Intraoperative Driving Pressure and Postoperative Pulmonary Complications After Abdominal Surgery – A Posthoc Propensity Score–Weighted Cohort Analysis of the LAS VEGAS Study Comparing Open to Closed Surgery

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Abstract

Background: It is uncertain whether associations between driving pressure (ΔP) during and occurrence of pulmonary complications after abdominal surgery depend on the surgical approach. Our primary objective was to test the time–weighted average ΔP (ΔP_{TW}) association with postoperative pulmonary complications and our secondary objective was to test the association between ΔP_{TW} and intraoperative Adverse Events.

Methods: We realized a posthoc retrospective propensity score weighted cohort analysis of the 'Local ASsessment of Ventilatory management during General Anesthesia for Surgery' (LAS VEGAS) study including patients undergoing abdominal surgery from the study database including data from 146 hospitals across 29 countries. The primary endpoint was a composite of postoperative pulmonary complications. The secondary endpoint was the occurrence of intraoperative adverse events.

Results: The analysis included 1,128 and 906 patients undergoing open or closed abdominal surgery repsectively. Absolute postoperative pulmonary complications rate was 5%. While driving pressure was lower in open abdominal surgery patients, time-weighted driving pressure was not different between groups. The association of ΔP_{TW} with occurrence of postoperative pulmonary complications was significant in both groups, with a higher risk ratio in closed than in open abdominal surgery patients (1.11 [95%CI 1.10 to 1.20], P<0.001 vs. 1.05 [95% CI 1.05 to 1.05; P<0.001; risk difference 0.05: [95%CI 0.04 to 0.06], P<0.001). ΔP_{TW} marginal effect estimation showed increased probability of pulmonary complication in both groups with a steeper increase in closed surgery patients at ΔP_{TW} above 20 $cmH_2O{\bullet}hour^{-1}$. The association of ΔP_{TW} with occurrence of intraoperative adverse events was also significant in both groups, with higher odds ratio in closed surgery (1.13 [95%CI 1.12 to 1.14]; P<0.001 vs. 1.07 [95%CI 1.05 to 1.10]; P<0.001; difference 0.05 [95%CI 0.03 to 0.07]; p<0.001).

Conclusions: Our results show how driving pressure represents a marker for pulmonary complications and adverse events in abdominal surgery regardless of surgical approach.

Trial registration: LAS VEGAS was registered at clinicaltrials.gov (trial identifier NCT01601223).

Introduction

The incidence of postoperative pulmonary complications varies between 9 and 40%, depending on definitions and studied populations, [1] and their occurrence is associated with increased morbidity and mortality.[2,3] Postoperative pulmonary complications can be prevented by reducing lung strain using a low tidal volume (V_T) [4] and sufficient positive end–expiratory pressure (PEEP).[5] Since the driving pressure, defined as the difference between plateau pressure and PEEP, is also strongly associated with the development of postoperative pulmonary complications, [5,6] titrating V_T and PEEP to minimise it could be an effective strategy to prevent pulmonary complications.

The respiratory system overall behaviour depends on its components properties, i.e., the artificial and native airways, lung tissue, and the chest wall consisting of the rib cage and the diaphragm. A part of the force applied during invasive ventilation is used to expand the chest wall, and another fraction to inflate the lungs.[7] When the chest wall elastance increases, e.g., during pneumoperitoneum, the driving pressure increases even when V_T is left unchanged.[8] This rise is interpreted as unharmful and may cause reluctance to target a low driving pressure in the presence of intraoperative pneumoperitoneum, i.e., during closed abdominal surgery. However, the cephalad shift of the diaphragm could induce or worsen atelectases, and the resulting increase in driving pressure is related with a rise in lung applied force.[9] Driving pressure effect during pneumoperitoneum can be thus mixed.

To determine and compare the exact associations between driving pressure and development of postoperative pulmonary complications in patients undergoing open abdominal surgery versus patients undergoing closed abdominal surgery, we reassessed the database of the 'Local ASsessment of Ventilatory management during General Anesthesia for Surgery' (LAS VEGAS) study. [10] The LAS VEGAS study was a prospective international observational study that showed a large proportion of surgery patients to be at an increased risk of pulmonary complications. It also showed intraoperative ventilation that consists of relatively high V_T and low PEEP.

The primary hypothesis tested in this analysis was that the association between driving pressure and development of pulmonary complications is weaker in closed abdominal surgery patients than in open abdominal surgery patients. Our primary objective was to test the time–weighted average driving pressure (ΔP_{TW}) association with postoperative pulmonary complications, and our secondary objective was to test the association between ΔP_{TW} and intraoperative adverse events.

Methods

Study design and setting

This is a posthoc analysis of the LAS VEGAS study database, [10] and was carried out in accordance to current guidelines and the recommendations of the statement for strengthening the reporting of observational studies in epidemiology (STROBE) (www.strobe-statemenent.org). The statistical analysis plan was predefined, updated and finalised before data extraction and is presented as **Additional File 1**. The LAS VEGAS study is a worldwide international multicentre prospective seven–day observational study describing intraoperative ventilation practice, occurrence of intraoperative complications and PPCs in the first five postoperative days, and hospital length of stay and mortality.

The study protocol was approved by the ethical committee of the Academic Medical Center, Amsterdam, the Netherlands (W12_190#12.17.0227). Each participating centre obtained approval from their institutional review board if needed, and patients were included after obtaining written informed consent when dictated by national or regional legislation. The LAS VEGAS study was partially funded and endorsed by the European Society of Anaesthesiology and registered at https://clinicaltrials.gov (NCT01601223, First posted date: 17/05/2012).

Inclusion and exclusion criteria

The LAS VEGAS study recruited patients undergoing general anaesthesia with mechanical ventilation for surgery consecutively during seven days in each participating centre between 14 January and 4 March 2013. Exclusion criteria of the LAS VEGAS study were: (1) age < 18 years, (2) invasive ventilation in the preceding month, (3) obstetric or ambulatory surgical interventions, and (4) cardiothoracic surgery cardiopulmonary bypass.

For the current posthoc analysis, the studied cohort is restricted to patients undergoing an abdominal intervention with sufficient data to calculate driving pressure at least at one time point other than induction of anaesthesia. Also, to increase the homogeneity of the compared patient cohorts, patients who had received intraoperative ventilation through an airway device other than a tracheal tube and patients under assisted or spontaneous ventilation mode were excluded. Patients in whom laparoscopy only assisted the surgery, i.e., surgeries that could not be classified as mere open or mere closed abdominal surgery, were also excluded from the current analysis.

Data recording and calculations

Full details on data collection can be found in the original paper [10] and **Additional File 2**. In the study database, ventilatory parameters at every hour of surgery, from induction up to the last hour of surgery were recorded.

Using the data as collected in the LAS VEGAS database, the following calculations were done for the current analysis. Driving pressure was calculated by subtracting PEEP from plateau pressure or inspiratory pressure at every hour in volume–controlled and pressure–controlled ventilated patients, respectively. ΔP_{TW}, i.e., the pressure that is proportional to the amount of time spent at each driving pressure in relation to the total time, was calculated by summing the mean values between consecutive time points multiplied by the time between those points and then dividing by the entire time. [11] Similarly, time–weighted average peak pressure and PEEP were determined. Details on calculations are provided in the **Additonal File 2 Figure S1**.

Definitions

The LAS VEGAS study had a rigid study protocol that was approved before data collection took place, as reported elsewhere. [10] The statistical analysis plan was written, updated, and finalised before data extraction. We used for this analysis severe postoperative pulmonary complications defined in the protocol as a collapsed composite of the following events: unexpected postoperative invasive or non–invasive ventilation, acute respiratory failure, acute respiratory distress syndrome, pneumonia, and pneumothorax. The occurrence of each type of complication was monitored until hospital discharge but restricted to the first five postoperative days.

Intraoperative adverse events were predefined and described in the protocol of the LAS VEGAS study as follows: any oxygen desaturation or lung recruitment manoeuvres performed to rescue from hypoxemia, any need for adjusting ventilator settings for reducing airway pressures or correction of expiratory flow limitation, any hypotension or need for vasoactive drugs, and any new cardiac arrhythmia. Since the simultaneous occurrence of various adverse events is frequent, we analysed them as an ordinal variable with a range spanning from zero to seven adverse events.

A detailed list of definitions of the composites of postoperative pulmonary complications and intraoperative adverse events is provided in **Additional File 2Table S1** and **Table S2**.

Endpoints

The primary endpoint was the composite of postoperative pulmonary complications. The secondary endpoint was the occurrence of one or more intraoperative adverse events.

Control of Bias

Bias controlling strategy is reported in **Additional File 2 Statistics**.

Analysis plan

The analysis plan was prespecified before data access, and we used data of all available patients in LAS VEGAS database without formal sample size calculation. Also, as the purpose of the analysis was exploring a physiological hypothesis, we did not specify any *a priori* effect size.

