Prevention of Respiratory Insufficiency after Surgical Management (PRISM) Trial:

A pragmatic randomised controlled trial of continuous positive airway pressure (CPAP) to prevent respiratory complications and improve survival following major abdominal surgery

Statistical Analysis Plan Version 2.0
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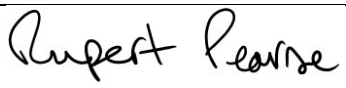
Signature	
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Contents

1. Administrative information 3
2. Introduction 4
2.1 Background 4
2.2 Purpose of statistical analysis plan 4
2.3 Inclusion/Exclusion criteria 4
3. Outcome Measures 5
3.1 Primary outcome 5
3.2 Secondary outcome 5
3.3 Process measures 5
3.4 Safety outcome measures 5
4. Study Methods 6
4.1 Trial design 6
4.2 Randomisation 6
4.3 Sample size 6
5. Analysis Principles 7
5.1 General analysis principles 7
5.2 Initial descriptive analysis 7
5.3 Primary outcome 9
5.4 Secondary outcomes 10
5.5 Process measures 10
5.6 Safety outcome measures 10
5.7 Graphs and other data summaries 11
5.8 Plan in case of non-convergence of analysis models 12
5.9 Plan in case of over-stratification 12
5.10 Subgroup analyses 13
5.11 Per-protocol analysis 13
6. Sensitivity Analysis 14
References 16
Appendix 1: Deriving outcomes and variables 17
Appendix 2: Dummy tables 21

1. Administrative information

Trial registration number: ISRCTN registry – ISRCTN56012545

This SAP is based on protocol version 1.6 (date: 10/04/2017)

Changes from previous version of SAP

- The previous version of the SAP inadvertently omitted the category '*resection of oesophagus (non-obesity surgery)*' as one of the categories of the minimisation variable *surgical procedure category*. This has been corrected in the randomisation and analysis sections.
- The previous SAP included the outcome 'Mechanical ventilation (invasive or non-invasive) within 30 days of randomisation' – this has been changed to 'Postoperative mechanical ventilation (invasive or non-invasive) within 30 days of randomisation', to clarify that this outcome refers to mechanical ventilation during the postoperative period
- Section 5.1 was updated to clarify that patients who were enrolled in PRISM for a repeat surgery despite previous enrolment would be included in the analysis
- In section 5.2.5 we have separated the category '*Administration of CPAP for less than 4 hours or with significant interruption for a patient in the treatment group (continuous interruption of more than 15 minutes would usually be considered prolonged)*.' into two separate categories: (i) *Administration of CPAP for less than 4 hours duration in the treatment group*; and (ii) *Administration of CPAP with significant interruption for a patient in the treatment group (continuous interruption of more than 15 minutes would usually be considered prolonged)*.
- We updated section 5.3 (describing the analysis of the primary outcome) to state that any categories with fewer than 15 patients for the variable *planned surgical procedure* will be combined with the category '*other intra-peritoneal surgery*' for analysis
- We updated section 5.3 (describing the analysis of the primary outcome) to state that missing baseline covariates will be handled using mean imputation or the missing indicator approach for analysis
- We added a per-protocol analysis using inverse-probability weighting for the primary outcome and following secondary outcomes: (a) pneumonia within 30 days of randomisation; (b) endotracheal re-intubation within 30 days of randomisation; (c) all-cause mortality within 30 days of randomisation. Full information is given in section 5.11.
- We added a new appendix (appendix 1) which details how at least 'one' comorbid disease, primary and secondary outcomes will be derived.
- We added a section on summarising CPAP information for the CPAP group (section 5.2.4)
- We added a plan in case of over-stratification when adjusting for covariates in the primary and secondary analysis models (section 5.9)

2. Introduction

2.1 Background

Prevention of Respiratory Insufficiency after Surgical Management (PRISM) is an international, multi-centre, parallel group, randomised controlled trial which aims to evaluate the clinical effectiveness of early post-operative continuous positive airway pressure (CPAP) administered as routine care compared to usual care in patients undergoing major abdominal surgery. The planned sample size is 4800 patients.

2.2 Purpose of statistical analysis plan

This document outlines the statistical analysis planned for the trial. It is important to set these out and to agree them in advance of inspecting the outcome data for the trial, so that data-derived decisions in the analysis are avoided. Any exploratory, post hoc or unplanned analysis will be clearly identified as such in the respective study analysis report. This SAP does not cover the cost and cost-effectiveness analysis, or the quality adjusted life years (QALY) at one-year after randomisation; these analyses will be planned in separate documents.

2.3 Inclusion/Exclusion criteria

Inclusion Criteria

Patients aged 50 years or over undergoing elective major intra-peritoneal surgery using an open surgical technique.

Exclusion Criteria

- Inability or refusal to provide informed consent
- Anticipated requirement for invasive or non-invasive mechanical ventilation for at least four hours after surgery as part of routine care
- Pregnancy or obstetric surgery
- Previous enrollment in PRISM trial
- Participation in a clinical trial of a treatment with a similar biological mechanism or related primary outcome measure

3. Outcome Measures

3.1 Primary outcome

- Composite endpoint of pneumonia, endotracheal re-intubation or death within 30 days of randomisation.

3.2 Secondary outcome

- Pneumonia within 30 days of randomisation
- Endotracheal re-intubation within 30 days of randomisation
- All-cause mortality within 30 days of randomisation
- Postoperative infection within 30 days of randomisation
- Postoperative mechanical ventilation (invasive or non-invasive) within 30 days of randomisation
- All-cause mortality within one year of randomisation

3.3 Process measures

In addition, we will use the following process measures (i.e. non-patient centred outcome measures), to facilitate comparison with other research:

- Re-admission to hospital within 30 days of randomisation
- Days in critical care (defined as either level 2 or level 3 critical care)
- Duration of hospital stay (days)

3.4 Safety outcome measures

Safety outcomes will quantify harm associated with CPAP (appendix). Presence or absence of the following pre-defined adverse events will be measured within 24 hours of the end of surgery in patients in the treatment group only:

- Interface intolerance due to excessive air leaks
- Pain
- Cutaneous pressure sore or pressure area
- Claustrophobia
- Oro-nasal dryness
- Hypercapnia
- Haemodynamic instability
- Vomiting
- Aspiration of gastric contents
- Other harm assessed as probably or definitely related to CPAP

4. Study Methods

4.1 Trial design

PRISM is an international, multi-centre, parallel group, randomised controlled trial with open study group allocation.

