Supplementary Appendix

Convalescent plasma treatment in patients with Covid-19: a systematic review and meta-analysis

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#### Appendix Table 1 Systematic search strategy

| PubMed | N= |
|--------|----|
| (("covid"[Title/Abstract] OR "covid-19"[Title/Abstract] OR "corona"[Title/Abstract] OR "sars"[Title/Abstract] OR "sars-cov-2"[Title/Abstract] OR "severe acute respiratory syndrome"[Title/Abstract] OR "ncov"[Title/Abstract] OR "2019-ncov"[Title/Abstract]) AND ("convalescent"[Title/Abstract] OR "convalescence"[Title/Abstract] OR "hyperimmune globulin therapy"[Title/Abstract] OR "passive antibody transfer"[Title/Abstract])) AND ("passive antibody therapy":ti,ab,kw OR "serotherapy":ti,ab,kw OR "hyperimmune globulin therapy":ti,ab,kw) AND (clinicaltrial [Filter])) | 2,467 |
| (("covid"[Title/Abstract] OR "covid-19"[Title/Abstract] OR "corona"[Title/Abstract] OR "sars"[Title/Abstract] OR "sars-cov-2"[Title/Abstract] OR "severe acute respiratory syndrome"[Title/Abstract] OR "ncov"[Title/Abstract] OR "2019-ncov"[Title/Abstract]) AND ("convalescent"[Title/Abstract] OR "convalescence"[Title/Abstract] OR "hyperimmune globulin therapy"[Title/Abstract] OR "passive antibody transfer"[Title/Abstract])) AND (clinicaltrial [Filter])) | 68 |

| Embase | |
|--------|------------------|
| ("covid-ab":ti OR "covid-19-ab":ti OR "corona-ab":ti OR "sars-ab":ti OR "sars-cov-2-ab":ti OR "severe acute respiratory syndrome-ab":ti OR "ncov-ab":ti OR "2019-ncov-ab":ti) AND ("convalescent-ab":ti OR "convalescence-ab":ti OR "hyperimmune plasma-ab":ti OR "immune plasma-ab":ti OR "passive immunization-ab":ti OR "plasma therapy-ab":ti OR "serotherapy-ab":ti OR "hyperimmune globulin therapy-ab":ti OR "passive antibody transfer-ab":ti) AND ("clinicaltrial":ti OR "randomized controlled trial":ti) | 2,616 |
| ("covid-ab":ti OR "covid-19-ab":ti OR "corona-ab":ti OR "sars-ab":ti OR "sars-cov-2-ab":ti OR "severe acute respiratory syndrome-ab":ti OR "ncov-ab":ti OR "2019-ncov-ab":ti) AND ("convalescent-ab":ti OR "convalescence-ab":ti OR "hyperimmune plasma-ab":ti OR "immune plasma-ab":ti OR "passive immunization-ab":ti OR "plasma therapy-ab":ti OR "serotherapy-ab":ti OR "hyperimmune globulin therapy-ab":ti OR "passive antibody transfer-ab":ti) AND ("clinicaltrial":ti OR "randomized controlled trial":ti) | 220 |

| Web of Science | |
|----------------|------------------|
| (TI=(corona) OR AB=(corona) OR TI=(covid) OR AB=(covid-19) OR TI=( Covid-19) OR AB=( Covid) OR TI=(sars) OR AB=(sars) OR TI=(sars-cov-2) OR AB=(sars-cov-2) OR T1=(severe acute respiratory syndrome) OR AB=(severe acute respiratory syndrome) OR TI=(ncov) OR AB=(ncov) OR TI=(2019-ncov) OR AB=(2019-ncov)) AND T1=(convalescent) OR T1=(convalescence) OR T1=( hyperimmune plasma) OR AB=( hyperimmune plasma) OR AB=( immune plasma) OR TI=( passive immunization) OR AB=( passive antibody transfer) OR TI=( plasma therapy) OR AB=( serotherapy) OR TI=( hyperimmune globulin therapy) OR AB=( hyperimmune globulin therapy) OR TI=( passive antibody transfer) OR AB=( passive antibody transfer)) | 2,822 |
| (TI=(corona) OR AB=(corona) OR TI=(covid) OR AB=(covid-19) OR TI=( Covid-19) OR AB=( Covid) OR TI=(sars) OR AB=(sars) OR TI=(sars-cov-2) OR AB=(sars-cov-2) OR T1=(severe acute respiratory syndrome) OR AB=(severe acute respiratory syndrome) OR TI=(ncov) OR AB=(ncov) OR TI=(2019-ncov) OR AB=(2019-ncov)) AND T1=(convalescent) OR T1=(convalescence) OR AB=( convalescent) OR T1=( hyperimmune plasma) OR AB=( hyperimmune plasma) OR AB=( immune plasma) OR AB=( passive immunization) OR AB=( passive antibody transfer) OR TI=( plasma therapy) OR AB=( serotherapy) OR TI=( hyperimmune globulin therapy) OR AB=( hyperimmune globulin therapy) OR TI=( passive antibody transfer) OR AB=( passive antibody transfer)) AND (TI=(trial) OR AB=(trial)) | 471 |