Continuous variables were reported as median and interquartile ranges; categorical variables expressed as n (%). Normality of distributions was assessed by inspecting quantile–quantile plots. If variables were normally distributed, the two–sample t–test was used, if not, the Wilcoxon rank sum test was used. For categorical variables, we used the Chi–square test or Fisher's exact test, or when appropriate as relative risks. Statistical uncertainty was expressed by showing the 95%–confidence intervals (CI).

We estimated whether ΔP_{TW} was associated with the occurrence of postoperative pulmonary complications with a weighted mixed–effect logistic regression and whether ΔP_{TW} was associated with intraoperative adverse events with a mixed ordinal regression. To fit every model, centres as a random intercept and an inverse probability weighting (IBW) factor computed from the covariate–balancing propensity score (CBPS) method to simultaneously optimise prediction of treatment assignment, i.e. ΔP_{TW} as a continuous variable, and confounders influence were introduced. [12] The CBPS procedure sets mean independence between treatment, i.e. ΔP_{TW}, and covariates to ensure covariate balancing and estimates the propensity score with the generalised method of moments method. For both outcomes, we fitted a model for each of the compared patient cohorts respectively, i.e., patients who underwent open surgery intervention and those who underwent a closed surgical intervention. We used a Wald z-test to test the difference between odds ratios from models fitted on closed and open surgery cohort. Models' goodness of fit was assessed by residual diagnosis based on scaled quantile residuals (R *DHARMa* package v. 0.2.4) and simulated residuals (R *sure* package v 0.2.0) for logistic and ordinal models, respectively.

To build the CBPS to relate exposure variable, i.e. ΔP_{TW}, with potential confounders, we included by clinical judgment the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) risk class, [13,14] and the average intraoperative V_T and then we performed feature selection with an augmented backward elimination selection method introducing 37 pre– and intraoperative variables (**Additional File 2 Statistics** for a detailed list). The selection was based on a sequential process where initially all variables entered the model and finally those pre– and intraoperative factors that yielded a change in the effect estimate > 0.1 and a significance criterion (alpha) < 0.1 were included. The algorithm stopped when all variables left in the model complied with both criteria. [15] We carried out a selection process of potential variables to avoid bias in the effect estimates using a comprehensive strategy to prevent the drawbacks of simple stepwise methods. [16] The internal validation of the model was assessed by bootstrap using five hundred generated samples and estimating the Area Under Curve (AUC) of the full and stepwise–selected variables models.

To further unravel the role of surgical approach, i.e., closed versus open abdominal surgery, on postoperative pulmonary complications we performed a sensitivity analysis fitting a mixed logistic regression with a random intercept for centre on a propensity score matched cohort. The propensity was used to match patients with a similar covariable structure using the R *matchit* package carrying out the matching with the nearest neighbour method with a caliper of 0.1 with a ratio of patients in the open surgery arm of 2 to 1. Full details on the covariables introduced in the propensity score matching procedure can be found in the **Additional File 2 Statistics**. To assess the type of surgery as an effect modifier, we carried out another sensibility analysis fitting a weighted mixed logistic regression model an all data, i.e. both surgery cohorts, introducing type of surgery as an independent variable and an interaction term between ΔP_{TW} and type of surgery.

Statistical significance was considered for two–tailed $P<0.05$. No imputation routine of missing values and no correction for multiple comparisons was prespecified; thus, all the findings should be viewed as exploratory. All analyses were performed with R 3.5.2 (The R Foundation for Statistical Computing, www.r-project.org).

Results

Patients

Of 2,034 abdominal surgery patients in the LAS VEGAS study, 1,218 (60%) patients underwent an open abdominal intervention, and 906 (40%) patients, a closed abdominal surgical procedure (**Figure 1**).

Baseline demographic data, surgery–related and intraoperative ventilation characteristics are presented in **Tables 1** and **2**, and **Figure 2**. Open abdominal surgery patients had higher ASA class and ARISCAT risk score, lower functional status, and fewer elective procedures, longer surgery times, less neuromuscular reversals, and received more intraoperative transfusions and fluids. Those on the lower abdomen were the most frequently performed interventions in the open abdominal surgery patients, while interventions on the upper abdomen were performed more often in closed abdominal surgery patients. ΔP_{TW} was not different between the open and closed surgery groups, (**Table 2**).

Primary and secondary outcome rates

In 102 (5%) patients, one or more postoperative pulmonary complications occurred, and their prevalence was higher in open surgery patients than in patients who underwent a closed surgical procedure (7 vs. 3%; P<0.001). Hypotension or need for vasopressors was more frequently observed during open surgery, while the need for airway pressure reduction was more often needed during closed surgery (**Table 3**).

Propensity score estimation variables

The variables that finally entered the propensity core and covariate balance assessment are detailed in the **Additional File 2 Statistics** and **Figure S2** and **S3**.

Association between driving pressure and occurrence of postoperative pulmonary complications

The association of ΔP_{TW} with the development of postoperative pulmonary complications was statistically significant in both surgical groups, however the association was stronger in closed abdominal surgery patients (odds ratio (OR), 1.17 [95%CI 1.16 to 1.19]; P<0.001; risk ratio (RR), 1.11 [95%CI 1.10 to 1.20], P<0.001) than in patients who underwent an open abdominal surgical intervention (OR, 1.07 [95%CI 1.06 to 1.08]; P<0.001; RR 1.05 [95% CI 1.05 to 1.05]). The association was stronger in closed compared to open abdominal surgery (difference between ORs: 0.09 [95%CI 0.07 to 0.10]; P<0.001; risk difference 0.05: [95%CI 0.04 to 0,06]), P<0.001. Residuals plot are reported in **Additional File Figure S4**.

Association between driving pressure and occurrence of adverse events

The association of ΔP_{TW} with the appearance of intraoperative AEs was statistically significant in both open and closed surgery patients, and also here the association was stronger in closed surgery patients (1.13 [95%CI 1.12 to 1.14]) than in patients who underwent an open abdominal intervention (1.07 [95%CI 1.05 to 1.10]), difference between ORs 0.05 [95%CI 0.03 to 0.07]; P<0.001.

Sensitivity analyses

The association of ΔP_{TW} with occurrence of postoperative pulmonary complications was statistically significant (OR, 1.08 [95%CI 1.06 to 1.09], P<0.001) with closed surgery patients having a lower probability of occurrence (OR, 0.14 [95%CI 0.12 to 0.16, P<0.001) with a statistical significant interaction between ΔP_{TW} and closed surgery (OR, 1.09 [95%CI 1.08 to 1.11], P<0.001). The marginal effect of ΔP_{TW} by type of surgery on postoperative pulmonary complication occurrence probability is showed in **Figure 3.** A rise in ΔP_{TW} was associated with increased probability of pulmonary complications in both types of surgery with a steeper increase in closed surgery patients for ΔP_{TW} above 20 $cmH_2O \bullet hour^{-1}$.

After matching, the resulting cohort consisted of 344 open surgery patients, and 254 closed surgery patients. Baseline characteristics between groups were well balanced (**Additional File 2Table S2** and **S3**). Type of surgery at matched levels of driving pressure was not associated with either outcome. (**Additional File 2Table S4** and **S5**).

Discussion

The analysis' main findings can be summarised as follows: (i.) the intraoperative ΔP_{TW} was not different between open and closed surgery groups, and (ii.) was associated with an increased risk of pulmonary complications occurrence of 10% and 5% for each additional $cmH2O \bullet hour^{-1}$ in closed and open surgery patients respectively; (iii.) was associated with the appearance of intraoperative adverse events, and (iv.) type of surgery has a modifying effect on the association between ΔP and postoperative pulmonary complications, although this was not confirmed in the matched cohort analysis.

This analysis uses the database of a worldwide international multicentre prospective observational study as a convenience sample, [10] strictly followed a plan, and was characterised by a robust method accounting for the multilevel data structure and allowing precise estimation and confounder control, even with seven or fewer events per confounder. [17,18] Also, the outcome of interest, i.e., severe postoperative pulmonary complications, was predefined, well–described, and largely followed the European Perioperative Clinical Outcome (EPCO) group definitions. [19]

A recent metanalysis of individual trials' on protective ventilation during general anaesthesia including patients undergoing cardiac and thoracic surgery found a significant association between driving pressure and the occurrence of pulmonary complications (OR 1.16, 95% CI 1.13 to 1.19; p<0·0001). [5] We found an almost identical association between driving pressure and pulmonary complications in closed abdominal surgery patients. Our results, thus, confirm that driving pressure might be a promising target for preventative interventions aiming at reducing pulmonary complications also in patients undergoing closed surgery. While the sensibility analysis with type of surgery as interaction confirmed the main analysis' results, the propensity score matched sensitivity analysis did not, although the matching process lead to a decrease in sample size thus limiting statistical power.

