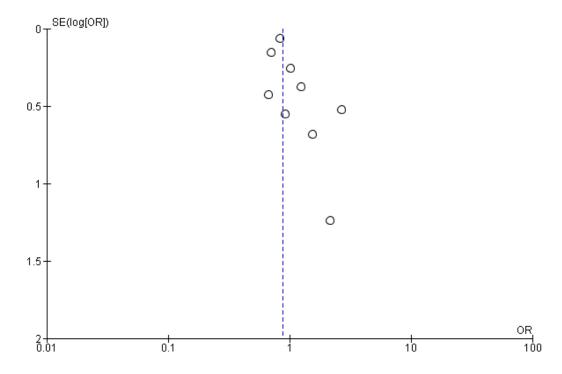


Supplementary Figure 1. The meta-regression plot regarding the effect of baseline CRP level and mortality outcome.

| Study or Subgroup                 | Tocilizumab            |           | Control     |         | Odds Ratio               |                         | Odds Ratio  |
|-----------------------------------|------------------------|-----------|-------------|---------|--------------------------|-------------------------|---|
|                                   | Events                 | Total     | Events      | Total   | Weight                   | ight IV, Random, 95% CI | IV, Random, 95% CI                                      |
| 1.1.1 Mandatory Hyp               | erinflamm              | atory p   | henotype    |         |                          |                         | 8   |
| Horby 2021                        | 621                    | 2022      | 729         | 2094    | 51.4%                    | 0.83 [0.73, 0.95]       |   |
| Salvarani 2020                    | 2                      | 60        | 1           | 63      | 0.5%                     | 2.14 [0.19, 24.21]      | 200   |
| Stone 2020                        | 9                      | 161       | 3           | 81      | 1.7%                     | 1.54 [0.41, 5.85]       |   |
| Veiga 2021                        | 14                     | 65        | 6           | 64      | 2.7%                     | 2.65 [0.95, 7.42]       |   |
| Subtotal (95% CI)                 |                        | 2308      |             | 2302    | 56.3%                    | 1.32 [0.65, 2.66]       | •   |
| Total events                      | 646                    |           | 739         |         |                          |                         |   |
| Heterogeneity: Tau <sup>2</sup> = | 0.25; Chi <sup>2</sup> | = 6.16,   | df = 3 (P   | = 0.10) | ; I <sup>2</sup> = 51%   |                         |   |
| Test for overall effect:          | Z = 0.77 (F            | = 0.44    | )           |         |                          |                         |   |
| 1.1.2 Others                      |                        |           |             |         |                          |                         |   |
| Gordon 2021                       | 98                     | 353       | 142         | 402     | 21.9%                    | 0.70 [0.52, 0.96]       | <del></del>   |
| Hermine 2020                      | 7                      | 63        | 8           | 67      | 2.5%                     | 0.92 [0.31, 2.71]       |   |
| Rosas 2021                        | 58                     | 294       | 28          | 144     | 10.2%                    | 1.02 [0.62, 1.68]       | 5 <del>. •</del>  |
| Salama 2021                       | 26                     | 249       | 11          | 128     | 5.1%                     | 1.24 [0.59, 2.60]       | # <del> </del>  |
| Soin 2021                         | 11                     | 91        | 15          | 88      | 4.0%                     | 0.67 [0.29, 1.55]       |   |
| Subtotal (95% CI)                 |                        | 1050      |             | 829     | 43.7%                    | 0.81 [0.64, 1.03]       | •   |
| Total events                      | 200                    |           | 204         |         |                          |                         | 7/0   |
| Heterogeneity: Tau <sup>2</sup> = | 0.00; Chi <sup>2</sup> | = 3.11,   | df = 4 (P   | = 0.54) | $1^2 = 0\%$              |                         |   |
| Test for overall effect:          | Z = 1.75 (F            | 80.0      | )           |         |                          |                         |   |
| Total (95% CI)                    |                        | 3358      |             | 3131    | 100.0%                   | 0.87 [0.73, 1.03]       | •   |
| Total events                      | 846                    |           | 943         |         |                          |                         | 76  |
| Heterogeneity: Tau <sup>2</sup> = | 0.01; Chi <sup>2</sup> | = 9.39,   | df = 8 (P   | = 0.31) | ; I <sup>2</sup> = 15%   |                         |   |
| Test for overall effect:          |                        |           |             |         |                          |                         | 0.01 0.1 1 10 10<br>Favours Tocilizumab Favours control |
| Test for subgroup diffe           | erences: Cl            | ni² = 1.6 | 5. df = 1 ( | P = 0.2 | 20), J <sup>2</sup> = 39 | .3%                     | Favours Tocilizumab Favours control                     |

Supplementary Figure 2. The subgroup analysis of all-cause mortality based upon mandatory hyperinflammatory phenotype at inclusion.



Supplementary Figure 3. The funnel plot for the included randomized controlled trials for all-cause mortality assessment.