4.2 Randomisation

Randomisation will occur after the participant has provided informed consent and up to four hours after the end of surgery. Participants will be centrally allocated to treatment groups (1:1) by a computer-generated dynamic procedure (minimisation) with a random component. Minimisation variables will be country, surgical procedure category and planned use of epidural anaesthesia. The surgical procedure categories are as follows: (a) resection of colon, rectum or small bowel; (b) resection of liver, pancreas or gall bladder; (c) resection of stomach (non-obesity surgery); (d) resection of oesophagus (non-obesity surgery); (e) obesity surgery; (f) vascular procedure; or (g) other intra-peritoneal surgery. Each participant will be allocated with 80% probability to the group that minimises between group differences in these factors among all participants recruited to the trial to date, and to the alternative group with 20% probability. To enter a patient into the PRISM trial, research staff at the site will log on to a secure web-based randomisation and data entry platform and complete the patient's details to obtain a unique patient identification number and allocation to a treatment group.

4.3 Sample size

The primary outcome is a composite endpoint of pneumonia, re-intubation, or death within 30 days of randomisation. The incidence of postoperative pneumonia in previous trials was 8.0% in the usual care group and 4.3% (relative risk reduction of 46%) in the treatment arm. However, the total number of patients included in these five trials was less than 600 patients. The incidence of postoperative pneumonia, admission to intensive care (a surrogate marker of re-intubation) and death in a large international cohort (n ~9000) was 11.7% for patients aged over 45 years [1]. In order to detect a reduction from 11.7% to 8.8% in the primary outcome measure (relative risk reduction of 25%), with 90% power, a type I error rate of 5%, and a loss to follow up rate of 4%, we would require a total sample size of 4800 patients (2400 per group). This sample size will allow us to detect a 26% relative risk reduction (7.7% vs. 5.7%) in the secondary outcome measure of mortality at one year after randomisation, with 80% power and a type I error rate of 5%. The sample size was calculated, using the '*power two proportions'* function in STATA 14.0 (StataCorp, College Station, USA).

5. Analysis Principles

5.1 General analysis principles

Analyses will follow the intention-to-treat principle: all randomised patients with a recorded outcome will be included in the analysis, and analysed to the treatment to which they were randomised [2, 3]. Patients will be included in the analysis, regardless of whether the treatment they received was compliant with the protocol. Patients with missing outcome data will be excluded from the analysis. Definitions of what constitutes a recorded outcome for each outcome can be found In Appendix 1. Patients who are re-randomised (i.e. enrolled in PRISM for a repeat surgery despite previous enrolment in PRISM) will be included in the analysis for both randomisations, and treated as independent observations [4, 5].

The magnitude of treatment effect estimate will be reported with 95% confidence interval for primary and secondary outcomes. All p-values will be two-sided, and a significance level of 5% will be used. For each outcome, summary statistics (e.g. mean (SD), number (%)) will be presented separately for each treatment arm.

5.2 Initial descriptive analysis

5.2.1 Representativeness of patients

All participating sites have been asked to keep a log of eligible patients not recruited to the trial. Reasons for non-participation will be categorised and summarised. Participation in the trial, treatment allocation and completeness of follow-up will be illustrated by a CONSORT flow diagram.[6]

5.2.2 Comparability of groups

Baseline demographic and clinical data for patients randomised to CPAP (treatment group) and usual care (usual care group) will be summarised but not subjected to statistical testing. Numbers (%) and means (SD) or medians (IQR) will be provided separately for each group. The treatment and usual care groups will be compared at entry for the following baseline characteristics:

- Demographic: age (years), gender (male/female)
- Co-morbid disease: (a) COPD; (b) asthma; (c) interstitial lung disease or pulmonary fibrosis; (d) bronchiectasis; (e) ischaemic heart disease; (f) diabetes mellitus; (g) heart failure; (h) liver cirrhosis; (i) active cancer; (j) previous stoke or TIA; (k) respiratory infections within the previous month; (l) HIV
- Current smoker
- ASA grade: I; II; III; IV

- Body mass index (kg/m^2)
- Minimisation criteria:
    - Planned surgical procedure: (a) resection of colon, rectum or small bowel; (b) resection of liver, pancreas or gall bladder; (c) resection of stomach (non-obesity surgery); (d) resection of oesophagus (non-obesity surgery); (e) obesity surgery; (f) vascular surgery; (g) other intra-peritoneal surgery
    - Country: (a) Italy; (b) Spain; (c) Sweden; (d) United Kingdom; (e) South Africa; (f) Norway
    - Planned use of epidural
- Surgical procedure performed: (a) Resection of colon, rectum or small bowel; (b) resection of liver, pancreas or gall bladder; (c) resection of stomach (non-obesity surgery); (d) resection of oesophagus (non-obesity surgery); (e) obesity surgery; (f) vascular procedure; (g) other intra-peritoneal surgery
- Pre-operative blood tests results: (a) haemoglobin (g/dL); (b) creatinine (µmol/L)
- ARISCAT score: ARISCAT is a risk index based on seven patient factors that evaluates risk for postoperative pulmonary complications in a patient [7, 8]. The seven factors are used to calculate this score are: age, oxygen saturation measured by pulse oximetry (SpO_2, %), pre-operative haemoglobin concentration, respiratory infection in the last month (yes/no), surgical incision category (peripheral/abdominal/thoracic), duration of surgery (hours) and emergency procedure (yes/no). ARISCAT score will be calculated for both groups and presented in the baseline data table. The component variables will be tabulated separately for reference. The ARISCAT Score and its individual components will only be summarised for patients who have all components of the score complete.

5.2.3 Clinical management

Clinical management for the treatment group and usual care group will be summarised but not subjected to statistical testing. Numbers (%) and means (SD) or medians (IQR) will be provided separately for each group. The treatment and usual care groups will be compared for the following clinical management characteristics:

- Surgery: open surgical technique; anaesthetic technique; mechanical ventilation during surgery
- Intravenous fluids during surgery: total intravenous fluid administered excluding blood products; total volume of blood products administered
- Planned and actual level of care on the first night after surgery
- Respiratory support after surgery within four hours of the end of surgery

5.2.4 CPAP after surgery

CPAP information for the CPAP group will be summarised. For each, summary statistics (e.g. mean (SD), median (IQR), number (%)) will be presented. The following CPAP characteristics will be reported:

- Duration of CPAP within 12 hours of the end of the surgery (minutes)
- Maximum airway pressure received within 12 hours after the end of surgery (cmH_2O)
- Primary method of CPAP delivery: face mask, helmet device, nasal mask

5.2.5 Protocol compliance

Numbers and percentages of protocol deviations will be reported. The following protocol deviations will be reported:

- Failure to administer CPAP to a patient in the treatment group
- Starting CPAP at a dose other than $5cmH_2O$ for a patient in the treatment group
- Administration of CPAP for less than 4 hours duration in the treatment group
- Administration of CPAP with significant interruption for a patient in the treatment group (continuous interruption of more than 15 minutes would usually be considered prolonged).
- Administration of CPAP to a patient in usual care group

We will report the number of patients in each treatment group with at least one of the above protocol deviations. In addition, a separate table as described above will be reported by the method which CPAP was delivered.