Respiratory driving pressure is an indicator of the amount of strain delivered to the respiratory system during mechanical ventilation. [7] Several studies investigated the effect of pneumoperitoneum on respiratory mechanics. Pneumoperitoneum was consistently found to decrease chest wall compliance, whereas lung compliance seems mostly spared by it. [20–27] Thus, inferring the amount of lung strain from plateau pressure and PEEP during pneumoperitoneum is challenging, since the part of the rise in plateau pressure caused by chest wall stiffening should not intensify lung it. [28] Consequently, a higher driving pressure during closed abdominal surgery could be less harmful or even ‘non–injurious’. The results of the current study reject this assumption, as a driving pressure rise was stronger associated with an increase in the occurrence of PPCs in closed abdominal surgery patients compared to open abdominal surgery.

Indeed, pneumoperitoneum can affect lung mechanics in several ways. [20–27] A cranial shift of the diaphragm during laparoscopic surgery increases alveolar collapse, especially in lung parts close to the diaphragm. This is particularly true in upper abdominal surgery, which was the most common surgical procedure in patients undergoing closed surgery in the here studied cohort. [29,30] PEEP may partially prevent this, and usually only when high PEEP is used. [31] In the patients studied here, mostly low PEEP was used, regardless of the group. Additional studies are needed to test how high PEEP affects the association between intraoperative driving pressure and postoperative pulmonary complications. Also, we found that driving pressure was higher in closed as compared to open abdominal surgery patients. However, since open abdominal surgeries lasted longer, ΔP_{TW} was remarkably similar in the two study groups, thus, at least in part, a higher absolute driving pressure was compensated by shorter duration of intraoperative ventilation, and vice versa. Indeed, the time–weighted parameter allows to estimate an exposure limit threshold to an injurious factor as in occupational health. The steeper increase in probability of pulmonary complications above a 20 $cmH_2O \bullet hour^{-1}$ can be related with increased atelectasis at low PEEP in this cohort of patients.

As expected, postoperative pulmonary complications occurred more frequently in open abdominal surgery patients. This could be explained by an increased baseline risk for pulmonary complications due to typical differences in patient characteristics but also given the duration and the type of surgery. However, this finding that pulmonary complications occurred more often in open abdominal surgery patients strengthens the current analysis since we observed the association even in a cohort of patients, i.e. closed abdominal surgery, at low risk for postoperative pulmonary complications and even after controlling for confounding effects with propensity score analysis.

Several intraoperative ventilation approaches, like the use of recruitment manoeuvres and higher PEEP, may result in a lower driving pressure. [32,33] Findings of a metanalysis including clinical trials on intraoperative ventilation suggest that PEEP titrations that resulted in a driving pressure rise increased the risk of postoperative pulmonary complications. [5] One randomised clinical trial showed an intraoperative PEEP strategy targeting the best compliance to reduce occurrence of pulmonary complications, though this was only a secondary endpoint in that study.[34] Thus, the best approach to minimise postoperative pulmonary complications is still debated.

ΔP_{TW} was associated with intraoperative adverse events in both closed and open surgery patients. Among adverse events, airway pressure reduction was more frequently needed in closed surgery group underlining the need of ventilation strategies aimed at lowering peak and plateau pressures in this group of patients reflecting unacceptable high airway pressure during surgery.

Several limitations must be acknowledged. Our used PPCs definitions are previous to those recently proposed, [1] although comparable. The LAS VEGAS study protocol did not include oesophageal pressure recording. Information regarding surgical positioning was not collected, and intra–abdominal pressure levels were not recorded in the database of the LAS VEGAS study. Both could influence ΔP. [35–37] Also, the granularity of airway pressure data is limited to hourly time points and time and driving pressure values are assessed as a whole thus we cannot estimate the effect of pressure alone. Furthermore, we only included patients intubated and ventilated in controlled mode, thus limiting our focus on a specific type of intraoperative airway device and ventilation mode, however still representative of most surgical patients. Of note, 25% of patients had a Body Mass Index (BMI) > 30. Extrapolation of the findings of this analysis to obese or morbidly obese patients should be done with some caution. Also, the original LAS VEGAS study was performed 7 years ago. Since then, there could have been changes in clinical practice, e.g., in the use of 'Enhanced Recovery After Surgery' (ERAS) pathways, as well as muscle relaxant monitoring during and reversal at the end of surgery. Although the time gap between research findings and practice changes usually lasts longer than a decade, [38–40] it still could be that more immediate changes may affect the here found associations. Finally, we did not set any a priori effect threshold nor multiple comparisons correction; hence the results' statistical significance and the exploratory nature of secondary outcome analysis must be confirmed in future trials.

Conclusions

Time–weighted driving pressure is associated with increased occurrence of postoperative pulmonary complications and intraoperative adverse events in abdominal surgery. These associations are stronger in closed abdominal surgery patients than in open abdominal surgery patients. In both patient categories, driving pressure could be a promising target for the prevention of postoperative pulmonary complications.

List Of Abbreviations

ΔP: driving pressure; $\Delta P_{TW:}$ time–weighted average ΔP; V_T: tidal volume; PEEP: positive end–expiratory pressure; STROBE: strengthening the reporting of observational studies in epidemiology; ARISCAT: Assess Respiratory Risk in Surgical Patients in Catalonia; AUC: Area Under Curve; RR: risk ratio; OR: odds ratio; BMI: Body Mass Index; EPCO: European Perioperative Clinical Outcome; ERAS: Enhanced Recovery After Surgery'

Declarations

Acknowledgments

None

Authors' Contributions

GM, ASN and MJS: Designed the study; GM, ASN, SNTH: Wrote the protocol; GM, ASN, LB, MJS: Collected the data from the original database; GM, ASN, ODC: Analyzed the data; GH, SJ, MH, GHM, MFVM, RMP, CP, WS, PS, HW, MWH, PP, MGdA, MJS: made substantial contribution to data interpretation; GM, wrote the manuscript under the supervision of PP and MJS.

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Availability of Data and Materials

The data as well as the code used for analysis are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The original study protocol was approved by the ethical committee of the Academic Medical Center, Amsterdam, the Netherlands (W12_190#12.17.0227). Each participating centre obtained approval from their institutional review board if needed, and patients were included after obtaining written informed consent when dictated by national or regional legislation

Consent for publication

Not applicable

Competing interests

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References

1. Abbott TEF, Fowler AJ, Pelosi P, et al. A systematic review and consensus definitions for standardised end-points in perioperative medicine: pulmonary complications. *British Journal of Anaesthesia*. 2018; **120**:1066–79.
2. Miskovic A, Lumb AB. Postoperative pulmonary complications. *British Journal of Anaesthesia* 2017; **118**:317–34.
3. Khuri SF, Henderson WG, DePalma RG, Mosca C, Healey NA, Kumbhani DJ. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Annals of Surgery* 2005; **242**:326–43.
4. Serpa Neto A, Hemmes SNT, Barbas CS V., et al. Protective versus Conventional Ventilation for Surgery. *Anesthesiology* 2015; **123**:66–78.
5. Neto AS, Hemmes SNT, Barbas CSV, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: A meta-analysis of individual patient data. *Lancet Respiratory Medicine* 2016; **4**:272–80.

6. Ladha K, Melo MFV, McLean DJ, Wanderer JP, Grabitz SD, Kurth T, Eikermann M. Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: Hospital based registry study. *British Medical Journal* 2015; **351**:h3646.
7. Williams EC, Motta-Ribeiro GC, Vidal Melo MF. Driving Pressure and Transpulmonary Pressure: How Do We Guide Safe Mechanical Ventilation? *Anesthesiology* 2019; **131**:155–63.
8. De Jong MAC, Ladha KS, Melo MFV, Staehr-Rye AK, Bittner EA, Kurth T, Eikermann M. Differential Effects of Intraoperative Positive End-expiratory Pressure (PEEP) on Respiratory Outcome in Major Abdominal Surgery Versus Craniotomy. *Annals of Surgery* 2016; **264**:362–9.
9. Wirth S, Biesemann A, Spaeth J, Schumann S. Pneumoperitoneum deteriorates intratidal respiratory system mechanics: an observational study in lung-healthy patients. *Surgical Endoscopy* 2017; **31**:753–60.
10. LAS VEGAS investigators. Epidemiology, practice of ventilation and outcome for patients at increased risk of postoperative pulmonary complications: LAS VEGAS - An observational study in 29 countries. *European Journal of Anaesthesiology* 2017;**34**: 492–507
11. Nichol A, Bailey M, Egi M, et al. Dynamic lactate indices as predictors of outcome in critically ill patients. *Critical Care* 2011; **15**:R242.
12. Imai L, Ratkovic M. CBPS: Covariate Balancing Propensity Score. *Journal of the Royal Statistical Society* 2014; **76**:243–63.
13. Canet J, Gallart L, Gomar C, et al. Prediction of Postoperative Pulmonary Complications in a Population-Based Surgical Cohort. *Anesthesilogy* 2010; **113**:1338–50.
14. Mazo V, Sabaté S, Canet J, et al. Prospective External Validation of a Predictive Score for Postoperative Pulmonary Complications. *Anesthesiology* 2014; **121**:219–31.
15. Dunkler D, Plischke M, Leffondré K, Heinze G. Augmented backward elimination: A pragmatic and purposeful way to develop statistical models. *PLoS One* 2014; **9**:1–19.
16. Myers J, Rassen J, Gagne J, et al. Effects of adjusting for instrumental variables on bias and precision of effect estimates. *American Journal of Epidemiology* 2011; **174**:1213–22.
17. Cepeda MS, Boston R, Farrar JT, Strom BL. Comparison of logistic regression versus propensity score when the number of events is low and there are multiple confounders. *American Journal of Epidemiolology* 2003; **158**:280–7.
18. Austin PC. Assessing the performance of the generalised propensity score for estimating the effect of quantitative or continuous exposures on binary outcomes. *Statistics in Medicine* 2018; **37**:1874–94.
19. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: A statement from the ESA-ESICM joint taskforce on perioperative outcome measur. *European Journal of Anaesthesiology* 2015; **32**:88–105.
20. Cinnella G, Grasso S, Spadaro S, et al. Effects of recruitment maneuver and positive end-expiratory pressure on respiratory mechanics and transpulmonary pressure during laparoscopic surgery.

