Prevention of Respiratory Insufficiency after Surgical Management:

PRISM trial

Site Initiation Presentation

Hospital name

Date

PRISM contacts

Chief Investigator: Rupert Pearse & Marco Ranieri

Research Fellow: Tom Abbott

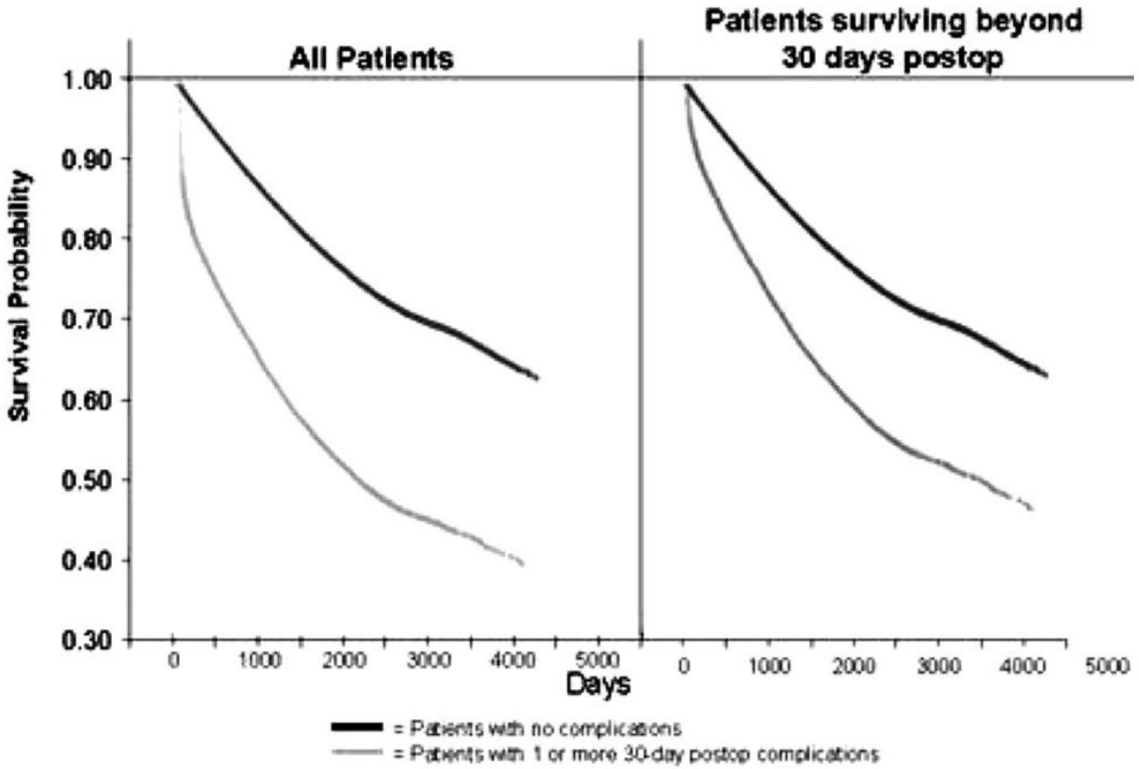
Senior Research Manager: Priyanthi Dias

Research assistant: Mari-Liis Pakats

PRISM Website: www.prismtrial.org

Contact email: admin@prismtrial.org