5.3 Primary outcome

The primary outcome will be analysed using a mixed-effect logistic regression model, with a random intercept for centre [9]. The model will be adjusted for the minimisation variables as fixed factors [10], which are country, planned use of epidural anaesthesia, and planned surgical category as follows: (a) resection of colon, rectum or small bowel; (b) resection of liver, pancreas or gall bladder; (c) resection of stomach (non-obesity surgery); (d) resection of oesophagus (non-obesity surgery); (e) Obesity surgery; or (f) vascular procedure; (g) Other intra-peritoneal surgery. For the minimisation variable planned surgical procedure, any category from (a)-(f) with fewer than 15 patients will be combined with other intra-peritoneal surgery. The model will also be adjusted for the following pre-specified baseline covariates [11-13]: age, gender (M/F), at least one co-morbid disease (chronic respiratory disease, ischaemic heart disease, diabetes mellitus, heart failure, liver cirrhosis, active cancer, and previous stroke or transient ischaemic attack), smoking status (current smoker) and ASA score (I & II

vs. III & IV). All covariates will be included in the model as fixed factors. Age will be included as a continuous variable, assuming a linear association with the outcome [14]. Categorical covariates with more than two categories (country, planned surgical category, ASA score) will be included using indicator variables. The magnitude of the treatment effect will be reported as an adjusted odds ratio with a 95% confidence interval. Missing data for baseline covariates will be handled using mean imputation for age, and a missing indicator will be added for missing data for categorical variables (gender, co-morbid disease, smoking status, and ASA score) [15].

5.4 Secondary outcomes

Secondary outcomes will be analysed using the same approach as the primary outcome (i.e. a mixed-effect logistic regression model, with a random intercept for centre), except they will adjust only for the minimisation variables apart from country (i.e. the model will be adjusted only for planned use of epidural anaesthesia and planned surgical category). This is to avoid over-stratification, as the expected event rate for these outcomes is low. This analysis strategy will be used for the following secondary outcomes:

1. Pneumonia within 30 days of randomisation
2. Endotracheal re-intubation within 30 days of randomisation
3. All-cause mortality within 30 days of randomisation
4. Post-operative infection within 30 days of randomisation.
5. Postoperative mechanical ventilation (invasive or non-invasive) within 30 days of randomisation.
6. All-cause mortality at one year after randomisation

5.5 Process measures

Summary measures will be presented separately for each treatment group. All patients with recorded data will be included in the summary. Formal statistical analysis will not be performed. Re-admission to hospital within 30 days of randomisation will be summarised by number (%). Days in critical care will be summarised for the subset of patients admitted to a critical care unit using mean (SD) and median (IQR). Duration of hospital stay will be summarised using mean (SD) and median (IQR).

5.6 Safety outcome measures

Each safety outcome measured will be summarised for patients in the CPAP group by the number (%). All patients with a recorded outcome will be included in the summary. In addition to this, 'other'

adverse events will be reported separately if prevalence is more than 1% across all participants in the trial.

5.7 Graphs and other data summaries

- The flow of study participants will be displayed in Consolidated Standards of Reporting Trials (CONSORT) diagram.
- 30-day and one-year survival of patients will be presented for both groups using Kaplan-Meier survival curves.
- Investigator self-assessment of blinding by treatment allocation will be presented as number (%).
- Duration of level 2 and 3 critical care stay within 30 days of randomisation for patients admitted to a critical care unit will be presented as mean (SD) and median (IQR).
- Data describing a predefined list of the most common post-operative complications occurring within 30 days of randomisation will be collected for all patients.

  The number and percentage of patients experiencing each of the following complications will be presented by (a) treatment allocation; (b) treatment allocation and Clavien-Dindo (CD) grade (I-II vs III-V); and (c) treatment allocation and CPAP delivery method for those in the CPAP group only. These summaries will not be subjected to any statistical testing. These complications are:

  Respiratory complications:
    - Pneumonia
    - Pleural effusion
    - Pneumothorax
    - Bronchospasm
    - Aspiration pneumonitis
    - Acute Respiratory Distress Syndrome (ARDS)

  Infective complications:
    - Surgical site infection (superficial)
    - Surgical site infection (deep)
    - Surgical site infection (organ space)
    - Urinary tract infection
    - Infection, source uncertain
    - Laboratory confirmed blood stream infection

Cardiac complications:

- Myocardial infraction
- Arrhythmia
- Cardiogenic pulmonary oedema
- Cardiac arrest with successful resuscitation

Other complications:

- Acute kidney injury
- Pulmonary embolism
- Stroke
- Acute psychosis or delirium
- Bowel infarction
- Anastomotic leak
- Perforation of viscus (e.g. bowel, gall bladder etc.)
- Postoperative haemorrhage
- Other postoperative haemorrhage
- Any other complication

5.8 Plan in case of non-convergence of analysis models

If the statistical models for any of the primary or secondary outcomes do not converge, then the following steps will be taken:

1. The model will be fitted without a random intercept for centre
2. As above, but excluding any additional covariates apart from minimisation variables
3. As above, but also excluding minimisation variables.

5.9 Plan in case of over-stratification

When adjusting for covariates in the primary or secondary analysis models, if there is a category within that covariate where no events have occurred in either of the treatment arms, the statistical model will exclude all patients within this category. To overcome this, this category will be merged with another category; this will be decided by the chief investigator who will be blinded to results. This will apply to the following covariates with three or more categories: (a) Country; (b) Planned surgical procedure. However, if all but one category within that covariate have no events recorded in one of the treatment arms then we will exclude this covariate from the model.

Covariates with only two categories will be excluded from the model if there is a category within that covariate where no events occurred in one of the treatment arms. Covariates with only two categories are: (a) planned use of epidural; (b) Gender (M/F); (c) at least one co-morbid disease (chronic respiratory disease, ischaemic heart disease, diabetes mellitus, heart failure, liver cirrhosis, active cancer, and previous stroke or transient ischaemic attack); (d) smoking status (current smoker); (e) ASA score (I & II vs. III & IV).

