**Supplement 6.** Summary of main clinical outcomes of the RCT and Quasi-RCT studies.

| **Study, Sample** | **Mortality Rate** | **Length of stay in ICU** | **Length of hospital stay** | **Mechanical ventilation (days)** | **Oxygenation, gas exchange and ventilation** | **Pneumonia Rate** |
| --- | --- | --- | --- | --- | --- | --- |
| InterventionN (%) | ControlN (%) | Intervention | Control | Intervention | Control | Intervention | Control | Intervention  | Control | InterventionN (%) | ControlN (%) |
| **RCT** |
| Gentilello et al. 18All = 65N (I) = 27N (C) = 38 | 7 (25.9) | 5 (13.2) | 16.8 ± 13.6 a | 15.0 ± 15.6 a | NR | NR | 8.5 ± 5.3 a | 10.0 ± 8.2 a | FiO2 >0.5 = 6 (22.2)\*PEEP > 5cmH20 = 6 (22.2)\* | FiO2 >0.5 = 16 (42.1)\*PEEP > 5cmH20 = 13 (34.2)\* | 5 (18.5) | 13 (34.2) |
| Demarest et al. 19All = 30N (I) = 16N (C) = 14 | 8 (50.0) | 6 (42.8) | 15.1 b | 11.4 b | NR | NR | NR | NR | NR | NR | 6 (37.5) | 8 (57.1) |
| Summer et al. 20All = 83N (I) = 41N (C) = 42 | 10 (24.4) | 11 (26.2) | 6.7 b | 11.6 b | NR | NR | NR | NR | PaO2 / FiO2 = 283 mmHg b | PaO2 / FiO2 = 282 mmHg b | 4 (9.3) | 7 (16.3) |
| Fink et al. 21All = 99N (I) = 51N (C) = 48 | 10 (19.6) | 8 (16.7) | 5 (1-32) c | 8 (2-74) c | 20 (2-201)c | 37 (5-612)c | 4 (0-32) c | 7 (0-74) c | NR | NR | 7 (13.7) | 19 (39.6) |
| Clemmer et al. 22All = 49N (I) = 23N (C) = 26 | 3 (13.0) | 5 (19.2) | 20.9 ± 16.15a | 13.9 ± 7.5 a | 27.1 ± 16.15 a | 19.0 ± 10.5 a | NR | NR | PaO2/PAO2 = 0.53 b | PaO2/PAO2 = 0.54 b | NR | NR |
| Nelson and Choi 23All = 100N (I) = 40N (C) = 60 | 4 (10.0) | 10 (16.7) | 8.6 ± 11.70a | 11.20 ± 15.40 a | 32.9 ± 30.2 a | 32.2 ± 28.2 a | 6.9 ± 8.9 a | 10.9 ± 15.2 a | NR | NR | NR | NR |
| deBoisblanc et al. 24All = 120N (I) = 69N (C) = 51 | 27 (39.1) | 14 (27.4) | 7.8 ± 0.8 d | 10.8 ± 1.4 d | 17.0 ± 2.2 d | 18.5 ± 1.9 d | 6.1 ± 0.9 d | 9.9 ± 1.8 d | NR | NR | 6 (9) | 11 (22) |
| Traver et al. 25All = 103N (I) = 44N (C) = 59 | 12 (27.3) | 19 (32.2) | 7.0 (2-43) c | 5.0 (2-53) c | 17.5 (3-98) c | 17.0 (3-74) c | 3.0 (O-28) c | 3.0 (O-24) c | NR | NR | 8 (18) | 17 (29) |
| Whiteman et al. 26All = 69N (I) = 33N (C) = 36 | NR | NR | 29.80 ± 27.52 a | 32 ± 46.53 a | NR | NR | 13.80 ± 11.49 a | 16.10 ± 20.60 a | NR | NR | 10(33) | 14 (38.8) |
| MacIntyre et al. 27All = 104N (I) = 53N (C) = 51 | 8 (15.1) | 7 (13.7) | NR | NR | NR | NR | NR | NR | NR | NR | 9 (17.3) | 13 (25.5) |
| Bahzad et al. 7All = 22N (I) = 12N (C) = 10 | NR | NR | 10 b | 18 b | NR | NR | NR | NR | PaO2/FiO2 after 72h = 163 mmHg bPulmonary compliance = 34.2 ml/cmH2O | PaO2/FiO2 after 72h = 152.7mmHg bPulmonary compliance = 32.2 ml/cmH2O | NR | NR |