Follow us on Twitter : @prismtrial

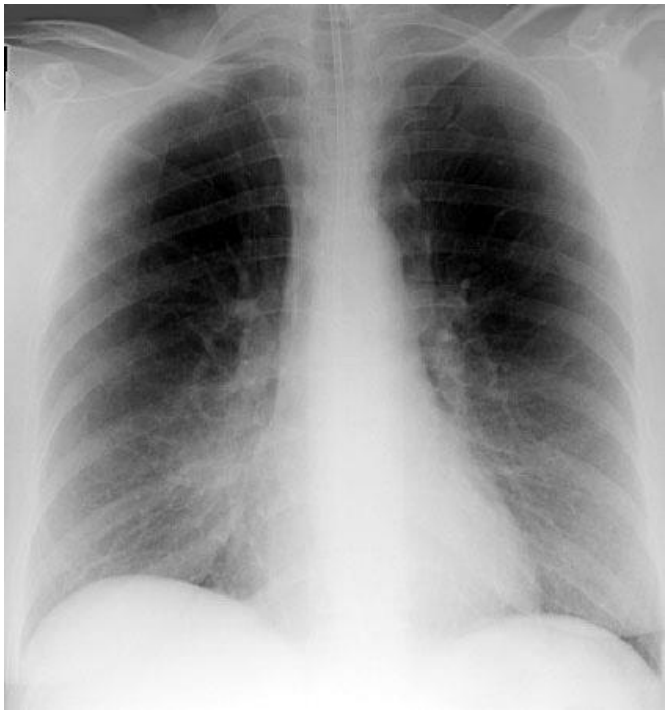


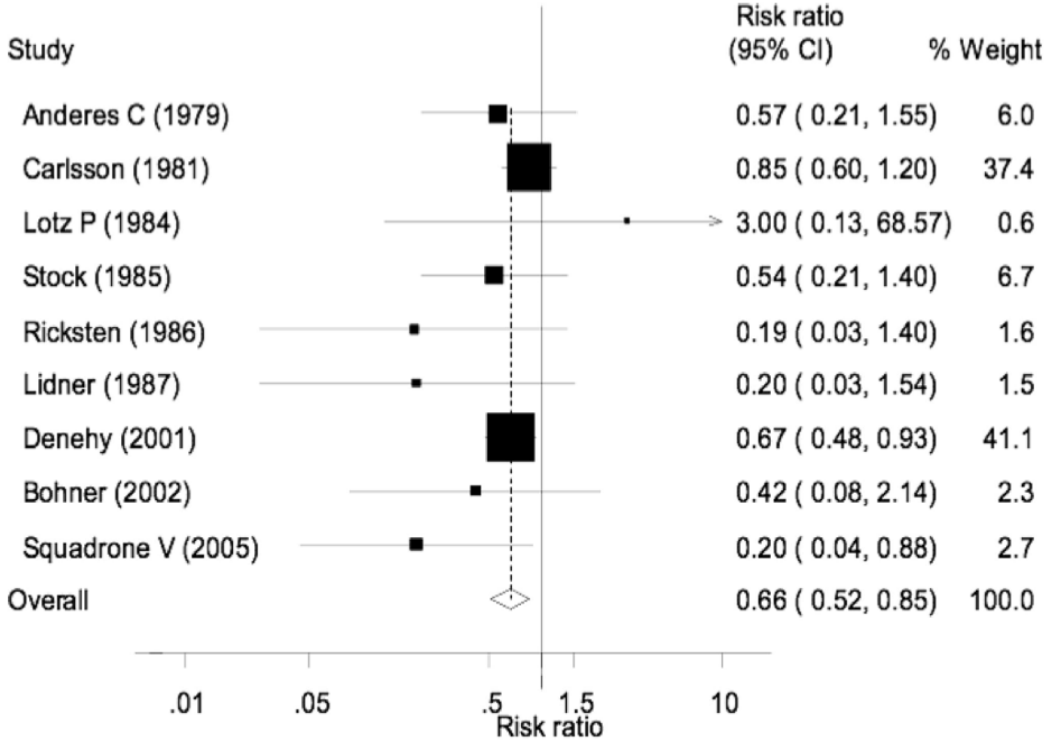
Postoperative complications decrease long-term survival

Khuri et al. Annals of surgery 2005; 242: 326-41.

The problem

- Atelectasis
- Pulmonary collapse
- Pneumonia
- Respiratory failure





CPAP may prevent respiratory failure after abdominal surgery

Ferreyra G et al *Ann Surg* 2008; 247: 617–626.