Anesthesiology 2013; **118**:114–22.

21. Fahy BG, Nagle SE, Njoku MJ, Flowers JL, Barnas GM. The Effects of Increased Abdominal Pressure on Lung and Chest Wall Mechanics During Laparoscopic Surgery. *Anesthesia and Analgesia* 1995; **81**:744–50.
22. Maracajá-Neto LF, Verçosa N, Roncally AC, Giannella A, Bozza FA, Lessa MA. Beneficial effects of high positive end-expiratory pressure in lung respiratory mechanics during laparoscopic surgery. *Acta Anaesthesiologica Scandinavica* 2009; **53**:210–7.
23. Mutoh T, Lamm WJE, Embree LJ, Hildebrandt J, Albert RK. Abdominal distension alters regional pleural pressures and chest wall mechanics in pigs in vivo. *Journal of Applied Physiology* 1991; **70**:2611–8.
24. Brandão JC, Lessa MA, Motta-Ribeiro G, et al. Global and Regional Respiratory Mechanics During Robotic-Assisted Laparoscopic Surgery. *Anesthesia and Analgesia* 2019; **129**:1564-1573.
25. Pelosi P, Foti G, Cereda M, Vicardi P, Gattinoni L. Effects of carbon dioxide insufflation for laparoscopic cholecystectomy on the respiratory system. *Anaesthesia*. 1996; **51**:744–9.
26. Kubiak BD, Gatto LA, Jimenez EJ, et al. Plateau and Transpulmonary Pressure With Elevated Intra-Abdominal Pressure or Atelectasis. *Journal of Surgical Research* 2010; **159**:e17–24.
27. Cortes-Puentes GA, Gard KE, Adams AB, Faltesek KA, Anderson CP, Dries DJ, Marini JJ. Value and limitations of transpulmonary pressure calculations during intra-abdominal hypertension. *Critical Care Medicine* 2013; **41**:1870–7.
28. Loring SH, Topulos GP, Hubmayr RD. Transpulmonary pressure: The importance of precise definitions and limiting assumptions. *American Journal of Respiratory and Critical Care Medicine* 2016; **194**:1452–7.
29. Andersson LE, Bååth M, Thörne A, Aspelin P, Odeberg-Wernerman S. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. *Anesthesiology* 2005; **102**:293–9.
30. Pereira SM, Tucci MR, Morais CCA, et al. Individual positive end-expiratory pressure settings optimise intraoperative mechanical ventilation and reduce postoperative atelectasis. *Anesthesiology* 2018; **129**:1070–81.
31. Mazzinari G, Diaz-Cambronero O, Alonso-Iñigo JM, et al. Intraabdominal Pressure Targeted Positive End-expiratory Pressure during Laparoscopic Surgery: An Open-label, Nonrandomized, Crossover, Clinical Trial. *Anesthesiology* 2020; **132**:667–677.
32. D'Antini D, Rauseo M, Grasso S, et al. Physiological effects of the open lung approach during laparoscopic cholecystectomy: Focus on driving pressure. *Minerva Anestesiologica* 2018; **84**:159–67.
33. Eichler L, Truskowska K, Dupree A, Busch P, Goetz AE, Zöllner C. Intraoperative Ventilation of Morbidly Obese Patients Guided by Transpulmonary Pressure. *Obesity Surgery* 2018; **28**:122–9.
34. Ferrando C, Soro M, Unzueta C, et al. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. *Lancet*

Respiratory Medicine 2018; **6**:193–203.

35. Gainsburg DM. Anesthetic concerns for robotic-assisted laparoscopic radical prostatectomy. *MinervaAnestesiologica* 2012 ;**78**:596–604.
36. Sharma KC, Brandstetter RD, Brensilver JM, Lung LD. Cardiopulmonary physiology and pathophysiology as a consequence of laparoscopic surgery. *Chest* 1996; **51**:810–15.
37. Fahy BG. Cardiopulmonary effects of laparoscopic surgery, revisited. *Chest* 1997; **111**:1787–8.
38. Lane-Fall MB, Cobb BT, Cené CW, Beidas RS. Implementation Science in Perioperative Care. *Anesthesiology Clinics* 2018; **36**:1–15.
39. Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. *Journal of the Royal Society of Medicine* 2011; **104**:510–20.
40. Wong A. Closing the gap: applying the Theoretical Domains Framework to improve knowledge translation. *Canadian Journal of Anaesthesia* 2017; **64**:569–573.

Tables

Table 1. Patients demographics and surgery–related characteristics

	All patients (N = 2.034)	Closed abdominal surgery (N = 906)	Open abdominal surgery (N = 1.128)	*P*–value	Absolute Difference
Age, years	54 [40 to 67]	49 [36 to 64]	58 [45 to 69]	< 0.001	9 [6 to 21]
Gender, male (%)	42% (846/2034)	34% (306/906)	48% (540/1128)	< 0.001	14% [9% to 18%]
Ethnicity, % (n/N)				0.194	
Caucasian Black Asian Other	88% (1787/2.030) 1% (20/2.030) 3% (58/2.030) 8% (165/2.030)	87% (786/902) 1% (6/902) 4% (33/902) 8% (77/902)	89% (1001/1.128) 1% (14/1.128) 2% (25/1.128) 8% (88/1.128)		
BMI (Kg•m^{-2})	26.2 [23.3 to 30.0]	26.7 [23.6 to 31.3]	25.8 [22.9 to 29.3]	< 0.001	0.8 [0.04 to 1.6]
Weight (kg)	75.0 [65.0 to 87.0]	77.0 [68.0 to 93.0]	74.0 [64.0 to 85.0]	0.001	3 [8 to 13]
PBW (kg)	60.6 [55.1 to 69.0]	59.7 [54.2 to 67.8]	61.5 [56.0 to 69.7]	< 0.001	1.82 [1.8 to 2]
ASA class, % (n/N)				< 0.001	
1 2 3 4 5	24% (495/2.028) 49% (989/2.028) 24% (488/2.028) 3% (53/2.028) 0% (3/2.028)	31% (276/904) 53% (477/904) 16% (146/904) 1% (5/904) 0% (0/904)	20% (219/1.124) 46% (512/1.124) 30% (342/1.124) 4% (48/1.124) 0% (3/1.124)		
ARISCAT score	26 [18 to 38]	18 [15 to 31]	34 [18 to 41]	< 0.001	16 [16 to 16]
ARISCAT class, % (n/N)				< 0.001	

< 26	51% (985/1.945)	68% (607/888)	36% (378/1.057)		
26–44	38% (741/1.945)	26% (231/888)	48% (510/1.057)		
> 44	11% (219/1.945)	6% (50/888)	16% (169/1.057)		
Preop. SpO_2 ,%	98 [96 to 99]	98 [96 to 99]	97 [96 to 99]	0.004	0 [0 to 3]
Current smoker, %	20% (413/2.034)	21% (79/906)	20% (222/1.128)	0.468	2% [3% to 7%]
Chronic comorbidity, % (n/N)					
Metastatic cancer	7% (138/2.034)	2% (22/906)	10% (116/1.128)	< 0.001	8% [5% to 9%]
Chronic kidney failure	4% (81/2.034)	1% (13/906)	6% (68/1.128)	< 0.001	5% [2% to 6%]
COPD	7% (138/2.034)	7.% (83/906)	6% (55/1.128)	0.290	1% [1% to 3%]
Heart failure	7% (143/2.034)	6% (53/906)	8% (90/1.128)	0.075	2% [1% to 4%]
OSAS	2% (42/2.034)	3% (27/906)	1% (15/1.128)	0.015	2% [1% to 3%]
Neuromuscular disease[a]	1% (17/2.034)	1% (6/906)	1% (11/1.128)	0.599	0.3% [0.3% to 1%]
Liver dysfunction	1% (29/2.034)	1% (5/906)	2% (24/1.128)	0.210	1% [1% to 2%]
Functional Status, % (n/N)				< 0.001	
Independent	92% (1872/2.034)	96% (867/906)	89% (1005/1.128)		
Partially dependent	7% (135/2.034)	4% (32/906)	9% (103/1.128)		
Totally dependent	1% (27/2.034)	1% (7/906)	2% (20/1.128)		
Preop. resp. infection,% (n/N)	5% (95/2.034)	4% (35/906)	5% (60/1.128)	0.150	2% [0.5% to 3%]
Preop. Hb ($g \bullet dl^{-1}$), % (n/N)	13.4 [12.2 to 14.0]	13.5 12.6 to 14.5]	13.3 [11.9 to 14.5]	< 0.001	0.2 [0.3 to 1]
Preop. anemia (Hb ≤ 10 g dl^{-1})	9% (1738/1.846)	3% (21/798)	8% (87/1.048)	< 0.001	5% [3% to 7%]