| Ahrens et al. 28All = 234N (I) = 97N (C) = 137 | 41 (42.3) | 58 (42.3) | 13.46 ± 13.21 a | 13.64 ± 11.33 a | NR | NR | 10.75 ± 12.23 a | 10.14 ± 10.62 a | NR | NR | 14(14.4) | 45 (32.8) |
| Staudinger et al. 29All = 150N (I) = 75N (C) = 75 | 28 (37.30) | 27 (36.0) | NR | NR | 25 ± 22 a | 39 ± 45 a | 8 ± 5 a | 14 ± 23 a | PaO2/FIO2= 241 ± 84 mmHg a | PaO2/FIO2 = 235 ± 95 mmHg a | 8 (11) | 17 (23) |
| Simonis et al. 30All = 89N (I) = 45N (C) = 44 | 12 (26.7) | 16 (36.4) | 15.8 (13.2; 18.4) e | 18.1 (15.0; 21.2) e | 18.1 (15.2; 21.0) e | 20.3 (16.6; 24.1) e | 248h (194; 391) e | 300h (232; 639) e | NR | NR | 10 (22) | 28 (63.6) |
| Bein et al. 6All = 27N (I) = 14N (C) = 13 | 2 (14.3) | 1 (7.7) | 15 (11–20) c | 17 (10–21) c | 27 (23–37) c | 31 (20–52) c | MV free days (Within 28 days) = 18 (13–20) c | MV free days (Within 28 days) = 14 (5–20) c | PaO2/FIO2= 320 (262–425) mmHg cPEEP = 12.0 (10.5–14.0) cmH20 cPplat = 20.0 (18.5–23.0) cmH20 c | PaO2/FIO2= 223 (183–292) mmHg cPEEP = 13.5 (12–14.8) cmH20 cPplat = 24.5 (22.0–26.0) cmH20 c | NR | NR |
| Hanneman et al. 4All = 15N (I) = 8N (C) = 7 | 2 (25.0) | 2 (28.6) | 11.1 (5.4 - 23.4) c | 8.2 (3.6 - 14.9) c | NR | NR | 6 ± 5 a | 5.2 ± 4.3 a | PaO2 = 105 ± 34 aFIO2 = 0.65 ± 0.24 a | PaO2 = 146 ± 114 aFIO2 = 0.71 ± 0.32 a | NR | NR |
| **Quasi - RCT** |
| Kirschenbaum et al. 31All = 37N (I) = 17N (C) = 20 | 1 (5.9) | 2 (10.0) | NR | NR | NR | NR | ICU = 21 ± 2.4 dAll = 55 ± 6 d | ICU = 20 ± 2.1 dAll = 58 ± 6 d | NR | NR | 3 (17.6) | 10 (50) |
| Wang et al. 32All = 70N (I) = 35N (C) = 35 | 6 (17.1) | 8 (22.9) | 22 ± 8 a | 27 ± 12 a | NR | NR | NR | NR | PaO2/FiO2 = 240 ± 80 mmHg a | PaO2/FiO2 215 ± 104 mmHg a | 0 (0) | 5 (14.3) |

a Data reported as mean and standard deviation; b Data reported as average only; c Data reported as median and range; d Data reported as mean and standard error; e Data provided as mean and 95% confidence interval; \* Data expressed in n (%)

Legends: RCT: Randomized controlled trials; N (I): Intervention sample; N (C): Control sample; ICU: Intensive care unit; FiO2: Fraction of inspired oxygen; PEEP: Positive end-expiratory pressure; NR: Not reported; PaO2/FiO2: Relationship between arterial oxygen pressure and fraction of inspired oxygen; PaO2/PAO2: Relationship between arterial partial pressure of oxygen and alveolar partial pressure of oxygen; PaO2: Blood pressure of oxygen; PaCO2: Blood pressure of carbon dioxide; MV: Mechanical ventilation.