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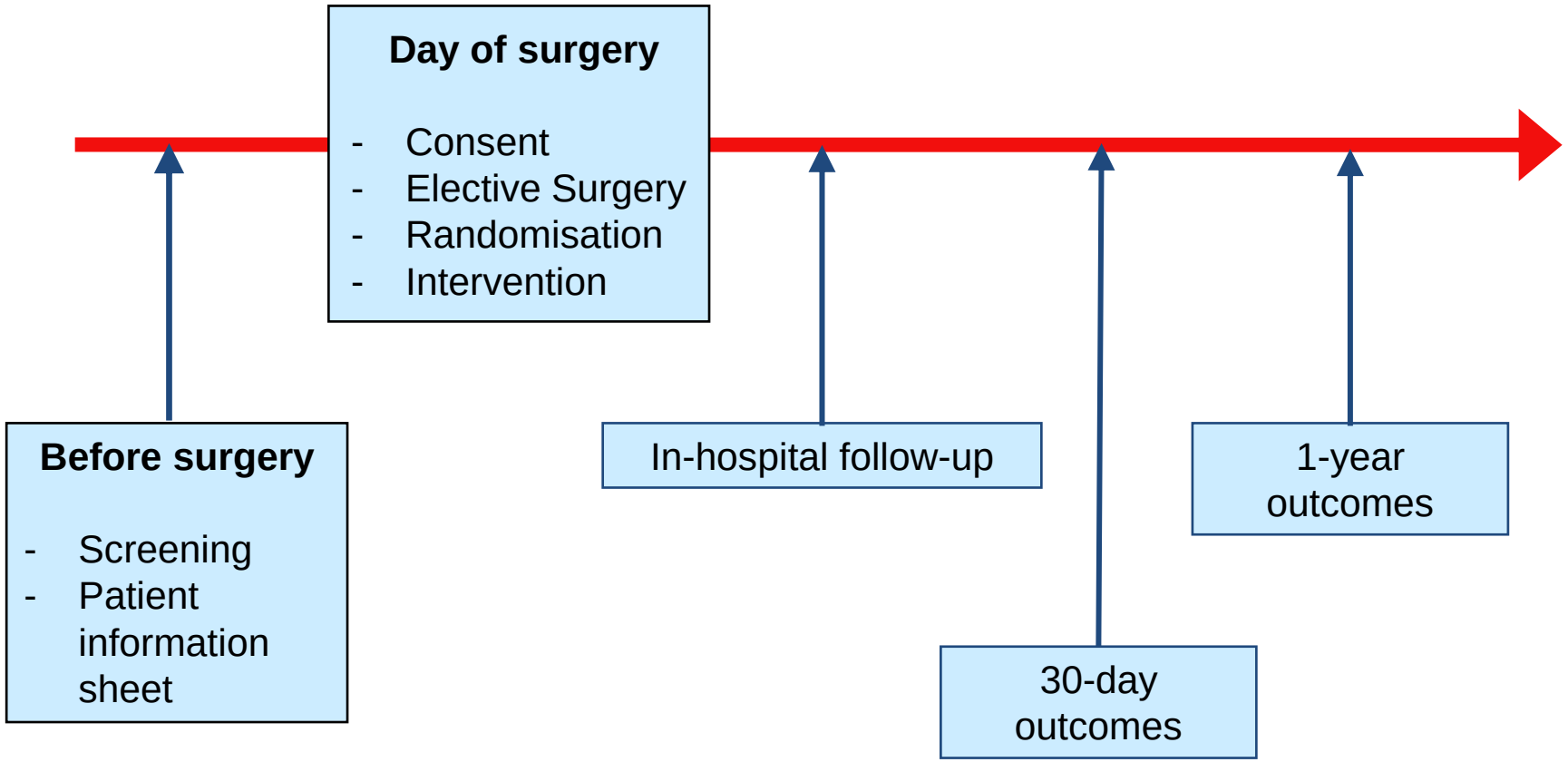
Objective

To determine whether early postoperative continuous positive airway pressure (CPAP) reduces the incidence of respiratory complications and improves one-year survival following major intra-peritoneal surgery.

Trial design

- International multi-centre randomised controlled trial
- Open study group allocation
- Sponsored by Queen Mary University of London (UK)
- Sample size = 4,800 patients
- Elective surgery only
- 50 sites (25 UK and 25 Italy)

Trial Design



Recruitment

- Aim to contact patients at least 24 hours prior to surgery
- Identify patients in the pre-admission or surgical outpatient clinic
- The first approach should be by a member of the clinical team
- Written informed consent must be obtained before surgery
- Keep a log of all the patients screening for participation.

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Informed consent

- PI or delegate
- Explain aims, methods and benefits/hazards
- Patient information sheet
- Informed consent form
- Consent must be given before the start of surgery

Inclusion criteria

- Age ≥50 years
- Elective major intra-peritoneal surgery
- Planned use of open technique

