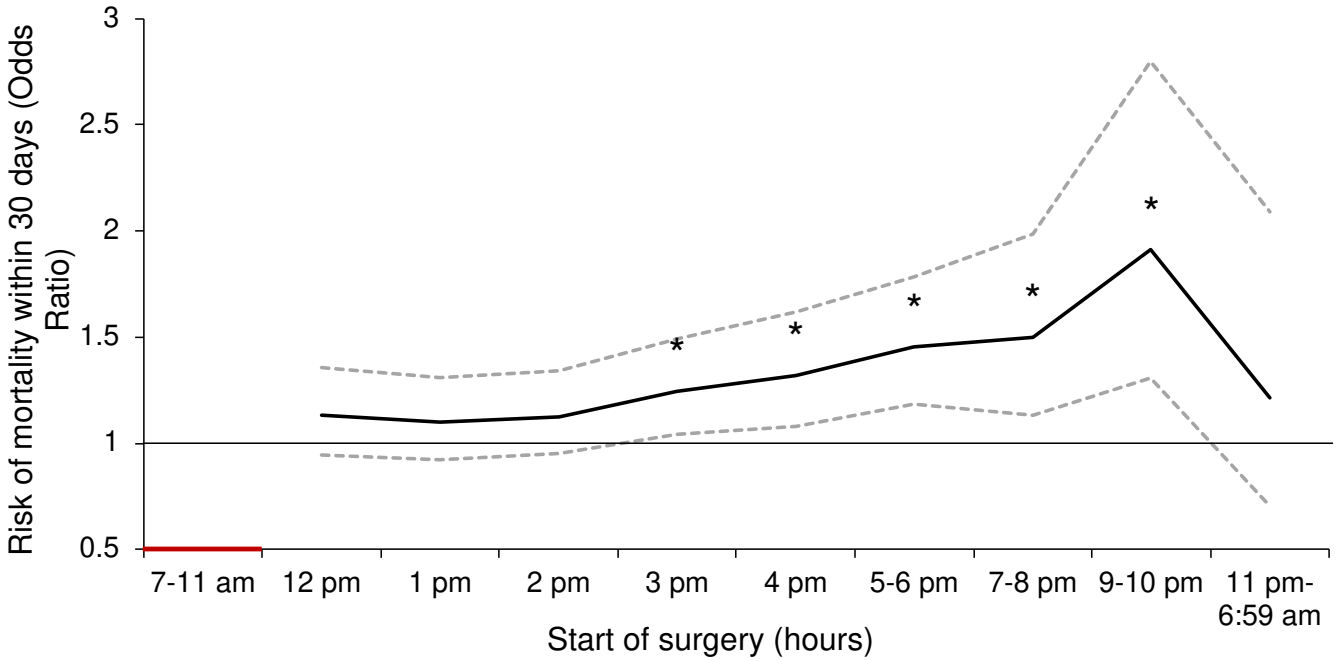
8 Supplemental figures

eFigure 1. Distribution of emergency and non-emergency cases throughout the day

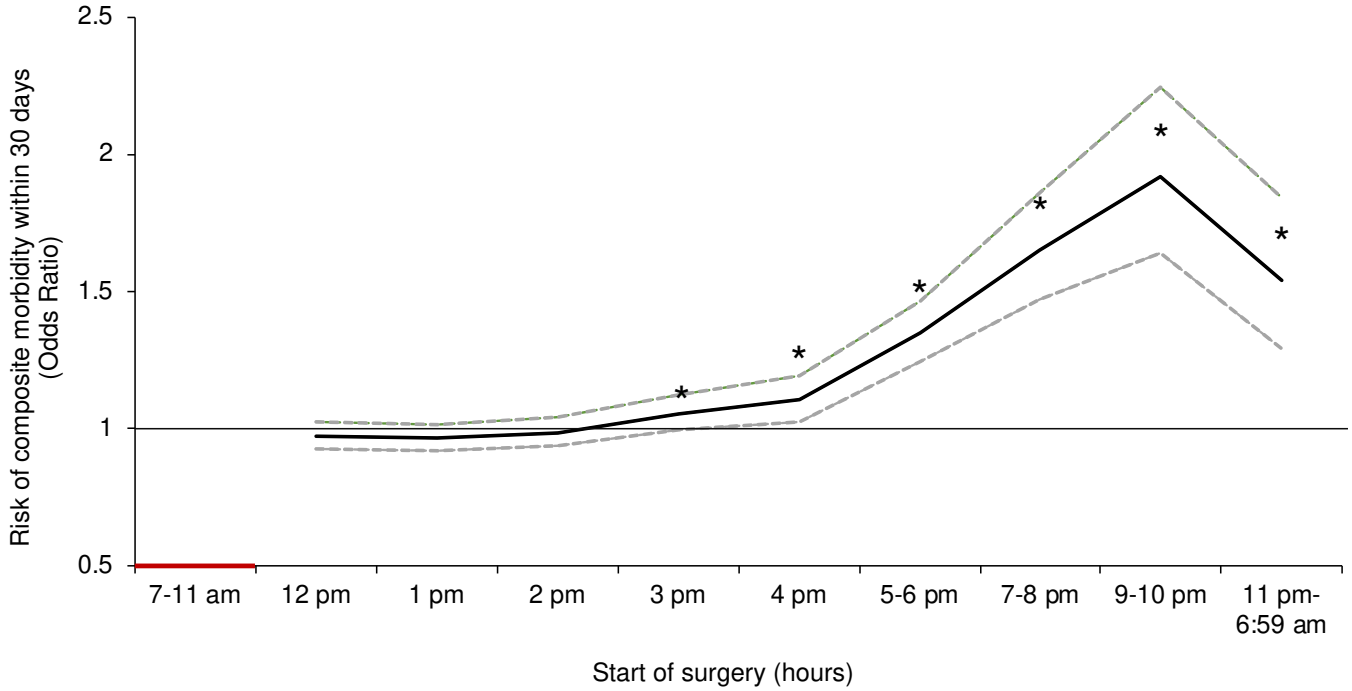


eFigure 2a. Adjusted odds ratios for mortality within 30 days of non-emergency surgery

Odds of 30-day mortality and morbidity after surgery started 3:00-10:59 pm and 3:00pm-6:59 am, respectively, were significantly higher ($p<0.05$) than after baseline risk morning hours from 07:00 to 11:59 h. The figure demonstrates adjusted odds ratios (—) and 95% confidence intervals (···) compared with baseline risk morning hours (_).

