## ONLINE SUPPLEMENTARY INFORMATION

**Table e1**. Summary of missing data by randomised treatment

| **CRF** | **Conservative oxygenation** | **Usual care** |
|---|---|---|
| 01.0 Registration | 0 | 0 |
| 02.0 Diagnosis | 0 | 0 |
| 03.0 Medical History | 0 | 0 |
| 04.1 Eligibility & Randomisation (Sealed Envelope) SE | 0 | 0 |
| 04.2 Randomisation | 0 | 0 |
| 05.1 & 05.2 APACHE II Score components | 1 | 0 |
| 06.1 & 06.2 SOFA | 0 | 0 |
| 07.1 & 07.2 & 07.3 Clinical Data I (Pre–Intervention) | | |
| PaO2 (kPa) | 0 | 2 |
| PaCO2 (kPa) | 0 | 2 |
| Mean inspiratory pressure ($cmH_20$) | 13 | 15 |
| Peak inspiratory pressure ($cmH_20$) | 0 | 1 |
| Positive End Expiratory Pressure (PEEP) ($cmH_2O$) | 0 | 1 |
| Mean airway pressure ($cmH_2O$) | 1 | 5 |
| Richmond Agitation Sedation Scale (RASS) Score | 1 | 0 |
| Alanine transaminase (ALT) (IU/L) | 0 | 1 |
| Aspartate transaminase (AST) (IU/L) | 7 | 7 |
| Prothrombin time (PT) (sec) | 7 | 7 |
| Activated Partial Thromboplastin Time (APTT) (sec) | 7 | 7 |
| 08.1 & 08.2 Clinical data II (Oxygen Measurements) | | |
| $F_IO_2$ (%) | 32 | 33 |
| $SpO_2$ (%) | 38 | 27 |
| $PaO_2$ (kPa) | 420 | 524 |
| $PaCO_2$ (kPa) | 424 | 524 |
| Number of hours 100% Oxygen boluses per day | 2 | 1 |
| 09.1 to 09.4 Clinical Data III (Bloods & Clinical Assessment) | 2 | 3 |
| Haemoglobin concentration (g/L) | 2 | 3 |
| Creatinine (µmol/L) | 3 | 3 |

| | | |
|---|---|---|
| Platelet count (x10 /L) | 2 | 3 |
| Total Bilirubin (µmol/L) | 3 | 3 |
| Lactate (mmol/L) | 2 | 3 |
| pH | 2 | 10 |
| Alanine aminotransferase (ALT) (IU/L) | 44 | 54 |
| Aminotransferase (AST) (IU/L) | 43 | 51 |
| Prothrombin time (PT) (sec) | 44 | 50 |
| Activated Partial Thromboplastin Time (APTT) (sec) | 2 | 3 |
| Mean arterial pressure (MAP) (mmHg) | 2 | 3 |
| Heart rate (beats per minute) | 2 | 3 |
| Number of packed red cells in the last 24 hours | 2 | 3 |
| Mode of mechanical ventilation | 2 | 3 |
| Total respiratory rate (breaths per minute) | 3 | 3 |
| Tidal volume (ml) | 92 | 113 |
| Mean inspiratory pressure ($cmH_20$) | 3 | 4 |
| Peak inspiratory pressure ($cmH_20$) | 3 | 5 |
| Positive End Expiratory Pressure (PEEP) ($cmH_2O$) | 22 | 22 |
| Mean airway pressure ($cmH_2O$) | 3 | 4 |
| Richmond Agitation Sedation Scale (RASS) Score | 3 | 4 |
| Glasgow Coma Scale (Score) | 117 | 122 |
| Fluid balance (ml) | | |
| 10.0 Blood sampling (Oxidative Stress) Day 2, 3, 5, 10 | | |
| Blood sample NOT taken | 10 | 14 |
| 11.0 End of intervention & Participant consent | 0 | 0 |
| 12.0 Survival Outcome | | |
| Participants with NO data (TOX018032) | 1 | 0 |
| 13.0 Adverse Events (AE) | | |
| Participants with NO reported adverse events | 5 | 5 |
| 14.0 Principal Investigator eSignoff | | |
| Participants with no eSignoff | 5 | 5 |