Exclusion criteria

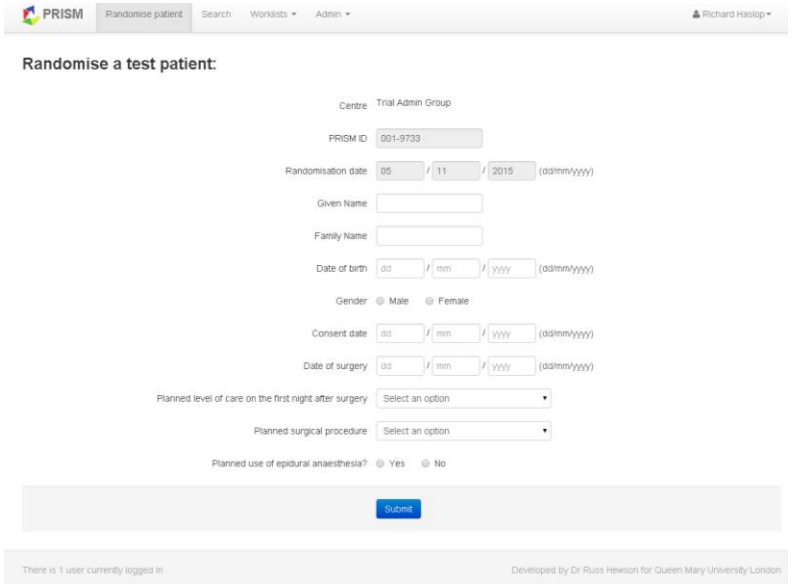
- Inability or refusal to provide informed consent
- Anticipated requirement for mechanical ventilation for at least four hours after surgery
- Pregnancy or obstetric surgery
- Previous enrolment in PRISM
- Current participation in a clinical trial of a treatment with a similar biological mechanism or related primary outcome measure
- Clinician refusal
- Contraindication to continuous positive airway pressure (CPAP)

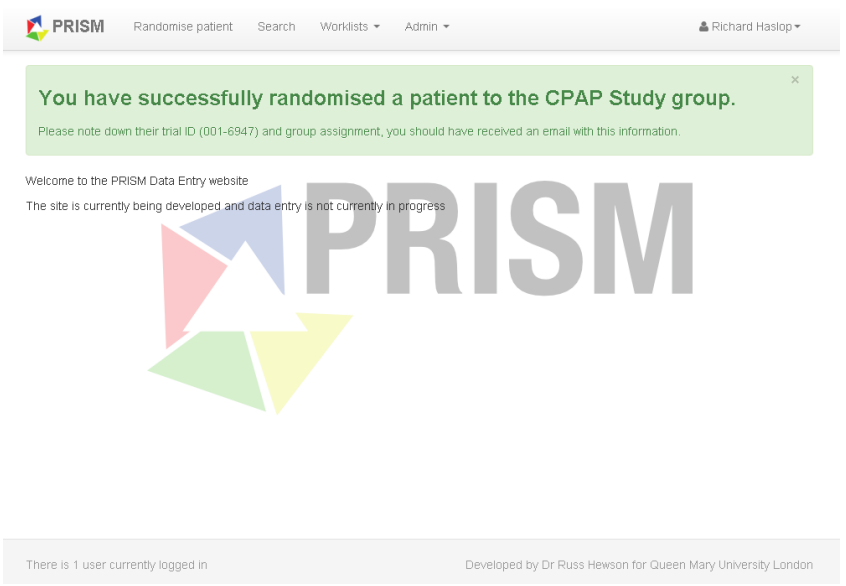
Randomisation

- After informed consent
- After the surgery has completed (up to 4h after the end of the surgical procedure)
- Via the PRISM online database
- Randomisation criteria:
  - Planned surgical procedure category
  - Planned use of epidural anaesthesia

Randomisation

- Register at http://database.prismtrial.org
- Enter “username” and “password” provided at registration





