

## **Appendix: definitions**

### **Clinical outcome measures**

#### **Primary outcome measure**

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

#### *Pneumonia*

Care will be taken to distinguish between tracheal colonisation, upper respiratory tract infections and early onset pneumonia. Pneumonia must meet the following criteria:

Two or more serial chest radiographs with at least one of the following features (one radiograph is sufficient for patients with no underlying pulmonary or cardiac disease):

- a) new or progressive and persistent infiltrate
- b) consolidation
- c) cavitation

AND at least one of the following:

- a) fever ( $>38^{\circ}\text{C}$ ) with no other recognised cause
- b) leucopaenia ( $< 4 \times 10^9/\text{L}$ ) or leucocytosis ( $>12 \times 10^9/\text{L}$ )
- c) for adults  $>70$  years old altered mental status with no other cause

AND at least two of the following:

- a) new onset of purulent sputum or change in character of sputum *or* increased respiratory secretions *or* increased suctioning requirements
- b) new onset *or* worsening cough *or* dyspnoea, or tachypnoea
- c) rales *or* bronchial breath sounds
- d) worsening gas exchange (hypoxia, increased oxygen requirement, increased ventilator demand)

### *Endotracheal re-intubation*

Re-insertion of an endotracheal tube after the patient has been extubated following the completion of the index surgical procedure. Endotracheal extubation is defined as an intentional clinical decision to remove an endotracheal tube. Extubation does not include accidental or inadvertent removal of an endotracheal tube. Re-intubation does not include intubation and anaesthesia for subsequent surgical procedures within the follow-up period, unless the patient is not extubated at the end of the later surgical procedure.

### **Secondary outcome measures (listed alphabetically)**

#### **Acute Kidney Injury**

According to the KIDGO consensus definition of moderate or severe acute kidney injury (2012):

- a) a two-fold increase in serum creatinine compared the preoperative baseline measurement
- b) or an increase in serum creatinine  $\geq 354 \mu\text{mol/L}$  ( $\geq 4.0 \text{ mg/dL}$ ) with an acute rise of  $> 44 \mu\text{mol/L}$  ( $0.5 \text{ mg/dL}$ )
- c) or oliguria of  $< 0.5 \text{ ml/kg/hour}$  for twelve consecutive hours
- d) or the initiation of new renal replacement therapy

Note: Cannot be diagnosed in patients with existing end stage renal failure.

#### **Acute psychosis or delirium**

An acute episode of severe confusion or personality change, which may result in hallucinations or delusional beliefs in the absence of a pre-existing diagnosis, which may account for the clinical symptoms and signs.

### **Acute respiratory distress syndrome**

According to the Berlin consensus criteria (2012):

- a) Within one week of a known clinical insult or new worsening respiratory symptoms
- b) AND bilateral opacities on chest imaging, not fully explained by effusions, lobar/lung collapse, or nodules
- c) AND respiratory failure not explained by cardiac failure or fluid overload (requires objective assessment e.g. echocardiogram to exclude hydrostatic oedema if no risk factors are present)
- d) AND supplemental oxygenation (requires correcting if altitude >1000m):
  - Mild:  $\text{PaO}_2:\text{FiO}_2$  26.7-40.0 kPa with PEEP or CPAP  $\geq 5\text{cmH}_2\text{O}$
  - Moderate:  $\text{PaO}_2:\text{FiO}_2$  13.3-26.6 kPa with PEEP  $\geq 5\text{cmH}_2\text{O}$
  - Severe:  $\text{PaO}_2:\text{FiO}_2 \leq 13.3$  kPa with PEEP  $\geq 5\text{cmH}_2\text{O}$

### **Anastamotic leak**

Demonstrated at laparotomy or by contrast enhanced radiograph or CT scan.

### **Aspiration pneumonitis**

Acute lung injury after the inhalation of gastric contents.

### **Bowel infarction**

Demonstrated at laparotomy.

## **Bronchospasm**

Newly detected expiratory wheeze treated with bronchodilators.

## **Cardiac events**

### *Myocardial infarction*

Increase in serum cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99<sup>th</sup> percentile upper reference limit and at least one of the following criteria:

- a) symptoms of new ischaemia
- b) new or presumed new significant ST segment or T wave ECG changes or new left bundle branch block
- c) development of pathological Q waves on ECG
- d) radiological or echocardiographic evidence of new loss of viable myocardium or new regional wall motion abnormality
- e) identification of intracoronary thrombus at angiography or autopsy

### *Arrhythmia*

ECG evidence of cardiac rhythm disturbance.

### *Cardiac arrest with successful resuscitation*

Cardiac arrest according to UK Resuscitation Council definition. Successful resuscitation is defined as return of spontaneous circulation for at least one hour.

### *Cardiogenic pulmonary oedema*

Appropriate clinical history and examination with consistent chest radiograph.