5.10 Subgroup analyses

A sub-group analysis will be performed for the primary outcome (composite of pneumonia, endotracheal re-intubation or death within 30 days of randomisation). The subgroup of interest will be planned surgical procedure category. This will comprise the following four groups:

- Lower gastrointestinal (resection of colon, rectum, or small bowel)
- Hepatobiliary (resection of liver, pancreas, or gall bladder)
- Upper gastrointestinal (resection of oesophagus, or resection of stomach (non-obesity surgery))
- Other (obesity surgery, vascular procedure, or other intra-peritoneal surgery)

The sub-group analysis will be performed using the same analysis model as for the primary outcome, except planned surgical procedure will be defined as above, instead of as in the minimisation procedure, and the model will include an interaction term between planned surgical procedure category and treatment arm.

The presence of an interaction will be tested using a Wald test assessing the interaction terms. The test will be considered significant at the 5% level. All patients with complete outcome data will be included in the subgroup analysis. Within each surgical procedure category, we will report summary statistics of the outcome by treatment arm, and a treatment effects and 95% confidence intervals. A p-value for the interaction test will also be reported.

5.11 Per-protocol analysis

A per-protocol analysis using inverse probability-weighting (IPW) [16] will be performed for the primary outcome and the following secondary outcomes: (a) pneumonia within 30 days of randomisation; (b) endotracheal re-intubation within 30 days of randomisation; (c) all-cause mortality within 30 days of randomisation. Participants who are non-adherent will be excluded from the

analysis; non-adherence is defined as (a) a participant in the intervention group who does not receive any CPAP; or (b) a participant in the usual care group who does receive CPAP. As post-randomisation exclusions can cause bias, we will use weighting to account for baseline risk factors that we expect to be joint determinants of adherence and the outcome. We will use the following baseline covariates to calculate weights: age, current smoker, ASA grade, COPD, interstitial lung disease, bronchiectasis, heart failure, liver cirrhosis, active cancer, previous stroke, respiratory infection within the previous month, planned surgical procedure, planned use of epidural, and BMI. Missing data for these baseline covariates will be handled using mean imputation for continuous variables and the missing indicator approach for categorical variables. The probability of non-adherence will be estimated from on a logistic regression model with non-adherence as the outcome, and the covariates mentioned above as fixed terms. Age and BMI will be included as linear terms. The weight is calculated as $\frac{1}{1-P(non-adherenc\ )}$; weights will be calculated separately in each treatment group. We will then use the same analysis model as for the main analysis, except we will include the Stata options [pw=weight], and vce(robust).

6. Sensitivity Analysis

We anticipate a very small amount of missing data for the primary outcome. If the level of missing data for the primary outcome exceeds 1% of randomised participants, we will perform a sensitivity analysis to assess the robustness of our analysis of the primary outcome data under the assumption that data is missing-not-at-random (MNAR) [2, 17-19]. For example, this could occur if patients who were discharged home and had no postoperative pneumonia were less likely to respond to their telephone follow-up after 30 days, than patients who did have a postoperative pneumonia.

We will perform a sensitivity analysis assuming the data is MNAR based on the following formula:

$$P(Y=1|X=x\ )= P(Y=1|X=x,obs)P(obs|X=x) + \ P(Y=1|X,unobs)P(unobs|X=x)$$

Where Y denotes the primary outcome (1=yes, 0=no) and X denotes the treatment allocation (1=treatment, 0=usual care), *obs* denotes that the patient's outcome was available, and *unobs* denotes that the patient's outcome was missing.

In this sensitivity analysis, the odds ratio for the treatment effect will be calculated by:

$$\frac{P(Y=1|X=1\ )/\left(1-P(Y=1|X=1\ )\right)}{P(Y=1|X=0\ )/\left(1-P(Y=1|X=0\ )\right)}.$$

$P(Y = 1|X = x, obs)$ will be estimated from the model used in the primary analysis using STATA's 'margins' command. $P(obs|X = x)$ and $P(unobs|X = x)$ will be estimated based on the number of patients with complete and incomplete outcome data in each treatment arm. The probability of an event amongst those with unobserved outcomes in the usual care group, $P(Y = 1|X = usual\ care, unobs)$, will be set at 0.05, 0.10 and 0.15. The probability of an event amongst those with unobserved outcomes in the treatment group, $P(Y = 1|X = treatment, unobs)$, will be set at $P(Y = 1|X = usual\ care, unobs) + \delta$. We will use the following values of δ: -0.02, -0.01, 0, +0.01, +0.02.

Confidence intervals will be calculated on the log scale using the standard errors for the log odds ratio from the complete case analysis then transformed to the odds ratio scale.

References

1. International Surgical Outcomes Study, g., *Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries.* Br J Anaesth, 2016. **117**(5): p. 601-609.
2. White, I.R., et al., *Strategy for intention to treat analysis in randomised trials with missing outcome data.* BMJ, 2011. **342**: p. d40.
3. Montori, V.M. and G.H. Guyatt, *Intention-to-treat principle.* CMAJ, 2001. **165**(10): p. 1339-41.
4. Kahan, B.C., et al., *A re-randomisation design for clinical trials.* BMC Med Res Methodol, 2015. **15**: p. 96.
5. Kahan, B.C., et al., *Re-randomization increased recruitment and provided similar treatment estimates as parallel designs in trials of febrile neutropenia.* J Clin Epidemiol, 2018. **97**: p. 14-19.
6. Schulz, K.F., et al., *CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials.* BMJ, 2010. **340**: p. c332.
7. Canet, J., et al., *Prediction of postoperative pulmonary complications in a population-based surgical cohort.* Anesthesiology, 2010. **113**(6): p. 1338-50.
8. Canet, J., et al., *Development and validation of a score to predict postoperative respiratory failure in a multicentre European cohort: A prospective, observational study.* Eur J Anaesthesiol, 2015. **32**(7): p. 458-70.
9. Kahan, B.C., *Accounting for centre-effects in multicentre trials with a binary outcome - when, why, and how?* BMC Med Res Methodol, 2014. **14**: p. 20.
10. Kahan, B.C. and T.P. Morris, *Improper analysis of trials randomised using stratified blocks or minimisation.* Statistics in Medicine, 2012. **31**(4): p. 328-340.
11. Kahan, B.C., et al., *The risks and rewards of covariate adjustment in randomized trials: an assessment of 12 outcomes from 8 studies.* Trials, 2014. **15**: p. 139.
12. Hernandez, A.V., E.W. Steyerberg, and J.D. Habbema, *Covariate adjustment in randomized controlled trials with dichotomous outcomes increases statistical power and reduces sample size requirements.* J Clin Epidemiol, 2004. **57**(5): p. 454-60.
13. Turner, E.L., et al., *Covariate adjustment increased power in randomized controlled trials: an example in traumatic brain injury.* J Clin Epidemiol, 2012. **65**(5): p. 474-81.
14. Kahan, B.C., et al., *A comparison of methods to adjust for continuous covariates in the analysis of randomised trials.* BMC Med Res Methodol, 2016. **16**: p. 42.
15. White, I.R. and S.G. Thompson, *Adjusting for partially missing baseline measurements in randomized trials.* Stat Med, 2005. **24**(7): p. 993-1007.
16. Hernán, M.A. and J.M. Robins, *Per-Protocol Analyses of Pragmatic Trials.* New England Journal of Medicine, 2017. **377**(14): p. 1391-1398.
17. Little, R.J., et al., *The prevention and treatment of missing data in clinical trials.* N Engl J Med, 2012. **367**(14): p. 1355-60.
18. Morris, T.P., B.C. Kahan, and I.R. White, *Choosing sensitivity analyses for randomised trials: principles.* BMC Med Res Methodol, 2014. **14**: p. 11.
19. Wood, A.M., I.R. White, and S.G. Thompson, *Are missing outcome data adequately handled? A review of published randomized controlled trials in major medical journals.* Clin Trials, 2004. **1**(4): p. 368-76.