**Table e2.** Summary of adverse event data by randomised treatment

| **Adverse event data**<br>24 participants had at least one AE | **Conservative oxygenaion**<br>n=37 | **Usual care**<br>n=38 |
|---|---|---|
| **Organ system** | | |
| Respiratory | 11 | 9 |
| Cardiovascular | 12 | 9 |
| Haematological | 2 | 2 |
| Renal | 4 | 3 |
| Gastrointestinal | 2 | 5 |
| Neurological | 4 | 6 |
| Other | 2 | 4 |
| **Event description** | | |
| Reintubation | 1 | 2 |
| Arterial desaturation | 6 | 3 |
| Arrhythmia | 6 | 5 |
| Requirement for inotropic support | 0 | 1 |
| Anaemia | 1 | 0 |
| Low platelet count | 0 | 1 |
| High white blood cell count | 1 | 1 |
| Acute kidney injury | 2 | 1 |
| Requirement for renal support | 1 | 2 |
| Diarrhoea | 0 | 1 |
| Failure to absorb enteral feed | 0 | 1 |
| Delirium | 1 | 2 |
| Other | 18 | 18 |
| **Serious event?** | | |
| No | 27 | 25 |
| Yes | 10 | 13 |
| **Event severity** | | |
| Mild | 14 | 14 |
| Moderate | 15 | 16 |
| Severe | 8 | 8 |
| **Causality** | | |

| | | |
|---|---|---|
| Not related | 10 | 15 |
| Unlikely | 23 | 21 |
| Possibly | 3 | 1 |
| Probably | 1 | 0 |
| Unknown | 0 | 1 |
| **Expectedness** | | |
| Unexpected | 21 | 23 |
| Expected | 15 | 12 |
| Unknown | 1 | 3 |
| **Outcome** | | |
| Resolved | 14 | 18 |
| Resolved with sequelae | 3 | 4 |
| Ongoing | 15 | 12 |
| Death | 5 | 4 |