Preop. creatinine (g•dl[-1])	0.8 [0.7 to 1.0]	0.8 [0.7 to 1.0]	0.9 [0.7 to 1.1]	< 0.001	0.04 [0.01 to 0.1]
Preop transfusion, % (n/N)	1% (23/2.034)	0% (3/906)	2% (20/1.128)	0.004	1% [0.5% to 1%]
Surgical procedure[b], % (n/N)					
Lower GI	26% (286/1.098)	14% (124/906)	31% (346/1.128)	< 0.001	17% [13% to 20%]
Upper GI, HBP	28% (303/1.098)	47% (429/906)	20% (222/1.128)	< 0.001	27% [23% to 31%]
Vascular surgery	2% (25/1.098)	0% (0/906)	3% (30/1.128)	< 0.001	2% [1% to 3%]
Aortic surgery	2% (19/1.098)	0% (0/906)	2% (20/1.128)	< 0.001	1% [1% to 2%]
Urological	19% (204/1.098)	9% (81/906)	14% (162/1.128)	< 0.001	5% [2% to 8%]
Gynaecological	18% (195/1.098)	26% (233/906)	17% (188/1.128)	< 0.001	9% [6% to 12%]
Endocrine surgery	1% (9/1.098)	1% (5/906)	1% (10/1.128)	0.443	0.3% [0.5% to 1%]
Transplant	2% (18/1.098)	0% (0/906)	2% (20/1.128)	< 0.001	2% [1% to 3%]
Neurosurgery	5% (52/1.098)	0% (1/906)	10% (109/1.128)	< 0.001	9% [8% to 11%]
Other procedure	3% (30/1.098)	5% (43/906)	19% (214/1.128)	< 0.001	14% [11% to 17%]
Urgency of Surgery[c], % (n/N)				< 0.001	
Elective	84% (1705/2.034)	87% (792/906)	81% (913/1.128)		
Urgent	12% (235/2.034)	9% (85/906)	13% (150/1.128)		
Emergency	4% (94/2.034)	4% (29/906)	6% (65/1.128)		
Duration of surgery[d], min	86 [55 to 149]	70 [50 to 110]	105 [65 to 172]	< 0.001	35 [21 to 43]
Duration of anaesthesia[e] , min	115 [80 to 190]	100 [71 to 147]	140 [91 to 205]	< 0.001	40 [20 to 60]
Time of surgery, %				<	0.2 [0.2 to 1]

(n/N)				0.843	
Daytime[f] Night–time	95% (1925/2034) 5% (109/2034)	95% (859/906) 5% (47/906)	95% (1066/1128) 5% (962/1128)		
Antibiotic prophylaxis, % (n/N)	80% (1.628/2.034)	73% (662/906)	84% (956/1.127)	0.005	11% [8% to 15%]
Mean arterial pressure, mmHg	82 [74 to 92]	84 [76 to 94]	80 [72 to 90]	< 0.001	4 [4 to 7]
Heart rate, beats•min	72 [63 to 82]	73 [64 to 82]	72 [62 to 83]	0.276	1 [3 to 11]
Intraop. procedures, % (n/N)					
Epidural anesthesia	12% (237/2.034)	3% (25/906)	19% (212/1128)	< 0.001	16% [13% to 18%]
Opioid				< 0.001	
Short–acting Long–acting Both	18% (367/2.015) 70% (1410/2.015) 12% (238/2.015)	22% (193/900) 62% (561/900) 16% (146/900)	16% (174/1.115) 76% (849/1.115) 8% (92/1.115)		
Neuromuscular Blockade	97% (1965/2.028)	97% (876/903)	97% (1089/1.125)	0.887	0.2% [0.1% to 1%]
Neuromuscular Monitoring	23% (474/2.032)	25% (230/906)	22% (244/1.126)	0.055	3% [0% to 7%]
Neuromuscular Reversal	41% (827/2.024)	49% (437/901)	35% (390/1.123)	< 0.001	14% [9% to 18%]
TIVA	10% (211/2.027)	11% (102/902)	10% (109/1.125)	0.266	1% [1% to 4%]
Transfusion	6% (113/2.034)	1% (13/906)	9% (100/1.128)	< 0.001	7% [6% to 9%]
Total Fluids (mL• kg^{-1})	18 [12 to 30]	15 [13 to 30]	23 [14 to 26]	< 0.001	8 [6 to 10]
Crystalloids (mL• kg^{-1})	17 [12 to 26]	14 [11 to 21]	20 [13 to 31]	< 0.001	5 [4 to 7]
Colloids (mL• kg^{-1})	7 [3 to 9]	4 [0 to 7]	7 [6 to 12]	< 0.001	3 [2 to 6]

Data are presented as median [25th–75th percentile] or % (n/N). For binary and continuous variables risk difference and median difference with 95% confidence intervals in square brackets are reported respectively.

Abbreviations: BMI, body mass index; ASA, American Society of Anaesthesiologists; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia risk index,[14,15] Hb, haemoglobin; GI: gastrointestinal; HBP, Hepatobiliopancreatic; SpO_2, peripheral oxygen saturation; CI, confidence interval.

[a]Neuromuscular disease affecting the respiratory system.

[b]The same patient may have more than one surgical indication

[c]Urgency of surgery is defined as *elective*: surgery that is scheduled in advance because it does not involve a medical emergency, *urgent*: surgery required within <48 hours, *emergent*: surgery performed when the patients' life or well being are threatened.

[d]Duration of surgery is the time between skin incision and closure of the incision.

[e]Duration of anaesthesia is the time between start of induction and tracheal extubation or discharge from operation room if the mechanical ventilation is continued.

[f]Daytime surgery is defined as anaesthesia induction between 8:00 a.m. and 19:59 p.m.

Table 2. Intraoperative ventilatory setting by group

	All patients (N = 2.034)	Closed abdominal surgery (N = 906)	Open abdominal surgery (N = 1.128)	*P*–value	Absolute Difference
Ventilation mode, % (n/N)				0.013	Pressure–controlled 4% [1% to 8%]
Volume–controlled	77% (1571/2.034)	79% (895/906)	75% (676/1.128)		
Pressure–controlled	23% (463/2.034)	21% (233/906)	25% (230/1.128)		
Tidal Volume					
Absolute (ml)	505 [465 to 570]	504 [462 to 570]	505 [465 to 572]	0.567	1 [24 to 25]
Per PBW ($ml \bullet kg^{-1}$)	8.0 [7.0 to 9.0]	8.5 [7.6 to 9.5]	8.2 [7.4 to 9.2]	0.001	0.2 [0.07 to 0.5]
Per ABW ($ml \bullet kg^{-1}$)	7.0 [6.0 to 8.0]	6.8 [5.8 to 7.7]	7.0 [6.1 to 7.9]	< 0.001	0.2 [0.1 to 0.4]
Minute ventilation ($L \bullet kg^{-1}$)	6.0 [6.0 to 7.0]	6.5 [5.8 to 7.2]	6.3 [5.5 to 7.0]	< 0.001	0.2 [0.1 to 0.4]
Respiratory system compliance					
Dynamic, $ml \bullet cm \bullet H_2O^{-1}$	26 [21 to 32]	25 [20 to 32]	27 [21 to 33]	< 0.001	2 [0 to 4]
Static, $ml \bullet cm \bullet H_2O^{-1}$	42 [35 to 50]	41 [33 to 50]	43 [36 to 51]	< 0.001	1 [0.4 to 2]
Routine recruitment maneuvers, % (n/N)	12% (238/2.029)	13% (119/905)	11% (119/1.124)	0.087	2% [1% to 5%]
FiO_2, %	50 [45 to 56]	54 [48 to 70]	50 [45 to 63]	< 0.001	4 [4 to 10]
SpO_2, %	99 [98 to 100]	99 [98 to 100]	99 [98 to 100]	< 0.001	0 [0 to 0]*
$EtCO_2$, kPa	4.0 [4.0 to 5.0]	4.6 [4.2 to 4.9]	4.3 [4.0 to 4.7]	< 0.001	0.2 [0.2 to 0.6]
Airway pressures					
Driving pressure					
Time–weighted average ($cmH_2O \bullet hour^{-1}$)	8 [6 to 11]	8 [6 to 11]	8 [6 to 10]	0.091	0.2 [0.09 to 1.2]
	14 [11 to 18]	16 [12 to	14 [11 to 17]	< 0.001	2 [2 to 7]