Appendix 1: Deriving outcomes and variables

Variables

At least 'one' co-morbid disease

- Equal to 1if:
  - At least one of the components of co-morbid disease is marked as 'yes'
- Equal to 0 if all of the components of co-morbid disease are marked as 'no'
- Missing if:
  - All components are missing
  - OR one or more components of co-morbid disease is missing, and all other components are marked as 'no'

Primary Outcome

Composite endpoint of pneumonia, endotracheal re-intubation or death within 30 days of randomisation.

- Equal to 1 if :
  - The patient experienced an event for one or more of the three components of the primary outcome (pneumonia, endotracheal re-intubation, death), even if data is missing for some of the other components (as in this case, the overall outcome is an event, regardless of the values of the missing components)
  - AND date of event is within 30 days of randomisation (for patients who experience an event for more than one of the three components, the primary outcome will be calculated based on the date of the first event)
- Equal to 0 if:
  - Data is available for each of the three components of the primary outcome
  - AND the patient did not experience an event within 30 days of randomisation
- Missing if:
  - Data is missing for all three components of the primary outcome
  - Data is missing for one or more components, and the patient did not experience an event within 30 days of randomisation for any of the observed components
  - One or more components is marked as 'yes' and is missing the date of the event, and the patient did not experience an event within 30 days of randomisation for the other component(s)

Secondary Outcomes

Pneumonia within 30 days of randomisation

- Equal to 1 if:
  - Pneumonia is marked as 'yes'
  - AND date of pneumonia is within 30 days of randomisation
- Equal to 0 if:
  - Pneumonia is marked as 'no'
  - OR pneumonia is marked as 'yes' and date of pneumonia is not within 30 days of randomisation
- Missing if:
  - Data is not available on whether the patient experienced an event or not
  - Pneumonia is marked 'yes' and missing date of pneumonia

Death within 30 days of randomisation

- Equal to 1 if:
  - Patient status at 30-day follow-up is dead
  - AND date of death is within 30 days of randomisation
- Equal to 0 if:
  - Patient status at 30-day follow-up is alive
  - OR patient status at 30-day follow-up is marked as 'dead' and date of death is not within 30 days of randomisation
- Missing if:
  - Patient status at 30-day follow-up is missing
  - Patient status at 30-day follow-up is marked as 'dead' and missing date of death

Endotracheal re-intubation within 30 days of randomisation

- Equal to 1 if:
  - Endotracheal re-intubation is marked as 'yes'
  - AND date of endotracheal re-intubation is within 30 days of randomisation
- Equal to 0 if:
  - Endotracheal re-intubation is marked as 'no'
  - OR endotracheal re-intubation is marked as 'yes' and date of endotracheal re-intubation is not within 30 days of randomisation
- Missing if:
  - Data is not available on whether the patient experienced an event or not
  - Endotracheal re-intubation marked as 'yes' and missing date of endotracheal re-intubation

All-cause mortality at one year after randomisation

- Equal to 1 if:
  - Patient status at one-year follow-up is dead
  - AND date of death is within one year of randomisation
- Equal to 0 if:
  - Patient status at one-year follow-up is alive
  - OR patient status at one-year follow-up is marked as 'yes' and date of death is not within one-year of randomisation
- Missing if:
  - Patient status at one-year follow-up is missing
  - Patient status at one-year follow-up is marked as 'dead' and missing date of death

Postoperative infection within 30 days of randomisation

This is defined as one or more of the following infections (more detail on the definition of each type of infection is available in the PRISM protocol):

1) Superficial surgical site infection
2) Deep surgical site infection
3) Organ space surgical site infection
4) Urinary tract infection
5) Infection, source uncertain
6) Laboratory confirmed blood stream infection
7) Pneumonia

- Equal to 1 if:
  - At least one of the components of postoperative infection is listed as occurring (i.e. listed under Clavien-Dindo grade I-V)
- Equal to 0 if:
  - All of the components of postoperative infection are "None"
- Missing if:
  - All components are missing
  - OR one or more of the components of postoperative infection is missing and all other components are "None"

Postoperative mechanical ventilation (invasive or non-invasive) with 30 days of randomisation

This consists of the following components:

1. Mechanical ventilation (invasive or non-invasive) within four hours of the end of surgery (page 5 of PRISM CRF)
2. Mechanical ventilation (invasive or non-invasive) after leaving the operating room (page 7 of the PRISM CRF)

- Equal to 1 if:
  - At least one of the components of mechanical ventilation is "Yes"
- Equal to 0 if:
  - All of the components of mechanical ventilation are "No"
- Missing if:
  - All of the components are missing
  - One or more components of mechanical ventilation is missing, and all other components are "No"

Appendix 2: Dummy tables

Table 1: Baseline patient characteristics

Baseline Characteristics	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Gender - no. (%)				
Male				
Female				
Age (years)				
Mean (SD)				
Median (IQR)				
Current Smoker - no. (%)				
[a]American Society of Anaesthesiology grade - no. (%)				
I				
II				
III				
IV				
[b]Chronic comorbid disease - no. (%)				
COPD				
Asthma				
Interstitial lung disease or pulmonary fibrosis				
Bronchiectasis				
Ischaemic heart disease				
Diabetes mellitus				
Heart failure				
Liver cirrhosis				
Active cancer				
Previous stroke or TIA				
Respiratory infection within the previous month				
HIV				
Planned surgical procedure - no. (%)				
Resection of colon, rectum or small bowel				
Resection of liver, pancreas or gall bladder				
Resection of stomach (non-obesity surgery)				
Resection of oesophagus (non-obesity surgery)				
Obesity surgery				
Vascular surgery				
Other intra-peritoneal surgery				
Planned use of epidural anaesthesia - no. (%)				
Country - no. (%)				
Italy				
Spain				
Sweden				
United Kingdom				
South Africa				
Norway				
Surgical procedure performed - no (%)				
Resection of colon, rectum or small bowel				
Resection of liver, pancreas or gall bladder				

Resection of stomach (non-obesity surgery)				
Resection of oesophagus (non-obesity surgery)				
Obesity surgery				
Vascular surgery				
Other intra-peritoneal surgery				
Pre-operative blood test results				
Haemoglobin (g/dL)				
Mean (SD)				
Median (IQR)				
Creatinine (µmol/L)				
Mean (SD)				
Median (IQR)				
Body Mass Index (kg/m^2)				
Mean (SD)				
Median (IQR)				
ARISCAT Score				
Mean (SD)				
Median (IQR)				

Abbreviations: SD, standard deviation; IQR, Interquartile range; COPD, chronic obstructive pulmonary disease.