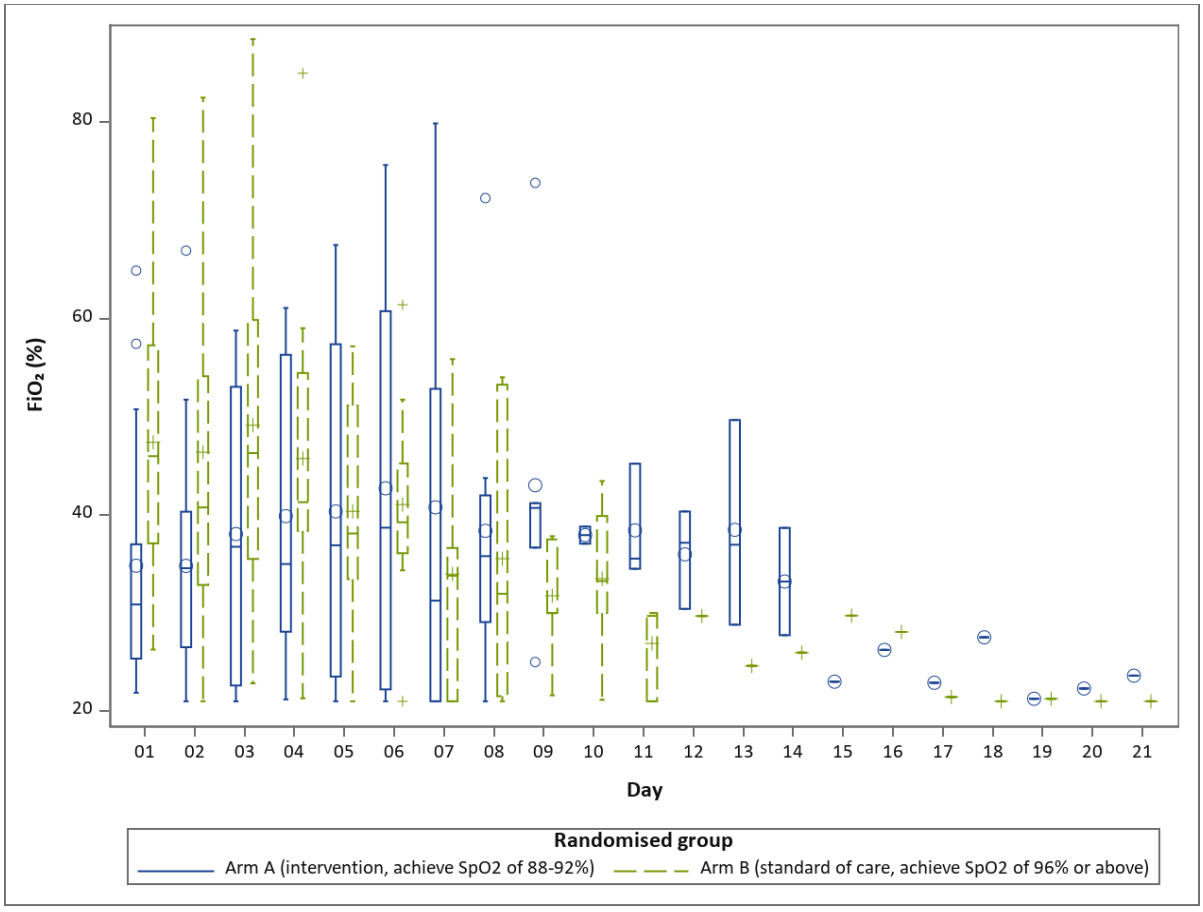
**Table e3**. Summary of protocol deviations

There were 22 protocol deviations in 15 participants:

- 19 procedure /assessment not done
- 1 procedure / assessment done, but out of window
- 2 others:
    - "Atrial fibrillation episode at 03:30 am, decision made to increase $F_IO_2$ to 40% by clinical team. Saturations were at 92%, $PaO_2$ at 9.1 kPa. Research team not informed. Saturations subsequently increased above target range. This was not followed for 3.5 hours. ICU research team discovered event at 07:00. DM (PI) present and informed of the situation, he discussed with the night team. Protocol recommenced."
    - "Bloods taken at 11:11 am on 14/05/18 - in the study Day 2 window. Due to confusion over study days, the processed bloods were stored in aliquots labelled for Day 3 samples."

