**e-Table 1.** Sensitivity analyses of FiO2 thresholds at a constant PaO2 limit of >80 mmHg to define unnecessary oxygen exposure.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **FiO2 threshold** | **Interquartile range of unnecessary oxygen exposure** | **% with unnecessary oxygen exposure** | **Interquartile OR of death (95% CI)** | **Interquartile difference in ventilator-free days score (95% CI)** | **Interquartile difference in hospital-free days score (95% CI)** |
| 0.3 | 0.2 – 0.9 | 82.1% | 1.10 (0.99 to 1.21) | -0.25 (-0.66 to 0.17) | -0.39 (-1.39 to 0.37) |
| 0.4 | 0 – 0.6 | 67.3% | 1.19 (1.08 to 1.32) | -0.77 (-1.21 to -0.33) | -1.26 (-2.14 to -0.38) |
| 0.5 | 0 – 0.38 | 49.3% | 1.20 (1.11 to 1.31) | -0.83 (-1.18 to -0.48) | -1.38 (-2.09 to -0.68) |
| 0.6 | 0 – 0.2  | 35.5% | 1.14 (1.08 to 1.21) | -0.56 (-0.81 to -0.31) | -0.96 (-1.46 to -0.46) |

**e-Table 2.** Sensitivity analyses of PaO2 thresholds at a constant FiO2 of >0.5 to define unnecessary oxygen exposure.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **PaO2 oxygenation goal threshold** | **Interquartile range of unnecessary oxygen exposure** | **% with unnecessary oxygen exposure** | **Interquartile OR of death (95% CI)** | **Interquartile difference in ventilator free-days score (95% CI)** | **Interquartile difference in hospital-free days score (95% CI)** |
| 80 | 0 – 0.38 | 49.3% | 1.20 (1.11 to 1.31) | -0.83 (-1.18 to -0.48) | -1.38 (-2.09 to -0.68) |
| 85 | 0 – 0.3 | 42.7% | 1.12 (1.05 to 1.21) | -0.46 (-0.75 to -0.17) | -0.72 (-1.31 to -0.13) |
| 90 | 0 – 0.2 | 37.8% | 1.08 (1.03 to 1.13) | -0.29 (-0.50 to -0.08) | -0.48 (-0.90 to -0.06) |
| 95 | 0 – 0.2 | 32.7% | 1.08 (1.03 to 1.14) | -0.28 (-0.50 to -0.06) | -0.43 (-0.87 to 0.01) |
| 100 | 0 – 0.1 | 29.2% | 1.04 (1.01 to 1.06) | -0.12 (-0.24 to -0.01) | -0.17 (-0.41 to 0.06) |

**e-Figure 1.** Time series of mean monthly cumulative above goal oxygen exposure at five days (left panel) and severity of ARDS (right panel). Left panel: Each “+” corresponds to a monthly estimate of mean cumulative above goal oxygen exposure. The solid line is a smooth function of cumulative excessive oxygen exposure with calendar time. Cumulative above goal oxygen exposure increased over time. The tidal volume and PEEP trials were conducted in the earlier years, during which we were more focused on ventilator management rules. Perhaps investigators and clinicians were more inclined to reduce FiO2 when arterial oxygenation exceeded the goal range during those trials. Right panel: Stacked barplot of severity with time suggests that there was a smaller proportion of severe cases in later years. There were no data available between 2006 and 2008.