[a] American Society of Anaesthesiology grades are defined as follows (grade 5 patients were not eligible for inclusion): 1, a healthy patient; 2, a patient with mild systemic disease that does not limit physical activity; 3, a patient with severe systemic disease that limits physical activity; and 4, a patient with severe systemic disease that is a constant threat to life.

[b] Patient may have more than one chronic co-morbid disease.

Table 2: Clinical management of study groups

Clinical management	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Open surgical technique used during surgery - no. (%)				
Anaesthetic technique - no. (%)				
General				
Epidural				
Spinal				
Endotracheal tube inserted				
Mechanical ventilation during surgery				
Recruitment manoeuvre - no. (%)				
Mechanical ventilation - no. (%)				
[a]Maximum positive end-expiratory pressure (cmH_2O)				
Mean (SD)				
Median (IQR)				
[a]Maximum set tidal volume (ml)				
Mean (SD)				
Median (IQR)				
[a]Maximum respiratory rate (min^{-1})				
Mean (SD)				
Median (IQR)				
[a]Maximum FiO_2 (%)				
Mean (SD)				
Median (IQR)				
Intravenous fluids during surgery				
Total volume of intravenous fluid administered excluding blood products (mL)				
Mean (SD)				
Median (IQR)				
Total volume of blood products administered (mL)				
Mean (SD)				
Median (IQR)				
Planned level of care on the first night after surgery - no. (%)				
Critical care unit level 3				
Critical care unit level 2				
Post- anaesthesia care unit				
Surgical ward				
Level of care on the first night after surgery - no. (%)				
Critical care unit level 3				
Critical care unit level 2				
Post- anaesthesia care unit				
Surgical ward				
Respiratory support after surgery (within 4 hours of the end of surgery) - no. (%)				
Invasive mechanical ventilation				
Non-invasive mechanical ventilation				
High flow nasal oxygen therapy				

Abbreviation: SD, standard deviation; IQR, Interquartile range

[a] Only summarised for patients who received mechanical ventilation during surgery

Table 3: Adherence and contamination

Adherence and contamination - no. (%)	Usual Care (n=XXXX)	CPAP (n=XXXX)
Patients with ≥ 1 treatment deviation	XX (XX.X %)	XX (XX.X %)
Total number of deviations	XXX	XXX
Number of treatment deviations per patient		
0	XXX (XX.X %)	XXX (XX.X %)
1	XXX (XX.X %)	XXX (XX.X %)
2	N/A	XXX (XX.X %)
3	N/A	XXX (XX.X %)
Types of deviations		
Participant in the intervention group did not receive CPAP	N/A	XXX (XX.X %)
CPAP administered for less than 4 hours duration	N/A	XXX (XX.X %)
CPAP administered with significant interruption	N/A	XXX (XX.X %)
CPAP started at a dose other than 5 cmH_2O	N/A	XXX (XX.X %)
Participant in the usual care group did receive CPAP	XXX (XX.X %)	N/A

Table 4: Adherence and contamination by CPAP delivery method

Adherence and contamination - no. (%)	CPAP[a] (n=XXXX)		
	Face mask (n=XXXX)	Helmet device (n=XXXX)	Nasal mask (n=XXXX)
Patients with ≥ 1 treatment deviation	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Total number of deviations	XXX	XXX	XXX
Number of treatment deviations per patient			
0	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
1	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
2	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
3	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Types of deviations			
Participant in the intervention group did not receive CPAP	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
CPAP administered for less than 4 hours duration	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
CPAP administered with significant interruption	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
CPAP started at a dose other than 5 cmH_2O	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)

[a]XXX patients had missing data on CPAP method out of XXXX patients randomised to the CPAP group

Table 5: Primary and secondary outcomes

Outcomes	Number of patients included in analysis - no. (%)		Summary measure		Adjusted odd ratios (95% CI)	P-value
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP		
Pneumonia, endotracheal re-intubation or death within 30 days of randomisation (primary outcome)						
Pneumonia within 30 days of randomisation						
Endotracheal re-intubation within 30 days of randomisation						
All-cause mortality within 30 days of randomisation						
Postoperative infection within 30 days of randomisation						
Postoperative mechanical ventilation (invasive or non-invasive) within 30 days of randomisation						
All-cause mortality within one year of randomisation						

Table 6: Complications within 30 days of randomisation

Complication	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Respiratory - no. (%)				
Pneumonia				
Pleural effusion				
Pneumothorax				
Bronchospasm				
Aspiration pneumonitis				
Acute respiratory distress syndrome (ARDS)				
Infections - no. (%)				
Surgical site infection (superficial)				
Surgical site infection (deep)				
Surgical site infection (organ space)				
Urinary tract infection				
Infection, source uncertain				
Laboratory confirmed blood stream infection				
Cardiac - no. (%)				
Myocardial infarction				
Arrhythmia				
Cardiogenic pulmonary oedema				
Cardiac arrest with resuscitation				
Other - no. (%)				
Acute kidney injury				
Pulmonary embolism				
Stroke				
Acute psychosis or delirium				
Bowel infarction				
Anastomotic leak				
Perforation of viscus				
Gastro-intestinal bleed				
Other postoperative haemorrhage				
Any other complication				

Table 7: Complications within 30 days of randomisation in the intervention group by CPAP delivery method