- Click “randomise patient” and enter relevant information

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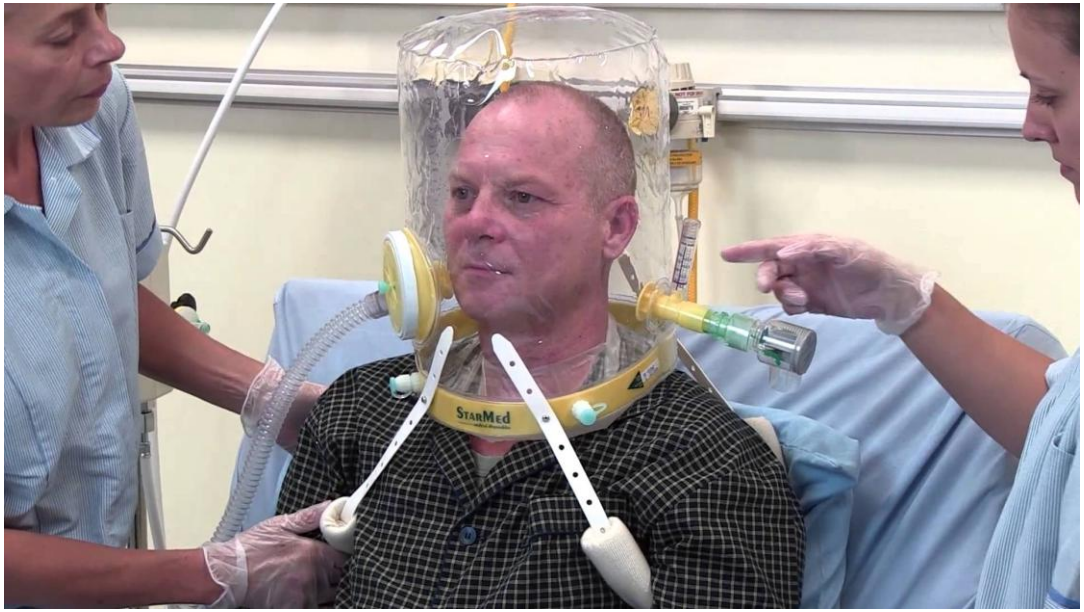
Intervention



CPAP for at least four hours, ideally started within four hours of completion of surgery