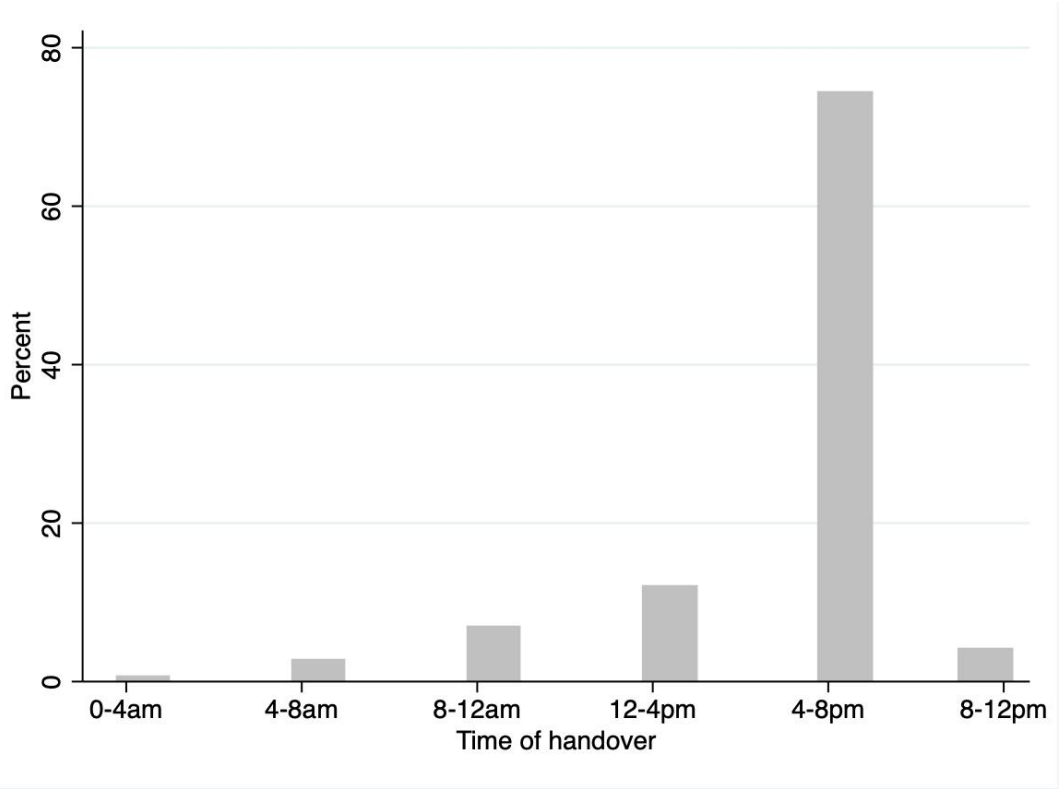


eFigure 2b. Adjusted odds ratios for 30-day morbidity within 30 days of non-emergency surgery



eFigure 3. Proportion of handovers between anaesthesiologists throughout the day

The percentage of handovers between anaesthesiologists occurring between 5 pm and 7 pm is 57 %. Overall, 65 % versus 35 % of handovers occurred during the night and day surgery periods, respectively. Patients undergoing night surgery were also disproportionately affected by multiple handovers (0.36 % of patients during day versus 0.99 % during night surgeries).



9 References

1. Althoff FC, Neb H, Herrmann E, et al. Multimodal Patient Blood Management Program Based on a Three-pillar Strategy: A Systematic Review and Meta-analysis. *Annals of surgery* 2019;269(5):794-804. doi: 10.1097/sla.0000000000003095 [published Online First: 2018/11/13]
2. Hallet J, Mahar AL, Tsang ME, et al. The impact of peri-operative blood transfusions on post-pancreatectomy short-term outcomes: an analysis from the American College of Surgeons National Surgical Quality Improvement Program. *HPB : the official journal of the International Hepato Pancreato Biliary Association* 2015;17(11):975-82. doi: 10.1111/hpb.12473 [published Online First: 2015/08/25]
3. Meybohm P, Herrmann E, Steinbicker AU, et al. Patient Blood Management is Associated With a Substantial Reduction of Red Blood Cell Utilization and Safe for Patient's Outcome: A Prospective, Multicenter Cohort Study With a Noninferiority Design. *Annals of surgery* 2016;264(2):203-11. doi: 10.1097/sla.0000000000001747 [published Online First: 2016/05/11]
4. Rohde JM, Dimcheff DE, Blumberg N, et al. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA* 2014;311(13):1317-26. doi: 10.1001/jama.2014.2726 [published Online First: 2014/04/03]
5. Jones PM, Cherry RA, Allen BN, et al. Association Between Handover of Anesthesia Care and Adverse Postoperative Outcomes Among Patients Undergoing Major Surgery. *JAMA* 2018;319(2):143-53. doi: 10.1001/jama.2017.20040
6. Kidney Disease: Improving Global Outcomes (KDIGO) KDIGO Clinical Practice Guideline for Acute Kidney Injury. Acute Kidney Injury Work Group: Kidney Int Suppl, 2012.