Maximum value (cmH_2O)		20]			
Minimum value (cmH_2O)	11 [9 to 14]	11 [9 to 15]	11 [9 to 14]	0.008	0 [0 to 17]
Coefficient of variation (%)	10 [5 to 20]	15 [6 to 26]	9 [4 to 15]	< 0.001	5 [4 to 8]
Peak pressure					
Time–weighted average ($cmH_2O \bullet hour^{-1}$)	12 [9 to 15]	11 [9 to 15]	12 [9 to 15]	0.414	0.2 [0.1 to 1.1]
Highest value (cmH_2O)	20 [17 to 24]	21 [18 to 26]	19 [16 to 23]	< 0.001	2 [2 to 10]
Lowest value (cmH_2O)	16 [14 to 20]	17 [14. to 20]	16 [14 to 20]	0.011	1 [1 to 3]
Coefficient of variation (%)	8 [4 to 15]	11 [5 to 19]	7 [3 to 12]	< 0.001	5 [3 to 6]
PEEP					
Time–weighted average ($cmH_2O \bullet hour^{-1}$)	2 [1 to 3]	2 [1 to 4]	2 [1 to 3]	0.019	0 [0 to 0]
Highest value (cmH_2O)	5 [2 to 5]	5 [2 to 5]	5 [2 to 5]	0.255	0 [0 to 0]
Lowest value (cmH_2O)	4 [0 to 5]	4 [0 to 5]	3 [0 to 5]	0.186	1 [1 to 5]
Coefficient of variation (%)	0 [0 to 22]	0 [0 to 22]	0 [0 to 22]	0.579	0 [0 to 0]

Data are presented as median [25^{th}–75^{th} percentile] or % (n/N). For binary and continuous variables risk difference and median difference with confidence intervals are reported respectively. Abbreviations: $EtCO_2$, end-tidal CO_2; FiO_2, fraction of inspired oxygen; SpO_2, peripheral oxygen saturation, OR, Odds ratio.

*Difference between groups is significant but very small and masked by rounding process.

Table 3. Intraoperative and postoperative outcomes.

	All patients (N = 2.034)	Closed abdominal surgery (N = 906)	Open abdominal surgery (N = 1.128)	*P*–value
Severe PPC (composite), % (n/N)	5% (102/2.034)	3% (28/906)	7% (74/1.128)	0.001
Intraoperative complications				
Desaturation	4% (73/2.026)	3% (26/903)	4% (47/1.123)	0.148
Unplanned rescue maneuvers	4% (87/2.026)	4% (41/903)	4% (46/1.123)	0.704
Need for ventilatory pressure reduction	4% (77/2.025)	6% (57/903)	2% (20/1.102)	< 0.001
Expiratory flow limitation	1% (14/2.015)	1% (12/898)	0% (2/1.117)	0.005
Hypotension	28% (562/2.027)	20% (182/903)	34% (380/1.124)	< 0.001
Use of vasopressors	23% (469/2.027)	17% (153/903)	28% (316/1.122)	< 0.001
New arrhythmia onset	1% (13/2.027)	0% (2/903)	1% (11/1.124)	0.065
Individual PCCs				
Acute respiratory failure	3% (58/2.034)	2% (21/906)	3% (37/1.128)	0.245
Need for mechanical ventilation	2% (44/2.034)	1% (11/906)	3% (33/1.128)	0.013
Acute respiratory distress syndrome	0% (6/2.034)	0% (0/906)	0% (6/1.128)	0.074
Pneumonia	0% (16/2.034)	0% (2/906)	1% (14/1.128)	0.019
Pneumothorax	0% (4/2.034)	0% (0/906)	0% (4/1.128)	0.186
In–hospital mortality	1% (22/1.892)	0% (3/838)	2% (19/1.054)	0.007
Length of stay (days)	3 [1 to 5]	1 [0 to 3]	5 [2 to 8]	< 0.001

Data are presented as median [25^{th}–75^{th} percentile] or % (n/N).

PPC, postoperative pulmonary complications.

Figures

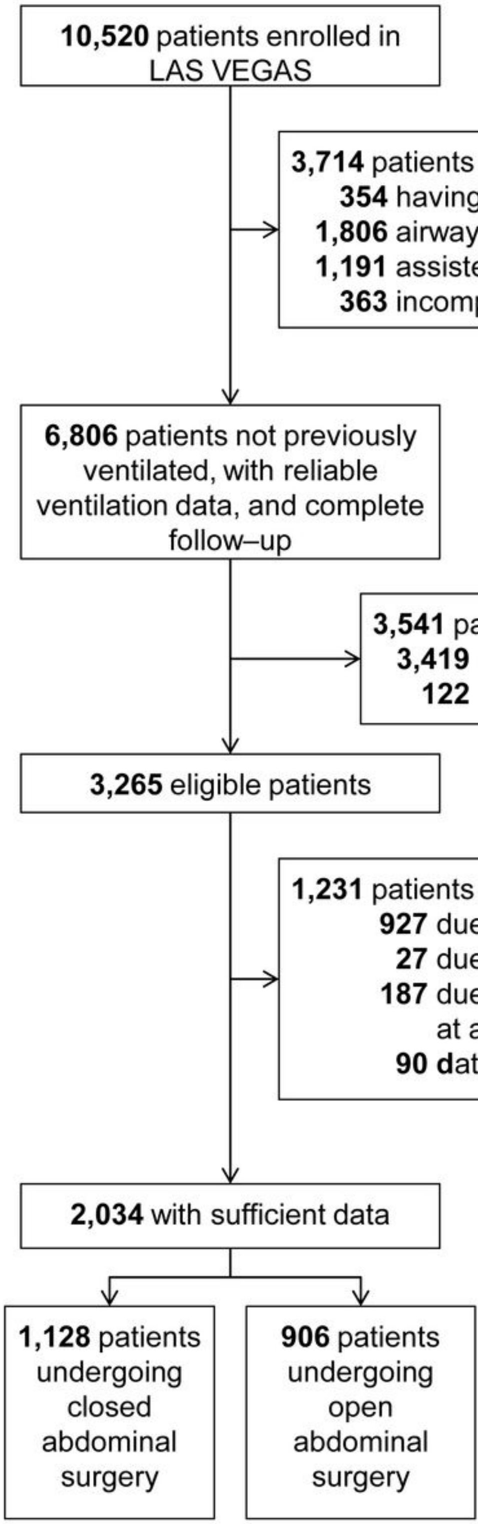

Figure 1

Patients' inclusion flowchart.