Complication	Number of patients included in analysis - no. (%)			Summary measure		
	CPAP[a] (n=XXXX)			CPAP		
	Face mask (n=XXX)	Helmet device (n=XXX)	Nasal mask (n=XXX)	Face mask	Helmet device	Nasal mask
Respiratory - no. (%)						
Pneumonia						
Pleural effusion						
Pneumothorax						
Bronchospasm						
Aspiration pneumonitis						
Acute respiratory distress syndrome						
Infections - no. (%)						
Surgical site infection (superficial)						
Surgical site infection (deep)						
Surgical site infection (organ space)						
Urinary tract infection						
Infection, source uncertain						
Laboratory confirmed blood stream infection						
Cardiac - no. (%)						
Myocardial infarction						
Arrhythmia						
Cardiogenic pulmonary oedema						
Cardiac arrest with resuscitation						
Other - no. (%)						
Acute kidney injury						
Pulmonary embolism						
Stroke						
Acute psychosis or delirium						
Bowel infarction						
Anastomotic leak						
Perforation of viscus						
Gastro-intestinal bleed						
Other postoperative haemorrhage						
Any other complication						

[a]XXX patients had missing data on CPAP method out of XXXX patients randomised to the CPAP group

Table 8: Complications within 30 days of randomisation by treatment allocation and Clavien-Dindo grade

Complication	Number of patients included in analysis - no. (%)		Summary measure					
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care			CPAP		
			I-II	III-V	Total	I-II	III-V	Total
Respiratory - no. (%)								
Pneumonia								
Pleural effusion								
Pneumothorax								
Bronchospasm								
Aspiration pneumonitis								
Acute respiratory distress syndrome (ARDS)								
Infections - no. (%)								
Surgical site infection (superficial)								
Surgical site infection (deep)								
Surgical site infection (organ space)								
Urinary tract infection								
Infection, source uncertain								
Laboratory confirmed blood stream infection								
Cardiac - no. (%)								
Myocardial infarction								
Arrhythmia								
Cardiogenic pulmonary oedema								
Cardiac arrest with resuscitation								
Other - no. (%)								
Acute kidney injury								
Pulmonary embolism								
Stroke								
Acute psychosis or delirium								
Bowel infarction								
Anastomotic leak								
Perforation of viscus								
Gastro-intestinal bleed								
Other postoperative haemorrhage								
Any other complication								

Table 9: Process measures

Process measures	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Re-admission to hospital within 30 days of randomisation - no. (%)				
Duration of primary hospital admission from randomisation (days)				
Mean (SD)				
Median (IQR)				
[a]Total duration of critical care stay within 30 days of randomisation (days)				
Number of patients admitted to a critical care unit - no. (%)				
Mean (SD)				
Median (IQR)				

Abbreviation: SD, standard deviation; IQR, interquartile range.

[a]Summarised only for patients admitted to critical care unit

Table 10: Critical care stay within 30 days of randomisation [a]

Critical Care Stay within 30 days of randomisation	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Number of patients admitted to a critical care unit - no. (%)				
Duration of level 2 critical care stay (days)				
Mean (SD)				
Median (IQR)				
Duration of level 3 critical care stay (days)				
Mean (SD)				
Median (IQR)				

Abbreviation: SD, standard deviation; IQR, interquartile range.

[a]Summarised only for patients admitted to critical care unit

Table 11: Summary of CPAP for patients randomised to the CPAP group

CPAP Characteristics	Number of patients included in analysis - no. (%)	Summary measure
	CPAP (n=XXXX)	CPAP
Number of patients who received CPAP - no. (%)		
Total duration of CPAP within 12 hours of the end of surgery (minutes)		
Mean (SD)		
Median (IQR)		
Maximum airway pressure received within 12 hours of the end of surgery (cmH_2O)		
Mean (SD)		
Median (IQR)		
Primary method of CPAP delivery - no. (%)		
Face mask		
Helmet device		
Nasal mask		
Extra research staff present to help deliver CPAP - no. (%)		
Staff administering CPAP used equipment to monitor airway pressures - no. (%)		
Staff administering CPAP used equipment to monitor FiO2 - no. (%)		
Patient had a nasogastric tube in situ during CPAP - no. (%)		

Abbreviation: IQR, interquartile range; SD, standard deviation; CPAP, continuous positive airway pressure

Table 12: Safety outcome measures

Adverse Events - no.(%)	CPAP (n=XXXX)
Patients with ≥ 1 adverse event	XX (XX.X %)
Total number of adverse events	XXX
Number of adverse events per patient	
0	XXX (XX.X %)
1	XXX (XX.X %)
2	XXX (XX.X %)
3	XXX (XX.X %)
4	XXX (XX.X %)
Type of adverse event	
Interface intolerance due to excessive air leak	XXX (XX.X %)
Pain	XXX (XX.X %)
Cutaneous pressure area	XXX (XX.X %)
Claustrophobia	XXX (XX.X %)
Oronasal dryness	XXX (XX.X %)
Hypercapnia	XXX (XX.X %)
Haemodynamic instability	XXX (XX.X %)
Vomiting	XXX (XX.X %)
Aspiration of gastric contents	XXX (XX.X %)
Other	XXX (XX.X%)

Table 13: Summary of 'other' safety outcomes with a prevalence of more than 1%

Other Adverse Events - no.(%)	CPAP (n=XXXX)
Total number of other adverse events	XXX (XX.X %)
Type of adverse event	
Other 1	XXX (XX.X %)
Other 2	XXX (XX.X %)
Other 3	XXX (XX.X %)
Other 4	XXX (XX.X %)
Other 5	XXX (XX.X %)

Table 14: Safety outcomes measures by CPAP delivery method

Adverse Events	CPAP[a] (n=XXXX)		
	Face mask (n=XXXX)	Helmet device (n=XXXX)	Nasal mask (n=XXXX)
Patients with ≥ 1 adverse event	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Total number of adverse events	XXX	XXX	XXX
Number of adverse events per patient			
0	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
1	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
2	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
3	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
4	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Type of adverse event			
Interface intolerance due to excessive air leak	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Pain	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Cutaneous pressure area	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Claustrophobia	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Oronasal dryness	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Hypercapnia	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Haemodynamic instability	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Vomiting	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Aspiration of gastric contents	XXX (XX.X %)	XXX (XX.X %)	XXX (XX.X %)
Other	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

[a]XXX patients had missing data on CPAP method out of XXXX patients randomised to the CPAP group

Table 15: ARISCAT Score

ARISCAT	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
ARISCAT Score				
Mean (SD)				
Median (IQR)				
Components				
Age (years) - no. (%)				
≥50				
51-80				
> 80				
Percentage peripheral oxygen saturation (SpO_2) - no. (%)				
≥ 96%				
91-95%				
≤90%				
Respiratory infection within the last month - no. (%)				
Preoperative anaemia (Hgb ≤10 g/dL) – no. (%)				
Surgical incision - no. (%)				
Upper abdominal				
Intrathoracic				
Peripheral				
Duration of surgery - no. (%)				
< 2 hours				
2-3 hours				
> 3 hours				
[a]Emergency procedure - no. (%)				