**Figure e1**

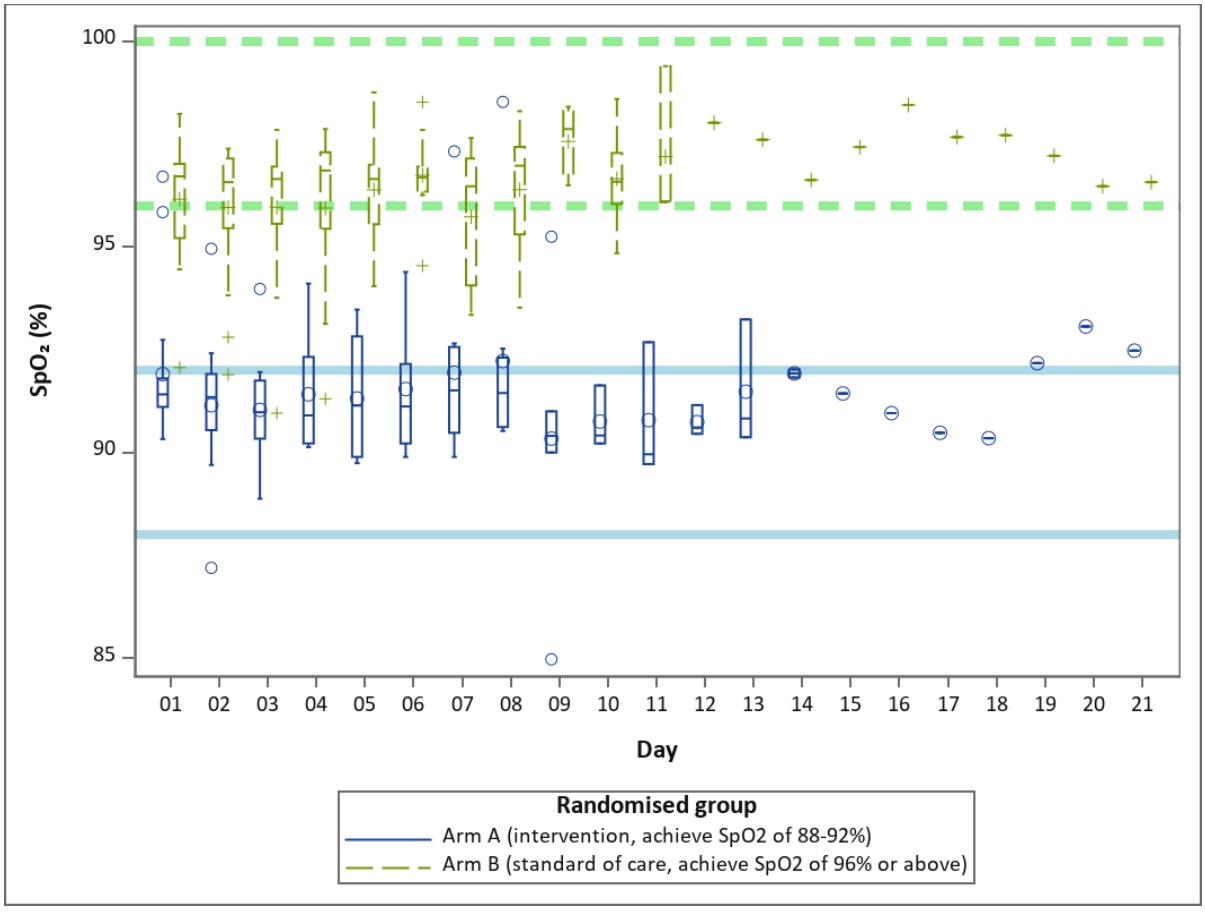
Daily time-weighted mean values for fractional inspired oxygen concentration in the conservative oxygen therapy and control groups




The bottom and top edges of the box indicate the intra-quartile range (IQR). The line inside the box indicates the median value. The marker inside the box indicates the mean value. The whiskers that extend from each box indicate the range of values that are outside of the intra-quartile range. However, they are close enough not to be considered outliers (a distance less than or equal to 1.5*IQR). Outliers are observations that are more extreme than the upper and lower whiskers (plus minus 1.5 IQR)