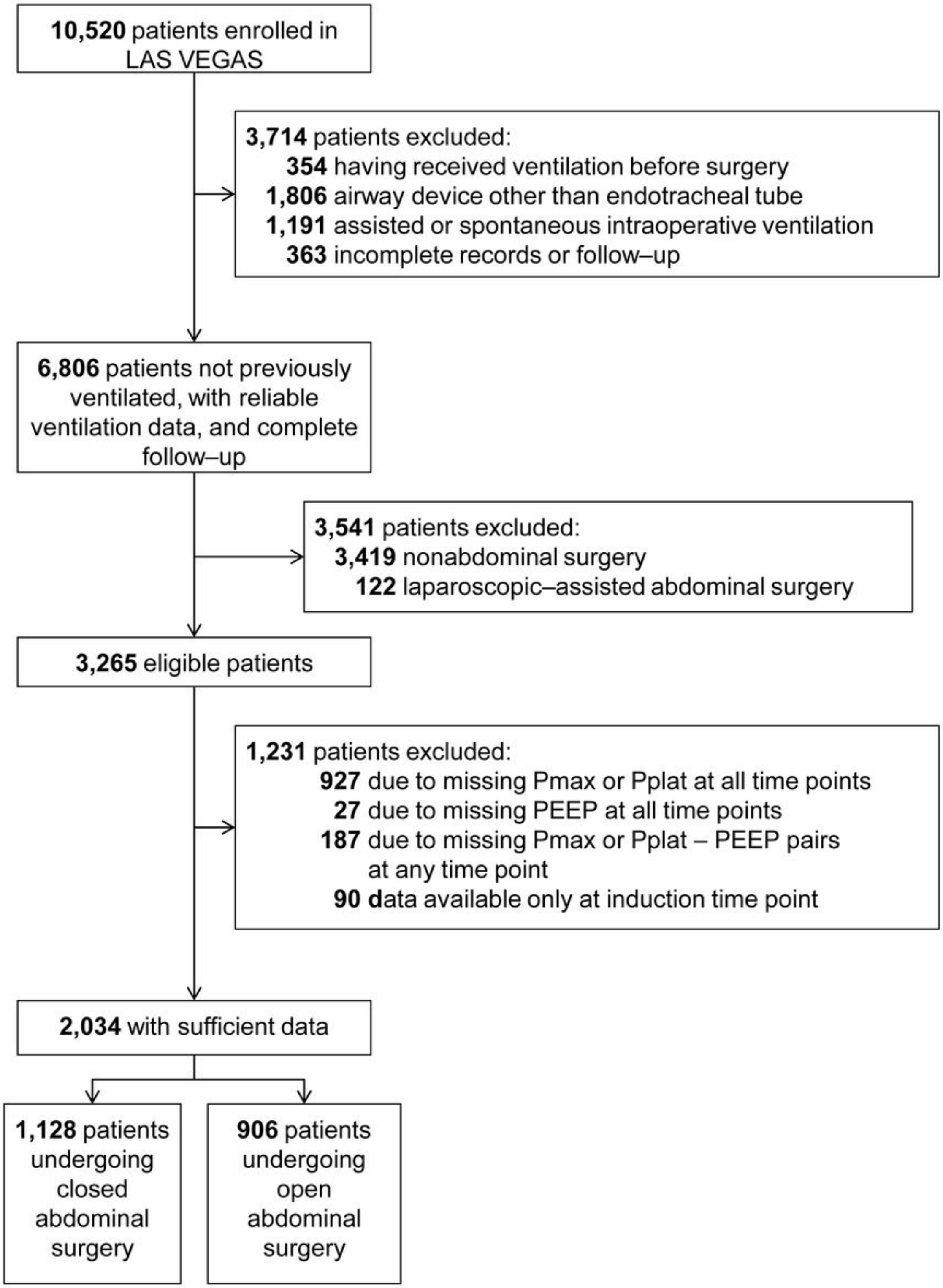

Figure 1

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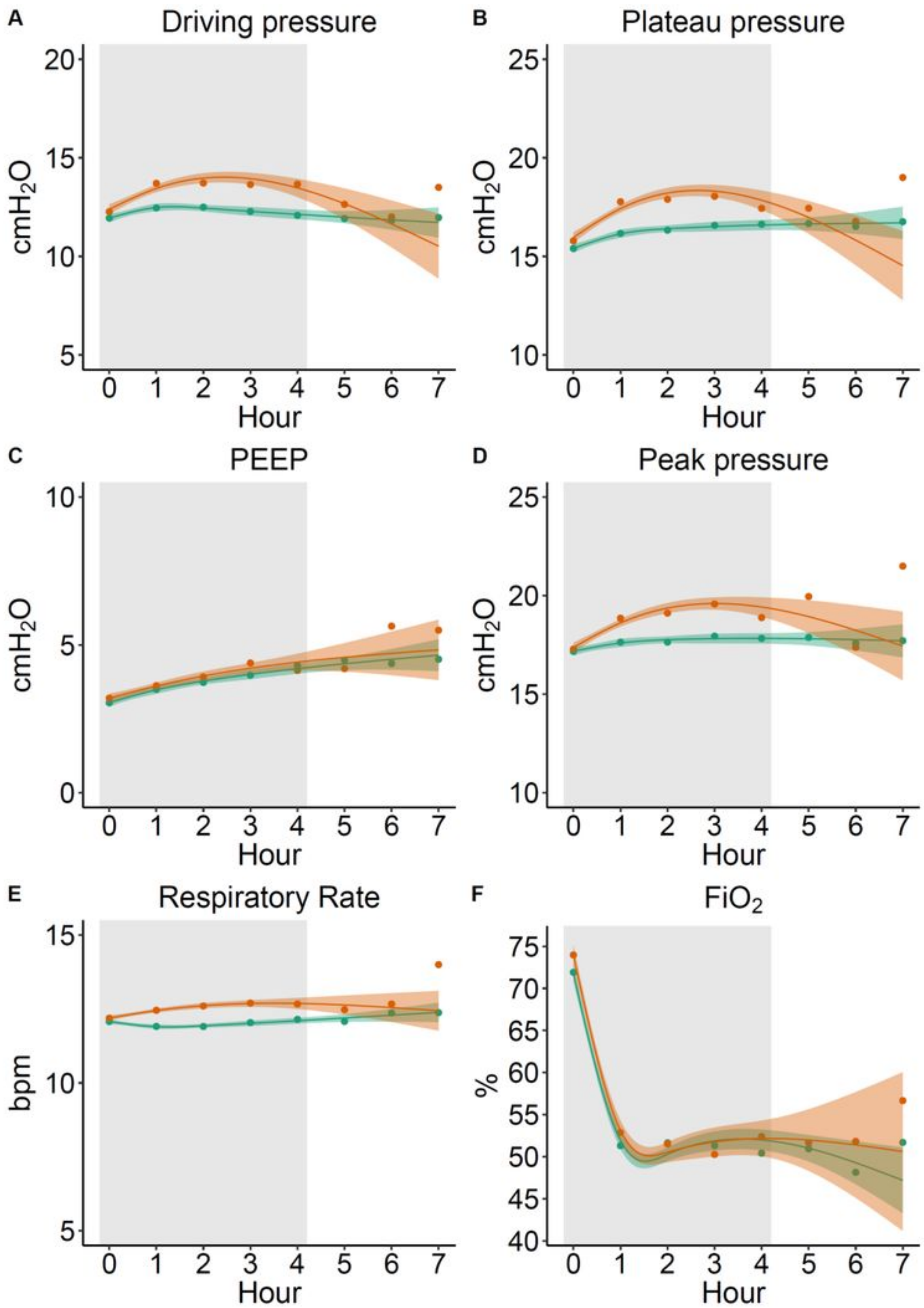
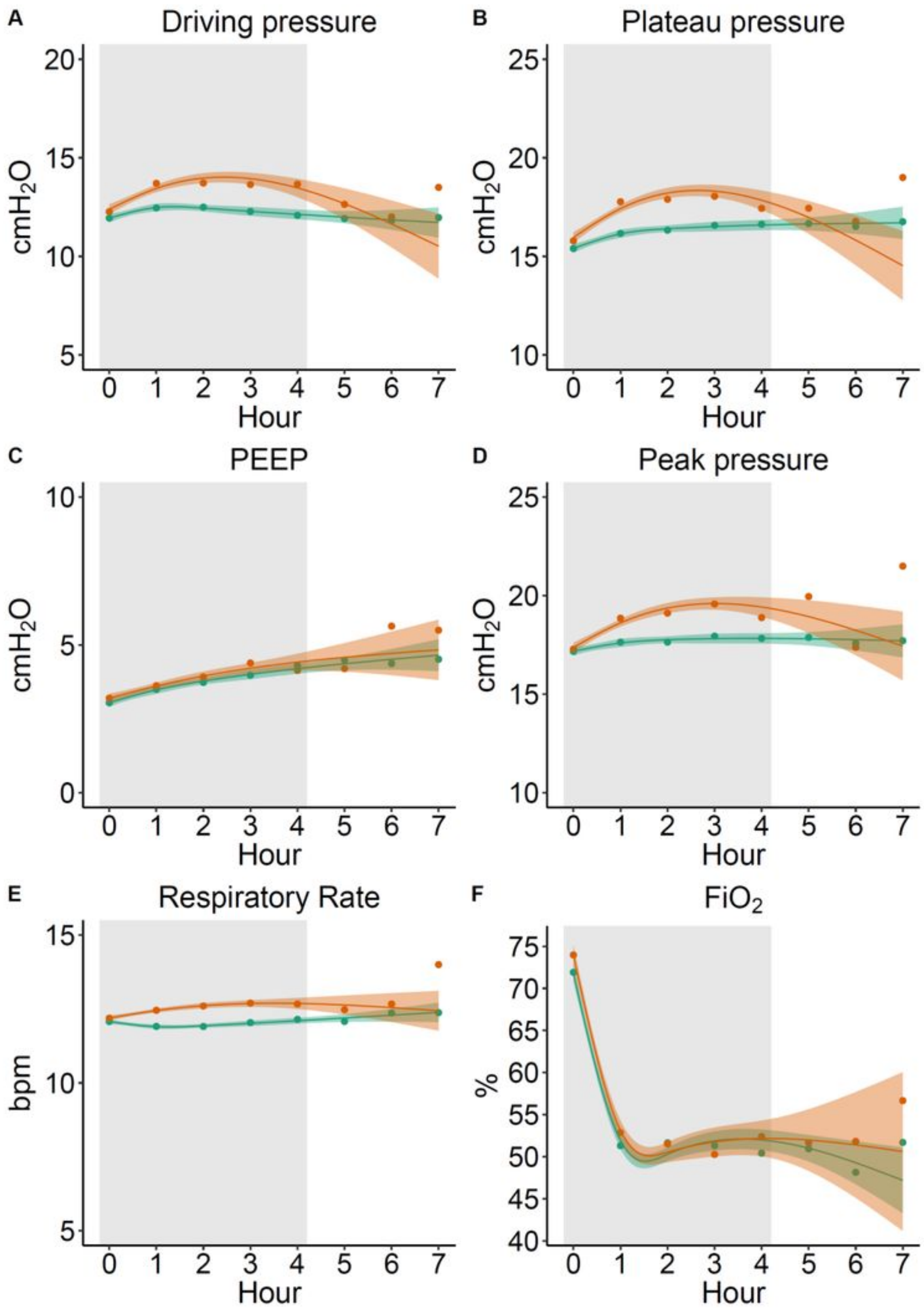


Time (hour)	0	1	2	3	4	5	6	7
Closed Surgery	775	906	433	175	78	30	10	2
Open Surgery	1019	1128	755	401	204	113	62	31
Total data points	1794	2034	1188	576	282	143	72	33

Figure 2

Mechanical ventilation settings over time. Green: open surgery, Orange: closed surgery. Hour 0 h represents the induction of general anaesthesia. Solid lines are means, and bandwidths is 95% bootstrapped confidence intervals. Gray boxes : More than 95% of data points represented.