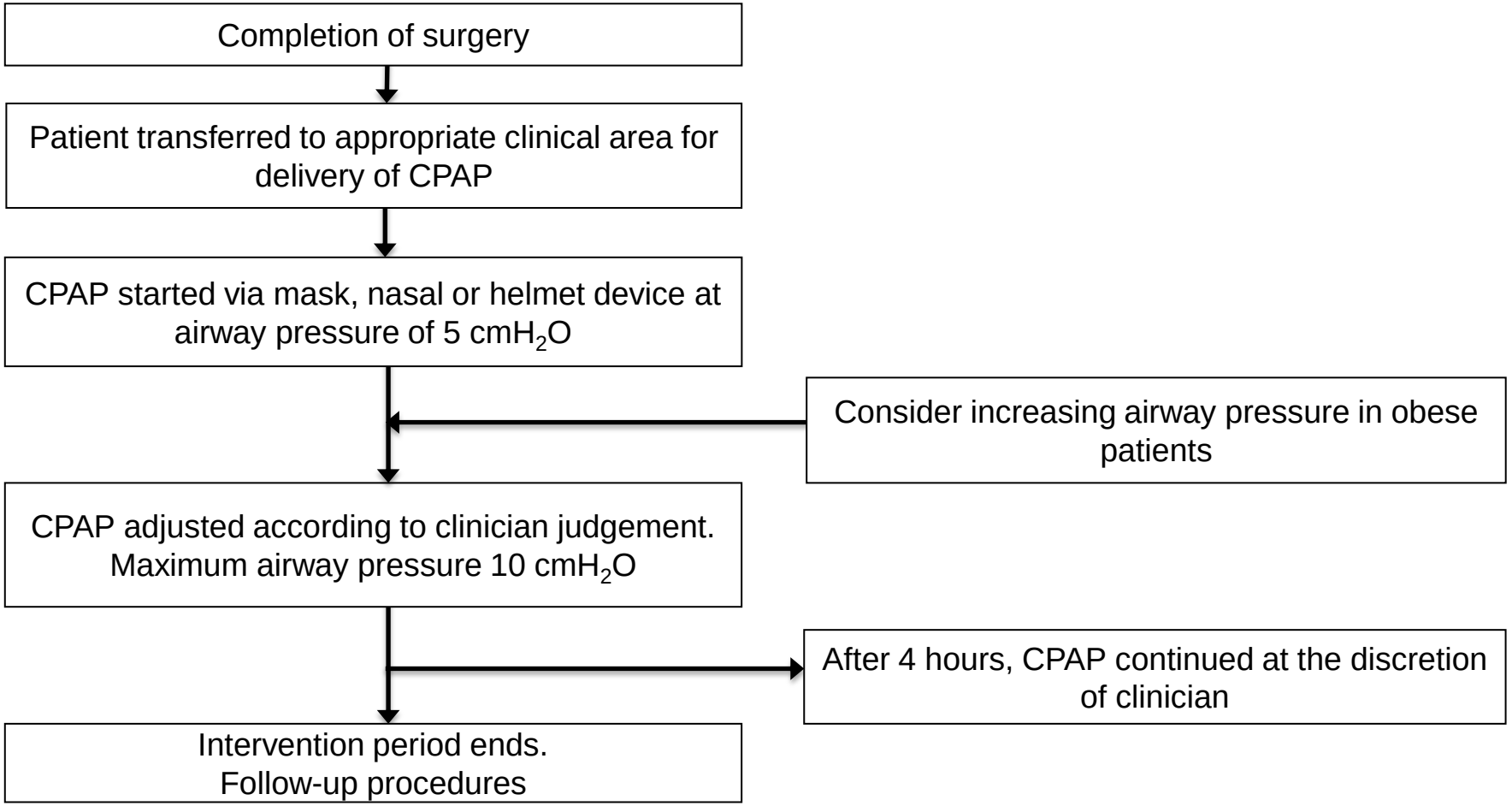
Intervention group

CPAP for at least four hours ideally started within four hours of the end of surgery

- Can be commenced up to 12h after the end of surgery
- Delivered by trained staff according to local policies
- Mask, nasal or helmet/hood delivery device
- Clinician can choose CPAP machine
- Minimum airway pressure 5cmH_2O
- Can be increased to maximum of 10cmH_2O

NB. HFNO is not considered CPAP

Intervention algorithm



Usual care group

Managed by clinical staff according to hospital policy

- Facemask oxygen is usual good practice
- Usual care patients receiving CPAP within 12 hours recorded as protocol deviation

Primary outcome

Pneumonia, endotracheal re-intubation or death within 30

days of randomisation

Secondary outcomes

- Pneumonia within 30 days of randomisation
- Endotracheal re-intubation within 30 days of randomisation
- Death within 30 days of randomisation
- Postoperative infection within 30 days of randomisation
- Mechanical ventilation (invasive or non-invasive) within 30 days of randomisation
- All-cause mortality at one year after randomisation
- Quality adjusted life years (QALY) at one year after randomisation

Follow-up

- Review a participant's medical record (paper or electronic) and contact them on the telephone to conduct brief interviews at 30 days and one year after randomisation
- Verified by the PI or designee
- After the completion of one-year follow up the PI or designee will lock each case so that no further data can be entered.

Quality of life

- EQ-5D(*3L*) questionnaire
- Simple descriptive profile and index value for health status
- Ask the patient each question on the list and record the appropriate answer on the CRF

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Questions…..?

Queen Mary
University of London

www.qmul.ac.uk

Data collection

Case Report Form (CRF) completion:

- Timely and accurate
- Entered into eCRF
- Logins to access the eCRF will be issued by the trial team

Minimising Bias

- Follow-up will be conducted by a member of research staff who is unaware of trial group allocation
- Complications will be verified by the local PI or designee who is unaware of trial group allocation

Self assessment of blinding

- To quantify the degree of blinding, research staff will make a self-assessment of blinding when collecting follow-up data
- Grade as one of the following options:
  - Suitably blinded
  - May have known study group allocation
  - Definitely knew study group allocation

Protocol deviations

- Failure to administer CPAP to patients in the intervention group.
- Starting CPAP at a dose other than 5cmH2O
- Administration of CPAP to a patient in usual care group.
- Administration of CPAP for less than 4 hours.
- Administration of CPAP with significant interruption for a patient in the intervention group.