**Figure e2**

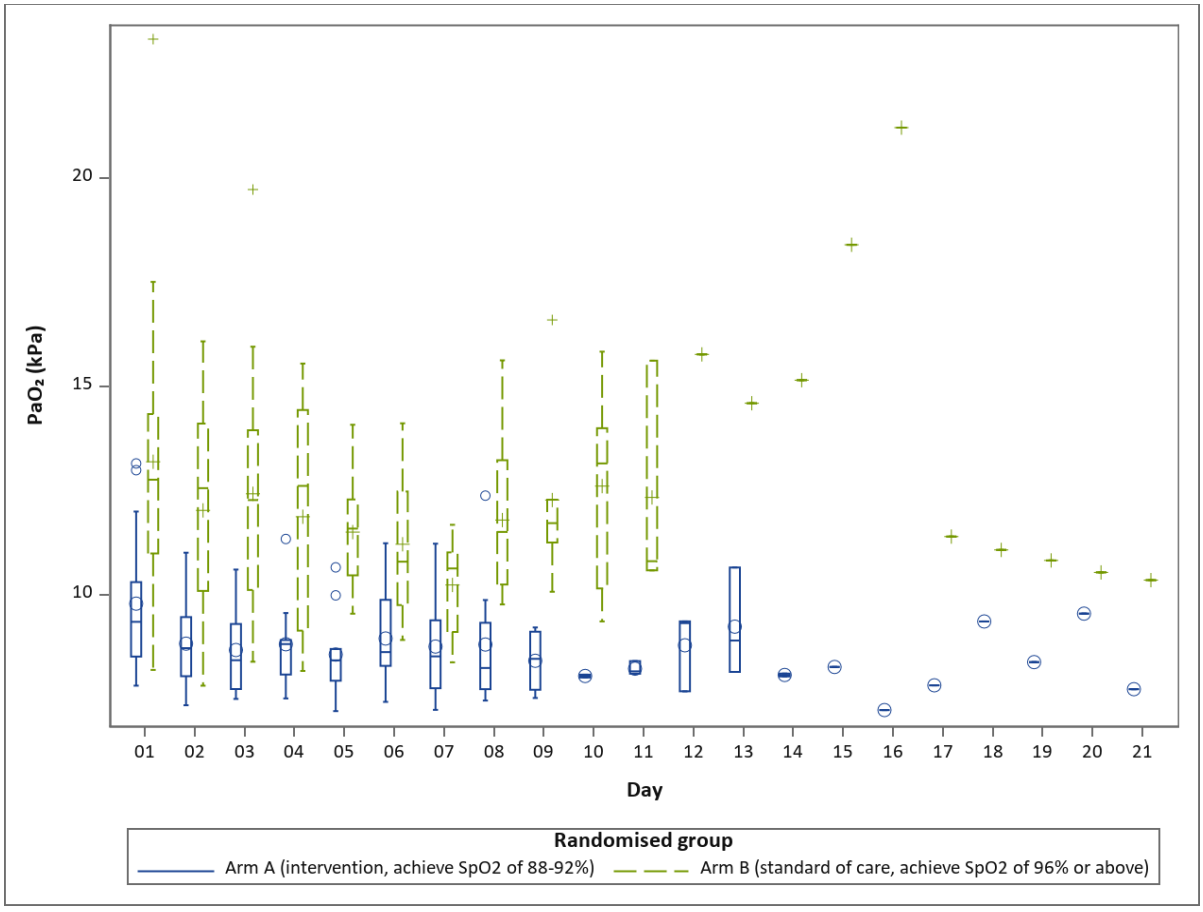
Daily time-weighted mean values for oxygen saturation in the conservative oxygen therapy and control groups.




The bottom and top edges of the box indicate the intra-quartile range (IQR). The line inside the box indicates the median value. The marker inside the box indicates the mean value. The whiskers that extend from each box indicate the range of values that are outside of the intra-quartile range. However, they are close enough not to be considered outliers (a distance less than or equal to 1.5*IQR). Outliers are observations that are more extreme than the upper and lower whiskers (plus minus 1.5 IQR). Horizontal lines show the protocol-specified minimum and maximum $SpO_2$ for each randomised arm (blue is intervention and green is control).

