OLA strategy for ARDS: Its effect on mortality depends on achieved recruitment (PaO2/FiO2) and mechanical power. Systematic Review and Meta-analysis with Meta-Regression.

2.- Supplementary Figures:
2.1. Figure S1: L’Abbè plot:

**FIGURE S1:** L’Abbè-plot. Group 1: OLA strategy. Group 2: Control ventilation. The arm-level outcomes for two experimental groups (e.g., treatment and control group) are plotted against each other. In the example below, the points show the log risk (of 28-day mortality) in the OLA strategy (Group1, x axis) and control ventilation (Group 2, y axis). Points falling on the solid diagonal line represent studies where the risk of infection did not differ between the two groups. Points falling below this line represent studies where the risk was lower in the OLA strategy group. The dashed line indicates the estimated effect based on the fitted model (which is linear on the log scale for the log risk ratio). Each trial is represented by a symbol of area proportional to its precision (inverse variance of RR). The distribution of the plotted points indicates the amount of heterogeneity present: some points are in the lower right quadrant, far from the estimated effect.
2.2.- Figure S2: Cumulative meta-analysis:

**FIGURE S2:** Cumulative Forest plot of comparison: OLA Strategy vs. Control Ventilation, outcome: 28-30th day Mortality.
2.3.- Figure S3: Correlation between Relative Mechanical Power and Relative Driving Pressure:

**FIGURE S3**: Correlation between Relative Mechanical Power (1\textsuperscript{st} day) and Relative Driving Pressure (1\textsuperscript{st} day). $R^2 = 0.709$, 95\% CI = 0.228 to 0.912, p.value = 0.00978
2.4.- Figure S4:

FIGURE S4: Effect of varying PaO2/FiO2 in the control group (3rd day) on RR of mortality.
2.5.- Figure S5:

<table>
<thead>
<tr>
<th>Author(s) and Year</th>
<th>Relative Risk [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amato, 1998</td>
<td>0.54 [0.31, 0.91]</td>
</tr>
<tr>
<td>Rainieri, 1999</td>
<td>0.60 [0.30, 1.21]</td>
</tr>
<tr>
<td>ALVEOLI, 2004</td>
<td>1.11 [0.83, 1.46]</td>
</tr>
<tr>
<td>ARIES, 2006</td>
<td>0.64 [0.40, 1.04]</td>
</tr>
<tr>
<td>EXPRES, 2008</td>
<td>0.89 [0.72, 1.11]</td>
</tr>
<tr>
<td>LOVES, 2008</td>
<td>0.90 [0.77, 1.05]</td>
</tr>
<tr>
<td>EPVent, 2008</td>
<td>0.43 [0.17, 1.07]</td>
</tr>
<tr>
<td>Huh, 2009</td>
<td>1.29 [0.64, 2.61]</td>
</tr>
<tr>
<td>Hodgson, 2011</td>
<td>1.50 [0.32, 7.14]</td>
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<tr>
<td>Pintado, 2013</td>
<td>0.53 [0.24, 1.15]</td>
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<tr>
<td>OLAnetwork, 2016</td>
<td>0.83 [0.51, 1.36]</td>
</tr>
<tr>
<td>ART, 2017</td>
<td>1.13 [1.00, 1.27]</td>
</tr>
<tr>
<td>EPVent-2, 2019</td>
<td>1.08 [0.72, 1.63]</td>
</tr>
<tr>
<td>PHARLAP, 2019</td>
<td>0.92 [0.49, 1.72]</td>
</tr>
</tbody>
</table>

Rel MP (1st day) = 0.50
Rel MP (1st day) = 1
Rel MP (1st day) = 1.5

FIGURE S4: Effect of varying Relative MP (1st day) on RR of mortality.
3.- Appendix:

Search strategies:

Cochrane Central Register of Controlled Trials (CENTRAL) CENTRAL searched via Cochrane Library Interface until March 2020.

- #1 MeSH descriptor: [Acute Respiratory Distress Syndrome, Adult] explode all trees 1343
- #2 MeSH descriptor: [Acute Lung Injury] explode all trees 426
- #3 MeSH descriptor: [Prone Position] explode all trees 286
- #4 MeSH descriptor: [Intermittent Positive-Pressure Ventilation] explode all trees 243
- #5 MeSH descriptor: [Positive-Pressure Respiration, Intrinsic] explode all trees 27
- #6 MeSH descriptor: [Respiratory Insufficiency] explode all trees 2664
- #7 MeSH descriptor: [Mortality] explode all trees 12784
- #8 ALI 4978
- #9 ARDS 1649
- #10 Open lung 8575
- #11 Lung recruitment 2508
- #12 Protective ventilation 931
- #13 ARF 544
- #14 ICU mortality 4879
- #15 (#1 or #2 or #3 or #6 or #8 or #9 or #13) 10210
- #16 #15 AND (#4 OR #5 OR #7 OR #10 OR #11 OR #12 OR #14) 1641
Medline searched via Ovid Interface until March 2020

1. exp Acute Lung Injury/ or exp Respiratory Distress Syndrome, Adult/ or (ALI or ARDS).ti,ab,kw. or (acute adj4 (lung injur* or distress syndrome)).mp. or ((severe or hypoxic) adj4 (respiratory and failure)).mp. 44625
2. exp Open Lung/ or exp Lung Recruitment/ or exp Protective Ventilation/ or exp Intermittent Positive-Pressure Ventilation/ or exp PEEP/ or exp Positive end-expiratory pressure/ 25662
3. 1 and 2 3288
4. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh. 1183216
5. 3 and 4 436
6. exp Intensive Care Unit/ 83098
7. exp Mortality/ 377806
8. 6 and 7 10501
9. 5 and 8 14
Embase search strategy

#1. 'acute lung injury':ti,ab,kw OR 'adult respiratory distress syndrome':ti,ab,kw OR ali:ti,ab,kw OR ards:ti,ab,kw 45,101

#2. 'open lung ventilation':ti,ab,kw OR 'prone positiv*':ti,ab,kw OR 'lung recruitment':ti,ab,kw OR 'lung recruitment maneuver':ti,ab,kw OR 'positive end expiratory pressure':ti,ab,kw OR 'peep':ti,ab,kw 21,756

#3. #1 AND #2 4,434

#4. 'randomized controlled trial':pt OR 'controlled clinical trial':pt OR 'randomized':ti,ab,kw OR 'clinical trials':ti,ab,kw OR 'trial':ti,ab,kw 1,497,826

#5. 'animals' OR 'humans and animals' 871,123

#6. #3 AND #4 1,029

#7. #6 NOT #5 873
**Search strategy for ISI Web of Science**

1# TS= (adult respiratory distress syndrome or acute lung injury or acute respiratory distress syndrome or ards or ali) 100.287

2# TS= (open lung ventilation OR prone position OR lung recruitment OR lung recruitment maneuver OR positive end expiratory pressure OR peep) 48.143

3# #2 AND #1 7.823

4# TS= (animals or humans and animals) 19.734.500

5# #3 NOT #4 3.568

6# TS= (randomized controlled trial OR controlled clinical trial OR randomized OR clinical trials OR trial) 2.429.297

7# #6 AND #5 1.045