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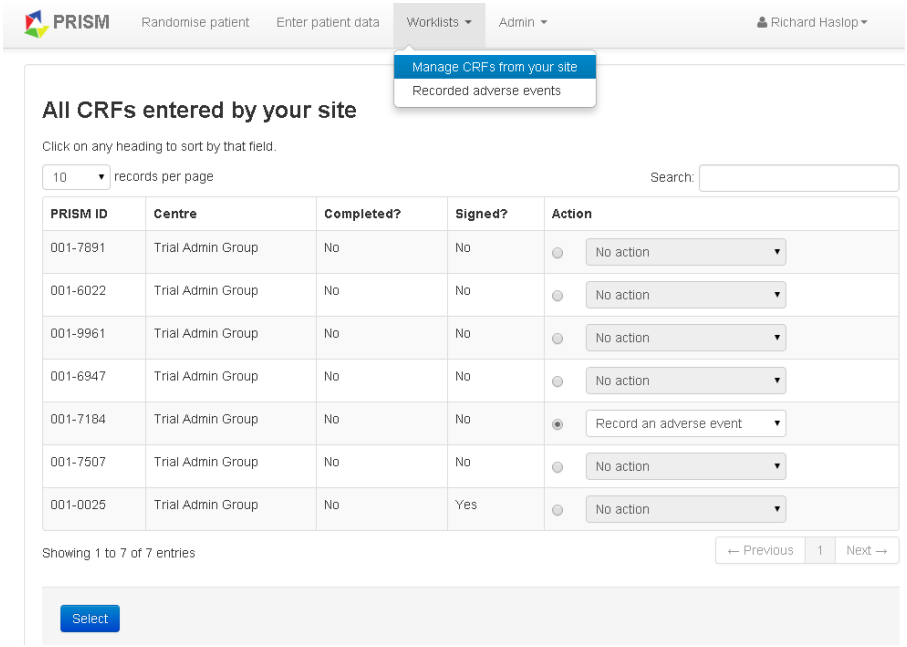
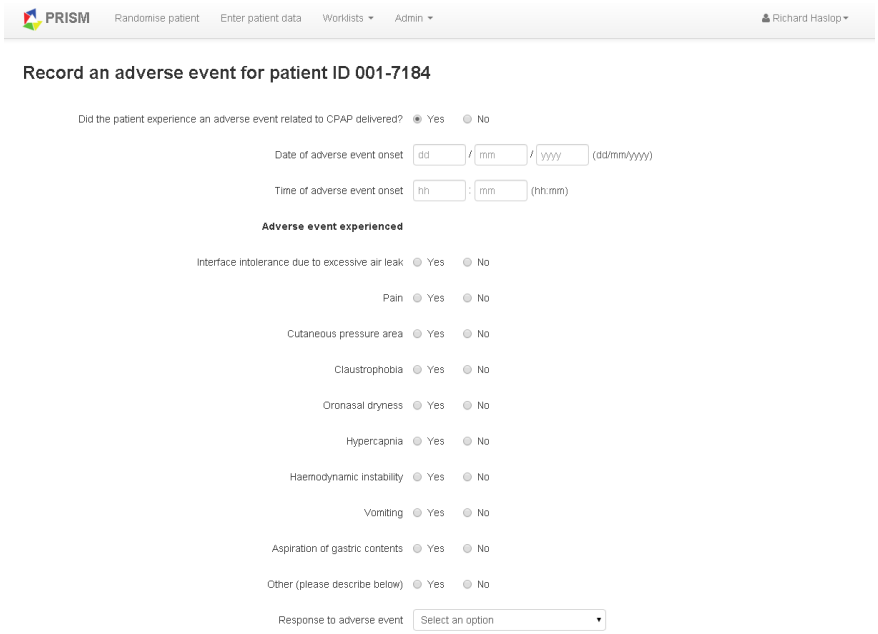
Adverse event reporting

- Only AEs **clearly related to the use of CPAP** will be reported
- PI responsible for confirming relatedness to CPAP
- Pre-defined AEs are listed in the AE SOP and protocol
- If AE does not fit into pre-defined categories record as ‘other’
- Clinician to decide if it is safe to continue using CPAP
- Please refer to the AE SOP