Abbreviation: SD, standard deviation; IQR, interquartile range

[a] All patients recruited in the trial were elective

Table 16: Pre-specified subgroup analyses for primary outcome

Planned surgical procedure	Number of patients included in analysis - no. (%)		Pneumonia, endotracheal re-intubation or death within 30 days of randomisation - no. (%)		Adjusted odds ratio (95% CI)	Test for interaction p-value
	Usual care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP		
Lower gastrointestinal (resection of colon, rectum, or small bowel)			XXX/XXXX (XX.X)	XXX/XXXX (XX.X)	X.XX (X.XX-X.XX)	X.XX
Hepatobiliary (resection of liver, pancreas, or gall bladder)			XXX/XXXX (XX.X)	XXX/XXXX (XX.X)	X.XX (X.XX-X.XX)	
Upper gastrointestinal (resection of oesophagus, or resection of stomach (non-obesity surgery))			XXX/XXXX (XX.X)	XXX/XXXX (XX.X)	X.XX (X.XX-X.XX)	
Other (obesity surgery, vascular procedure, or other intra-peritoneal surgery)			XXX/XXXX (XX.X)	XXX/XXXX (XX.X)	X.XX (X.XX-X.XX)	

Table 17: Results of sensitivity analysis for data being missing not at random of primary outcome within 30 days of randomisation

Proportion with missing data in usual care assumed to have an event	Proportion with missing data in intervention group assumed to have an event	Odds ratio (95% CI)
0.05	0.03	
	0.04	
	0.06	
	0.07	
0.10	0.08	
	0.09	
	0.11	
	0.12	
0.15	0.13	
	0.14	
	0.16	
	0.17	

Table 18: Per-protocol analysis using inverse probability weighting

Outcome	Number of patients included in analysis - no. (%)		Summary measure		Adjusted odd ratios (95% CI)	P-value
	Usual Care[a] (n=XXXX)	CPAP[b] (n=XXXX)	Usual Care	CPAP		
Pneumonia, endotracheal re-intubation or death within 30 days of randomisation (primary outcome)						
Pneumonia within 30 days of randomisation						
Endotracheal re-intubation within 30 days of randomisation						
All-cause mortality within 30 days of randomisation						

[a] Excludes XXX/XXXX patients who received CPAP in the usual care group

[b] Excludes XXX/XXXX patients who received no CPAP in the intervention group

Table 19: Summary of investigators' self-assessment of blinding

Investigator self-assessment of blinding - no. (%)	Number of patients included in analysis - no. (%)		Summary measure	
	Usual Care (n=XXXX)	CPAP (n=XXXX)	Usual Care	CPAP
Suitably blinded				
May have known the study group allocation				
Definitely knew the study group allocation				

Figure 1: Information for CONSORT flow diagram

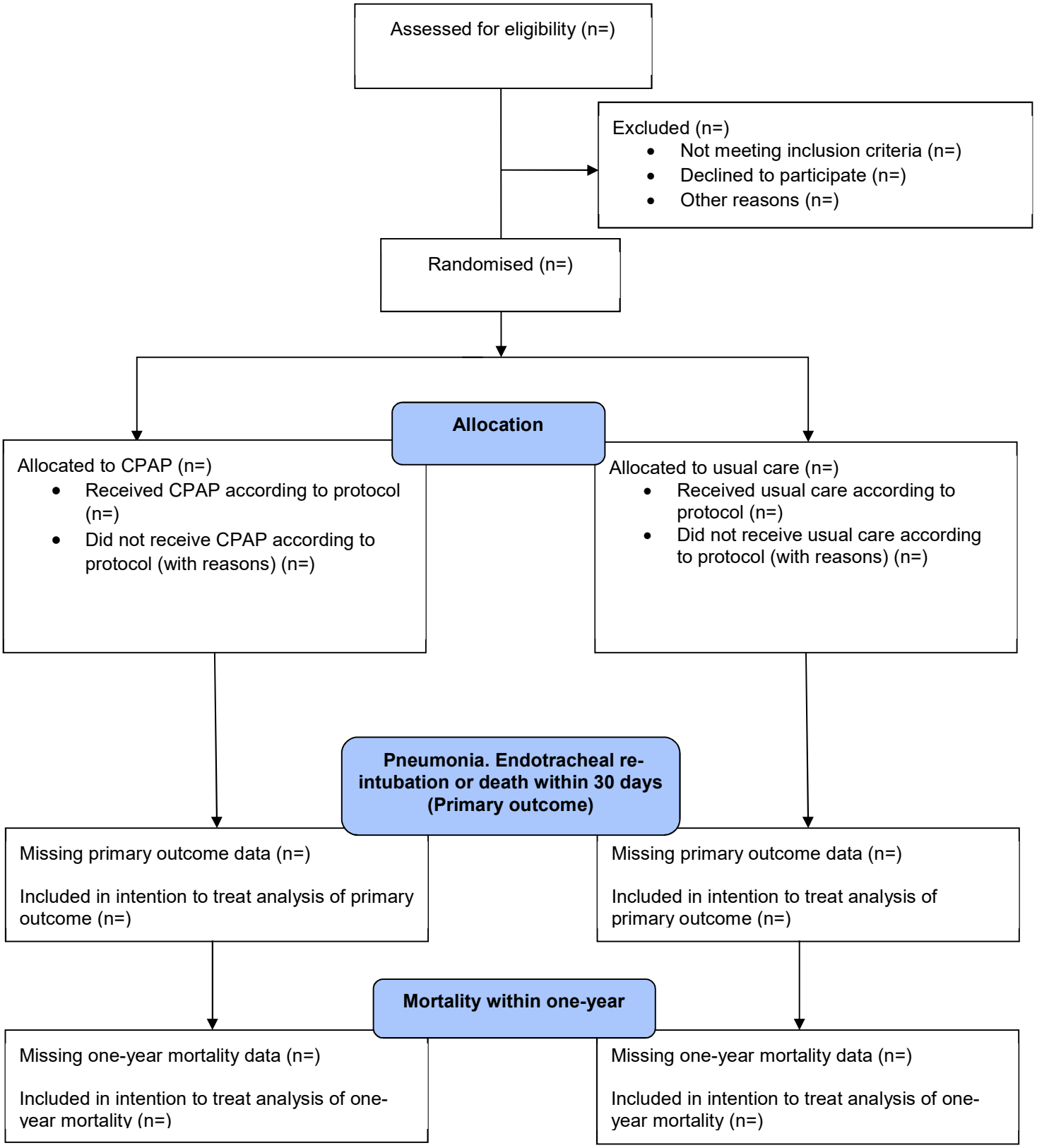

Figure 2: Kaplan-Meier survival curves by treatment allocation for (a) 30 days and (b) one-year following randomisation