## **Infective complications**

### *Infection, source uncertain*

Strong clinical suspicion of infection but the course has not been confirmed. Requires two or more of the following criteria:

- a) core temperature  $<36^{\circ}\text{C}$  or  $>38^{\circ}\text{C}$
- b) white cell count  $>12 \times 10^9/\text{L}$  or  $<4 \times 10^9/\text{L}$
- c) respiratory rate  $>20$  breaths per minute or  $\text{PaCO}_2 < 4.5 \text{ kPa}$
- d) pulse rate  $>90$  beats per minute

### *Urinary tract infection*

This is a simplified version of the CDC criteria taken from the ESA-ESICM consensus on perioperative outcome measures (Jammer et al. 2014).

Urinary tract infection is defined as a positive urine culture of  $\geq 10^5$  colony forming units per ml with no more than two species of micro-organisms AND with at least one of the following signs or symptoms:

- a) fever ( $>38^{\circ}\text{C}$ )
- b) urgency
- c) frequency
- d) dysuria
- e) suprapubic tenderness

- f) costo-vertebral angle pain or tenderness with no other recognised cause

*Surgical site infection (superficial)*

A superficial surgical site infection must meet the following criteria:

Infection occurs within 30 days after the operative procedure AND involves only skin and subcutaneous tissue of the incision AND patient has at least one of the following:

- a) purulent drainage from the superficial incision;
- b) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision;
- c) at least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness, or heat, and superficial incision is deliberately opened by surgeon, unless incision is culture-negative;
- d) diagnosis of superficial incisional surgical site infection by the surgeon or attending physician.

*Surgical site infection (deep)*

A deep incisional surgical site infection must meet the following criteria:

Infection occurs within 30 days after the operative procedure AND involves deep soft tissues (e.g., fascial and muscle layers) of the incision AND patient has at least one of the following:

- a) purulent drainage from the deep incision but not from the organ/space component of the surgical site
- b) a deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C) or localised pain or tenderness, unless incision is culture-negative

- c) an abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathological or radiologic examination
- d) diagnosis of a deep incisional surgical site infection by a surgeon or attending physician

An infection that involves both superficial and deep incision sites should be classified as a deep incisional surgical site infection.

*Surgical site infection (organ/space)*

An organ/space surgical site infection involves any part of the body, excluding the skin incision, fascia, or muscle layers that is opened or manipulated during the operative procedure. An organ/space surgical site infection must meet the following criteria:

Infection occurs within 30 days after the operative procedure AND appears related to the previous surgery AND the infection involves any part of the body, excluding the skin incision, fascia, or muscle layers opened or manipulated during the operative procedure AND patient has at least one of the following:

- a) purulent drainage from a drain that is placed through a stab wound into the organ/space;
- b) organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/ space;
- c) an abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination;
- d) diagnosis of an organ/space surgical site infection by a surgeon or attending physician.

*Laboratory-confirmed bloodstream infection*

Requires at least one of the following criteria:

- a) Patient has a recognised pathogen cultured from one or more blood cultures and the organism cultured from blood is not related to an infection at another site.
  
- b) Patient has a fever ( $>38^{\circ}\text{C}$ ), chills, or hypotension and at least one of the following:
  - a. Common skin contaminant is cultured from two or more blood cultures drawn on separate occasions;
  
  - b. Common skin contaminant is cultured from at least one blood culture from a patient with an intravascular line, and the physician institutes appropriate antimicrobial therapy;
  
  - c. Positive antigen blood test.

**Perforated viscus**

Demonstrated at laparotomy or by contrast enhanced radiograph or CT scan. For example perforated bowel, gall bladder etc.

**Pleural effusion**

Radiological evidence of significant fluid accumulation in the pleural cavity. Most commonly this will be detected using a chest radiograph or an ultrasound scan.



**Pneumothorax**

Air in the pleural cavity with no visceral bed surrounding the visceral pleura. Usually results from damage to the pleural membranes or lung tissue.

**Postoperative haemorrhage***Gastro-intestinal bleed*

Unambiguous clinical evidence or endoscopy showing blood in gastro-intestinal tract.

*Other postoperative haemorrhage*

Overt blood loss, not from the gastro-intestinal tract, requiring transfusion of two or more units of blood in two hours.

**Pulmonary embolism**

A new blood clot or thrombus within the pulmonary arterial system identified by computed tomography pulmonary angiogram (CTPA) with an appropriate clinical history.

**Stroke**

Clinical diagnosis with confirmation by computed tomography (CT) scan.

## Definitions of pre-defined adverse events related to CPAP

### *Interface intolerance due to excessive air leak*

Air leaks associated with delivery device sufficient to prevent effective CPAP. Subjective assessment by clinician.

### *Pain*

Pain associated with contact of delivery device against the skin, sufficient to prevent effective CPAP. Subjective assessment of severity by the investigator.