Adverse event reporting

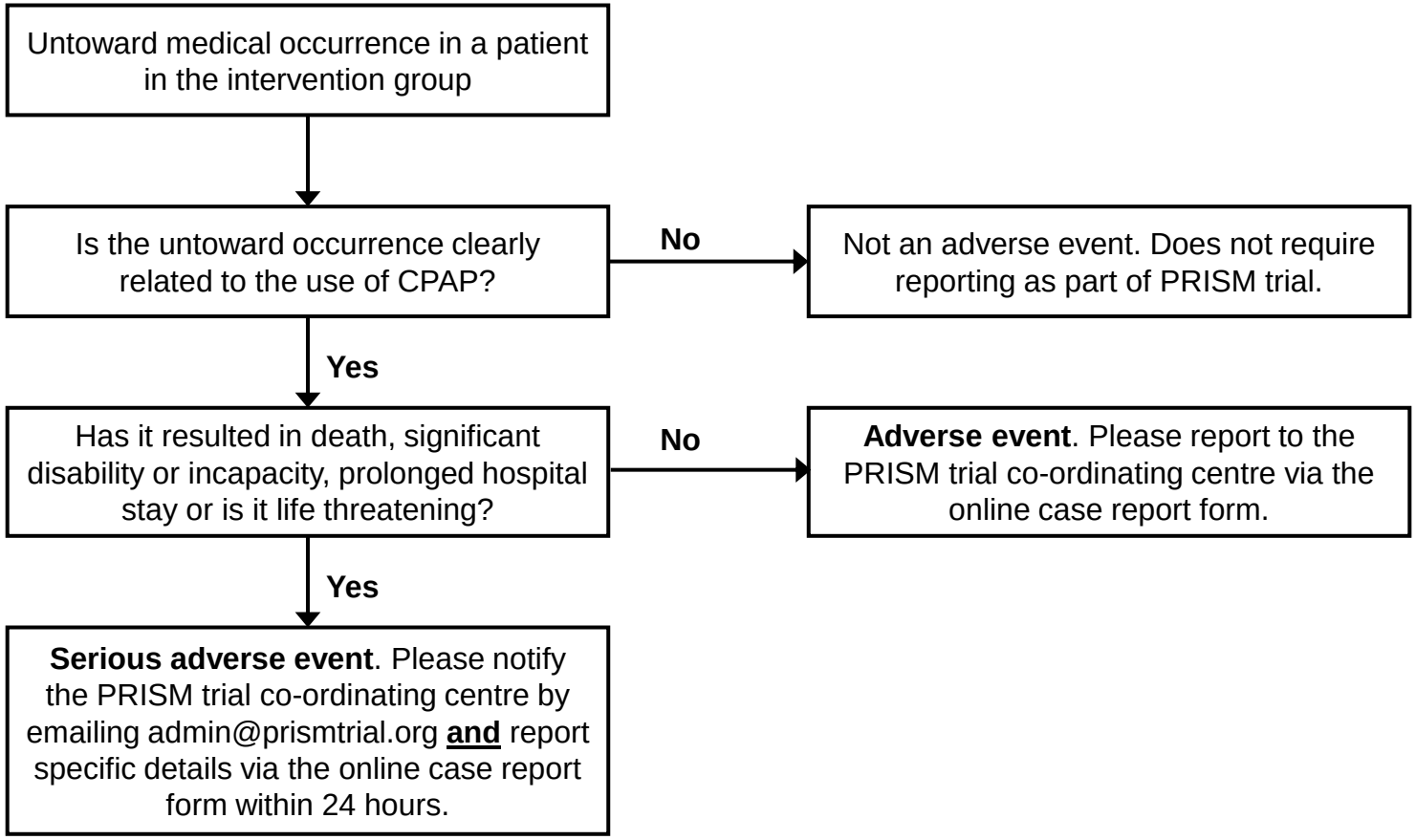




SAE reporting

- Report potential SAEs to the trial coordinating centre within 24 hours
- Must be assessed by PI (or suitably qualified nominee) as **probably or definitely caused by CPAP** and meet at least one of the following criteria:
    - Results in death
    - Is life threatening
    - Clearly prolongs hospital stay
    - Causes significant disability or incapacity
- CI will assess and discuss with PI as required

SAE reporting



Withdrawal

- All study participants are free to withdraw from the study at any time.

- All randomised patients will be included in the final analysis on an intention to treat basis, unless they specifically ask for their data not to be included.

- Record a reason using discontinuation form

Patient identifiable information

- Will be collected and entered on to the secure data entry web portal
- Please do not send any patient identifiable information by email to the trial office e.g. name, address, date of birth, hospital number, national insurance number etc. **Use only the PRISM trial ID to identify a participant.**

Monitoring

- Each site will receive 3 monitoring visits:
  - Site initiation visit
  - After 10 patients recruited or at 1 year, whichever is sooner
  - Closeout visit
- 100% Source Data Verification (SDV) up to 30 day follow-up for up to 10 patients at each visit. At closeout, patients monitored at first visit will have 1 year data verified
- Possible ad-hoc visits
- Site self assessment for random selection of 20% of patients

Study Procedures

- Screening & enrolment log to be completed
- Investigator Site File (ISF)
- Delegation log signed
- Standard Operating Procedures (SOPs)
- Copies of all investigators CVs & GCP/RGF certificates must be filed in the ISF

Trial Initiation

When R&D approval is in place and all documentation has been sent to us, the trial can begin.

Please send the following prior to activation:

- Localised patient documentation (PIS, ICF, GP letter)
- Signed protocol agreement
- PI CV&GCP
- R&D approval letter
- Completed delegation log
- Signed SIV checklist (at this meeting or after)
- The PI must register on the trial database and enter general site information.

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Key points

- Each site must have regulatory approval
- Randomise after the surgery has finished
- Informed consent must be obtained
- Timely entry of CRF data into the eCRF

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Last chance for questions...