**Figure e3**

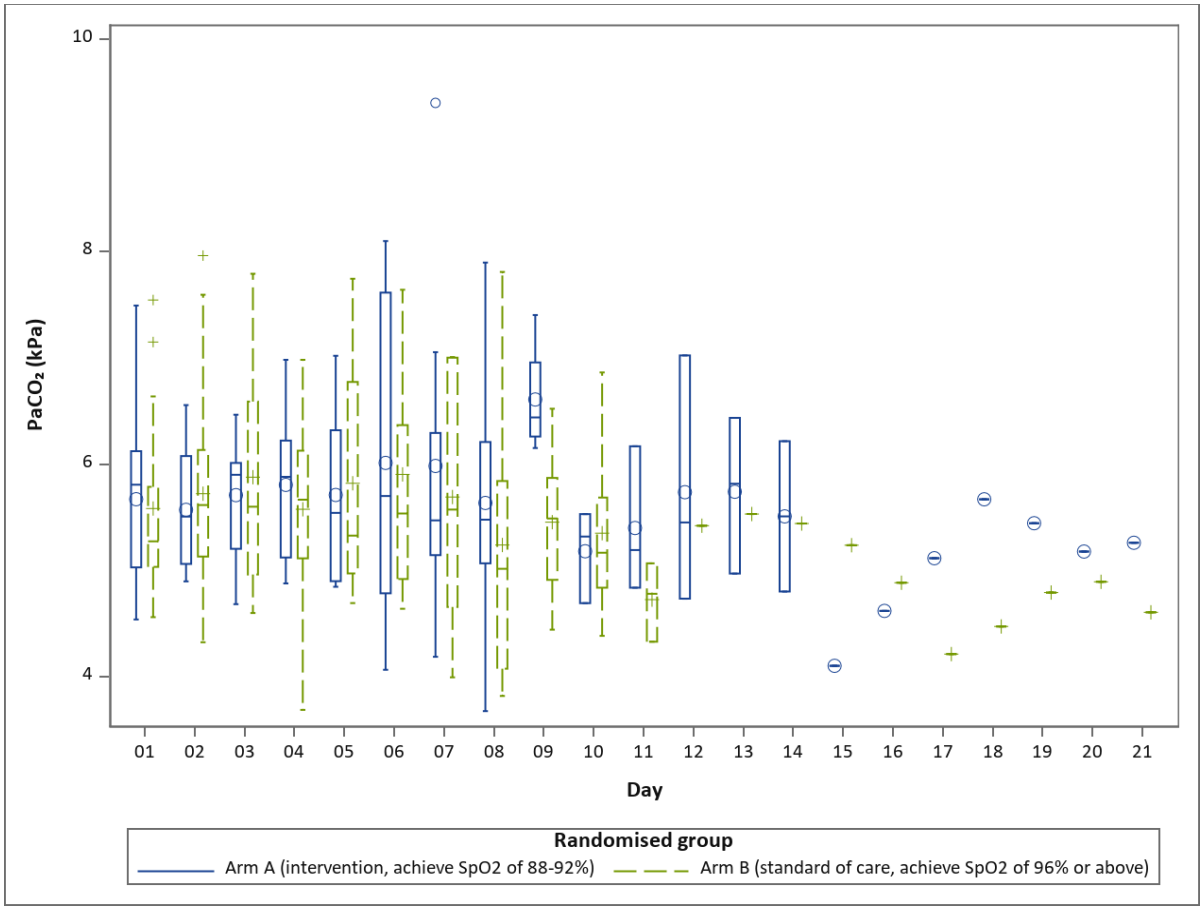
Daily time-weighted mean values for arterial partial pressure of oxygen in the conservative oxygen therapy and control groups




The bottom and top edges of the box indicate the intra-quartile range (IQR). The line inside the box indicates the median value. The marker inside the box indicates the mean value. The whiskers that extend from each box indicate the range of values that are outside of the intra-quartile range. However, they are close enough not to be considered outliers (a distance less than or equal to 1.5*IQR). Outliers are observations that are more extreme than the upper and lower whiskers (plus minus 1.5 IQR)

**Figure e4.**

Daily time-weighted mean values for arterial partial pressure of carbon dioxide in the conservative oxygen therapy and control groups




The bottom and top edges of the box indicate the intra-quartile range (IQR). The line inside the box indicates the median value. The marker inside the box indicates the mean value. The whiskers that extend from each box indicate the range of values that are outside of the intra-quartile range. However, they are close enough not to be considered outliers (a distance less than or equal to 1.5*IQR). Outliers are observations that are more extreme than the upper and lower whiskers (plus minus 1.5 IQR)