### *Cutaneous pressure sore or pressure area*

Pressure sore or pressure area associated with contact of the delivery device against the skin. Assessment of severity to be completed by investigator and reported on page two of the supplementary adverse event form according to Waterlow grading<sup>16</sup>:

- a) Grade 1: discolouration of intact skin, not affected by light pressure
- b) Grade 2: partial thickness skin loss/damage involving the dermis or epidermis
- c) Grade 3: Full thickness skin loss/damage involving the subcutaneous tissue but not the underlying fascia.
- d) Grade 4: Full thickness skin loss/damage with extensive destruction and necrosis of the underlying tissue.

### *Claustrophobia*

Claustrophobia associated with the delivery device sufficient to prevent effective CPAP. Subjective assessment of severity by investigator.

### *Oronasal dryness*

Oronasal dryness associated with delivery device sufficient to prevent effective CPAP. Subjective assessment of severity by the investigator.

### *Hypercapnia*

Hypercapnia *directly resulting* from CPAP and sufficient to prevent effective CPAP. This should not include hypercapnia not directly caused by CPAP. Subjective assessment by investigator and to record peak PaCO<sub>2</sub> on page two of the supplementary adverse event form.

### *Haemodynamic instability*

Systolic blood pressure of less than 70 mmHg *or* need for inotropic drugs to maintain systolic blood pressure higher than 85 mmHg for two hours or more, *or* electrocardiogram evidence of ischemia or significant ventricular arrhythmias.

### *Vomiting*

Vomiting, which is sufficient to prevent effective CPAP. Subjective assessment of severity by investigator.

### *Aspiration of gastric contents*

Inhalation of regurgitated gastric contents directly related to CPAP.

## **Other definitions**

### **Active cancer**

A current diagnosis of cancer excluding non-melanoma skin cancers. A previous diagnosis of cancer where the patient underwent curative treatment with remission is not considered active cancer. A surgical procedure where the indication is a presumed diagnosis of cancer, but which has not yet been confirmed with histology, should be considered active cancer.

### **Cancer surgery**

#### *Intended to be a curative treatment*

The surgical procedure is intended to cure the cancer.

#### *Intended to be palliative treatment*

The surgical procedure is not intended to cure the cancer. For example surgical debulking in metastatic disease, partial removal of a tumour or for the purpose of pain or other symptom control.

### **End of surgery**

Completion of surgery. Usually marked by suturing of the wound and application of dressing(s).

### **Intraoperative recruitment manoeuvre**

A technique used by the anaesthetist to transiently increase the transpulmonary pressure. This is usually by increasing tidal volume or inspiratory pressure for at least one breath.

### **Levels of care after surgery**

#### *Level 3 care: Critical care unit*

A clinical area capable of providing invasive mechanical ventilation or support to at least two organ systems.

*Level 2 care: Critical care unit or step-down unit*

A clinical area capable of providing support to a single organ system, but not including invasive mechanical ventilation, which is considered level 3 care.

*Post-anaesthesia care unit (PACU)*

Short-stay clinical area dedicated to caring for patients that are recovering from anaesthesia. If the PACU is providing level 2 care then level 2 care should be recorded on the CRF.

*Surgical ward*

Hospital ward environment not offering single-organ support or dedicated to patients recovering from anaesthesia.

*Critical care unit admission*

Either level two or level three care, as defined above.

**Open surgical technique**

Open abdominal surgery is usually distinguished from laparoscopic by the fact that for laparoscopic surgery the incision is only large enough to remove the resected specimen. Some procedures may involve the use of a laparoscope as well as an open incision, where the incision is larger than required to remove the specimen – this is considered open surgery.

**Preoperative oxygen saturation (SpO<sub>2</sub>)**

Pulse-oximetry on room air before surgery.

**Primary hospital admission**

The hospital admission for elective surgery during which the participant was randomised as part of the PRISM trial. The duration of the primary hospital stay

should be calculated from the date of randomisation.

## **Respiratory support**

### *Invasive mechanical ventilation*

Positive pressure ventilation via an endotracheal tube or supraglottic airway device.

### *Non-invasive mechanical ventilation*

Positive pressure mechanical ventilation via a face-mask, hood or helmet, or nasal device. However, Continuous Positive Airway Pressure (CPAP) is not considered non-invasive mechanical ventilation.

### *High flow nasal oxygen*

Humidified oxygen therapy delivered via large-bore nasal prongs at flow rates greater than 50 litres per minute.

## **Maximum positive end expiratory pressure (PEEP) during surgery**

The maximum pressure, above atmospheric pressure, that exists at the end of expiration and provided by mechanical ventilation.

## **Maximum set tidal volume (V<sub>t</sub>) during surgery**

The maximum volume of air displaced between inspiration and expiration during mechanical ventilation as set on the ventilator.

## **Start of surgery**

Time of the induction of anaesthesia before the surgical procedure.