7. Mehta RL, Kellum Ja Fau - Shah SV, Shah Sv Fau - Molitoris BA, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. (1466-609X (Electronic))
8. Shin CH, Long DR, McLean D, et al. Effects of Intraoperative Fluid Management on Postoperative Outcomes: A Hospital Registry Study. (1528-1140 (Electronic))
9. Santer P, Zheng S, Hammer M, et al. Ventilatory frequency during intraoperative mechanical ventilation and postoperative pulmonary complications: a hospital registry study. (1471-6771 (Electronic))
10. Schaefer MS, Raub D, Xu X, et al. Association between propofol dose and 1-year mortality in patients with or without a diagnosis of solid cancer. (1471-6771 (Electronic))
11. Kork F, Spies C, Conrad T, et al. Associations of postoperative mortality with the time of day, week and year. *Anaesthesia* 2018;73(6):711-18. doi: 10.1111/anae.14228 [published Online First: 2018/02/24]
12. National Center for Biomedical Ontology, Current Procedural Terminology [Available from: http://bioportal.bioontology.org/ontologies/CPT.
13. Bulletin of the American College of Surgeons, 2016 CPT coding changes and their effects [Available from: http://bulletin.facs.org/2016/01/2016-cpt-coding-changes-and-their-effects.
14. Dalton JE, Kurz A Fau - Turan A, Turan A Fau - Mascha EJ, et al. Development and validation of a risk quantification index for 30-day postoperative mortality and morbidity in noncardiac surgical patients. (1528-1175 (Electronic))
15. Brueckmann B, Villa-Uribe Jl Fau - Bateman BT, Bateman Bt Fau - Grosse-Sundrup M, et al. Development and validation of a score for prediction of postoperative respiratory complications. (1528-1175 (Electronic))

16. McLean DJ, Diaz-Gil D Fau - Farhan HN, Farhan Hn Fau - Ladha KS, et al. Dose-dependent Association between Intermediate-acting Neuromuscular-blocking Agents and Postoperative Respiratory Complications. (1528-1175 (Electronic))

Effects of Night Surgery on Postoperative Mortality and Morbidity - A Multicentre Cohort Study

Supplemental Digital Content 2

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page*
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	7 Supplemental Digital Content 1, section 6.1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-7 Supplemental Digital Content 1, section 2-6, eTables 1, 2, 11, 16
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 Suppelemtal Digital Content 1, section 1, 4
Bias	9	Describe any efforts to address potential sources of bias	4-7; Supplemental Digital Content 1, section 6
Study size	10	Explain how the study size was arrived at	4, 8 Figure 1 Supplemental Digital Content 1, section 3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-8 Supplemental Digital Content 1, section 2,

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	4-8 Supplemental Digital Content 1, section 2-7
		(b) Describe any methods used to examine subgroups and interactions	4-6 Supplemental Digital Content 1, section 4-6, eTables 5-16
		(c) Explain how missing data were addressed	4, 7 Supplemental Digital Content 1, section 3
		(d) If applicable, explain how loss to follow-up was addressed	n.a.
		(e) Describe any sensitivity analyses	6, 7 Supplemental Digital Content 1, section 4-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8 Figure 1 Supplemental Digital Content 1, section 3
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 9 Table 1 Table 2 eTables 3-5
		(b) Indicate number of participants with missing data for each variable of interest	Figure 1
		(c) Summarise follow-up time (eg, average and total amount)	n.a.
Outcome data	15*	Report numbers of outcome events or summary measures over time	7-9 Table 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-9 Tables 2-4 eTable 2
		(b) Report category boundaries when continuous variables were categorized	Supplemental Digital Content, section 2 eTable 2
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n.a.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11 Tables 3-4 eTables 5, 6, 7, 8, 9, 10, 12, 13, 14, 15
Discussion			

Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

n.a. = not applicable

* Pages according to page numbers in the manuscript.