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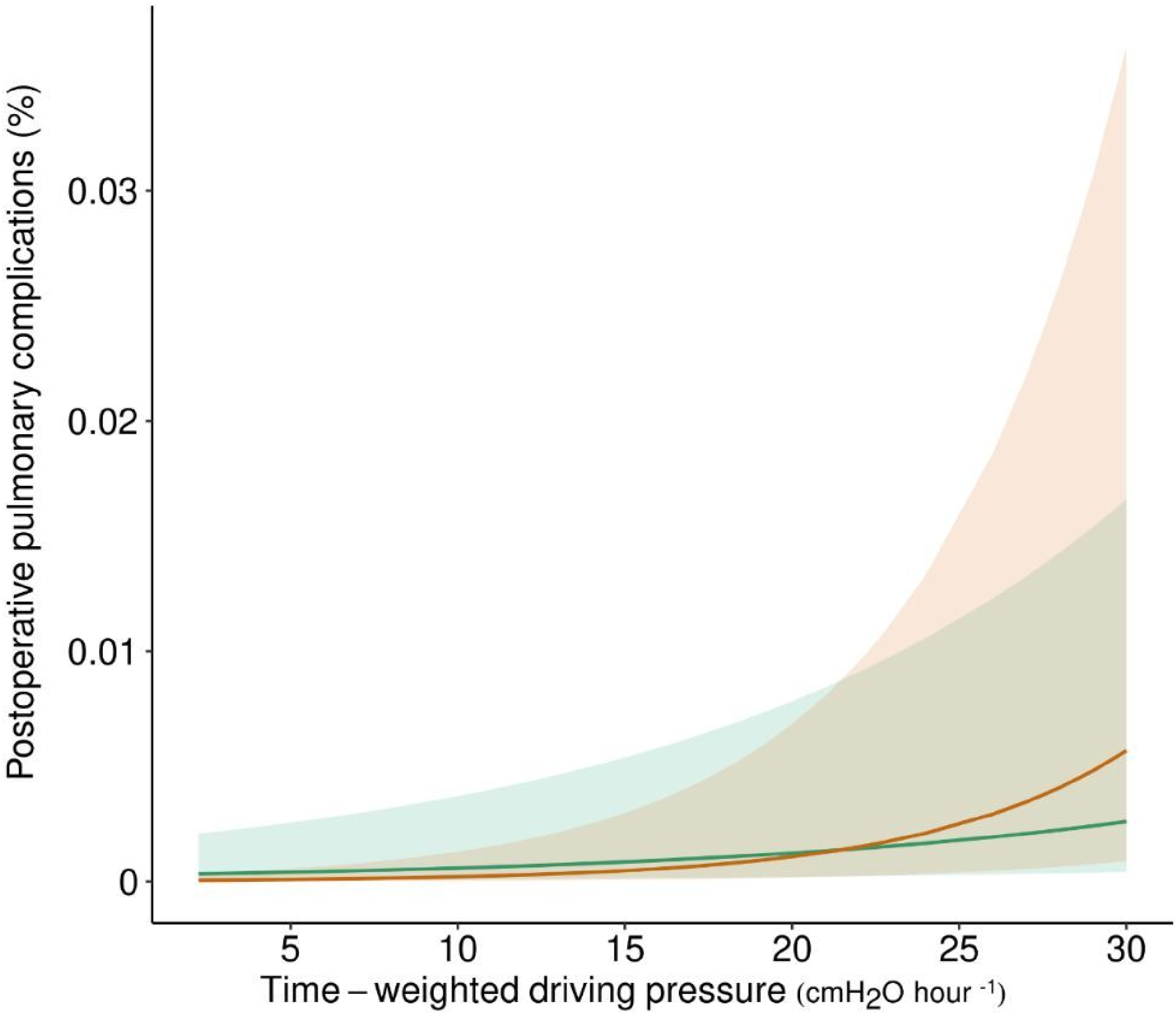

Figure 3

Marginal effect plot of time–weighted average driving pressure on the probability of occurrence of postoperative pulmonary complications by type of surgery. Green: open surgery, Orange: closed surgery; solid lines are estimated marginal mean effect and bandwidths are 95% confidence intervals.

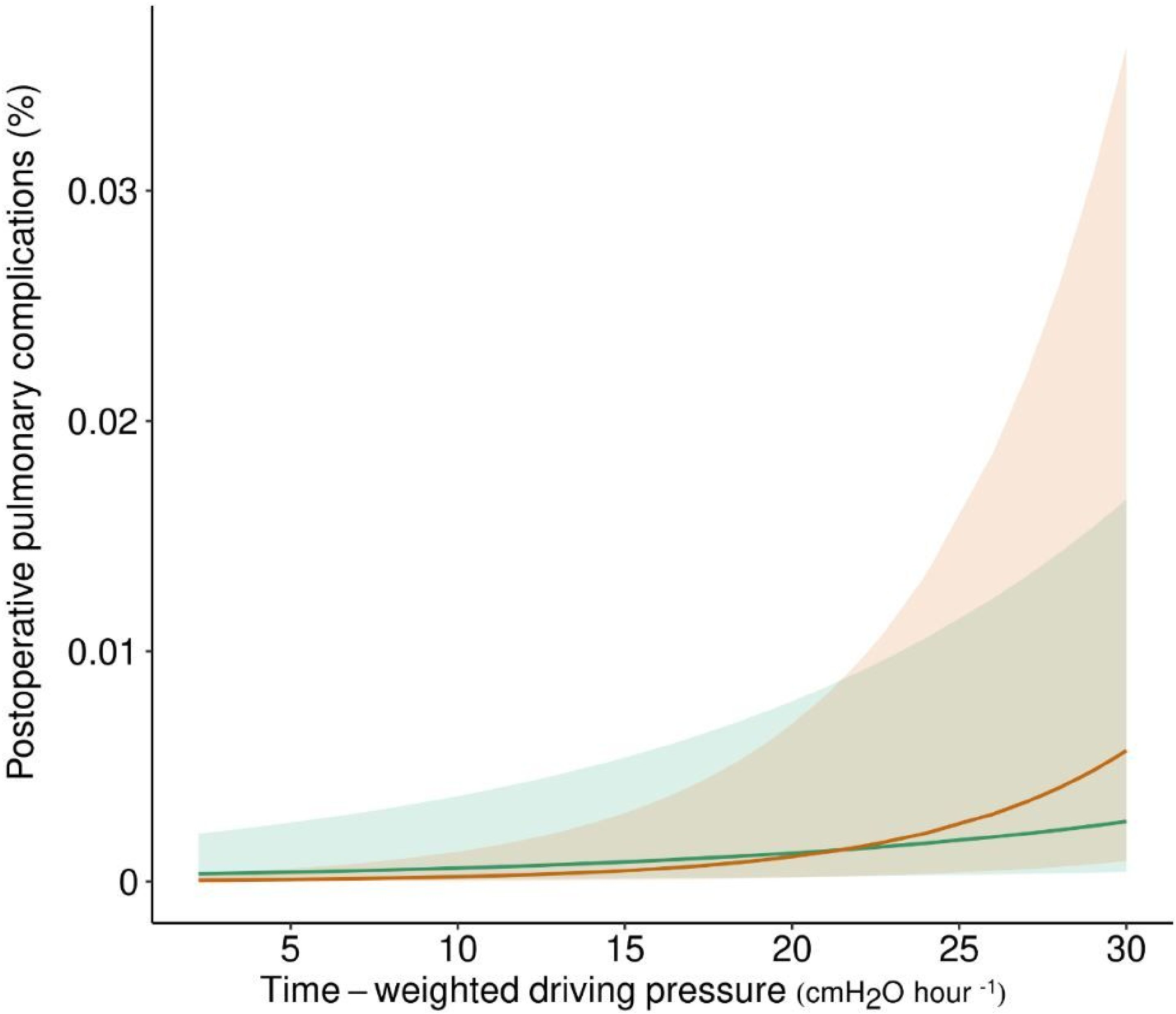

Figure 3

Marginal effect plot of time–weighted average driving pressure on the probability of occurrence of postoperative pulmonary complications by type of surgery. Green: open surgery, Orange: closed surgery; solid lines are estimated marginal mean effect and bandwidths are 95% confidence intervals.

Supplementary Files

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