| Cochrane Library | |
|------------------|------------------|
| ((corona):ti,ab,kw OR (covid):ti,ab,kw OR (Covid-19):ti,ab,kw OR (Covid19):ti,ab,kw OR (sars):ti,ab,kw OR (sars-cov-2):ti,ab,kw OR (sars-cov-1):ti,ab,kw OR (sars-cov-2):ti,ab,kw OR (severe acute respiratory syndrome):ti,ab,kw OR (ncov):ti,ab,kw) AND ( "convalescent":ti,ab,kw OR "convalescence":ti,ab,kw OR "hyperimmune plasma":ti,ab,kw OR "immune plasma":ti,ab,kw OR "passive immunization":ti,ab,kw OR "plasma therapy":ti,ab,kw OR "serotherapy":ti,ab,kw OR "hyperimmune globulin therapy":ti,ab,kw OR (passive antibody transfer):ti,ab,kw) | 536 |
| ((corona):ti,ab,kw OR (covid):ti,ab,kw OR (Covid-19):ti,ab,kw OR (Covid19):ti,ab,kw OR (sars):ti,ab,kw OR (sars-cov-2):ti,ab,kw OR (sars-cov-1):ti,ab,kw OR (sars-cov-2):ti,ab,kw OR (severe acute respiratory syndrome):ti,ab,kw OR (ncov):ti,ab,kw) AND ( "convalescent":ti,ab,kw OR "convalescence":ti,ab,kw OR "hyperimmune plasma":ti,ab,kw OR "immune plasma":ti,ab,kw OR "passive immunization":ti,ab,kw OR "plasma therapy":ti,ab,kw OR "serotherapy":ti,ab,kw OR "hyperimmune globulin therapy":ti,ab,kw OR (passive antibody transfer):ti,ab,kw) AND TRIALS | 530 |

| MedRxiv | |
|--------|------------------|
| ((covid*) OR (corona*) OR (sars*)) AND ( convalescence*) | 433 |
| ((covid*) OR (corona*) OR (sars*)) AND ( convalescence*) AND ((randomized controlled trial) OR (RCT)) | 206 |
## Appendix Table 2: Study design of included trials

| Study          | Countries                        | Design                               | Primary Efficacy Outcome Parameters                                                                 | Secondary Efficacy Outcome Parameters                                                                 | Safety Outcome Parameters                                                                 | Inclusion criteria                                                                 | Exclusion criteria                                                                 | Symptom onset before enrollment |
|----------------|----------------------------------|--------------------------------------|------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------|
| REMAP-CAP      | Australia, Canada, United Kingdom, and United States | open-label, adaptive RCT                      | respiratory and cardiovascular organ support-free days up to day 21                                     | (1) hospital survival (2) severe COVID-19 cases                                                  | not reported                                                                           | (5) hospitalized patients admitted to hospital with acute illness due to confirmed COVID-19 | (1) death is declared to be imminent and inevitable during the next 24 hours AND no one of the patient’s attending physician, attending nurse, or attending hospital staff was not able to make a decision about life-sustaining treatment (2) no admit to the ICU (3) patients admitted to hospital with acute illness due to confirmed COVID-19 and left against medical advice. | n.a.                           |
| CONCOR-1       | Canada, United States and Brazil | multicenter, open-label, randomized controlled trial | composite of iminophagia or death by day 30                                                              | (1) time to iminophagia (2) death (3) severe COVID-19 cases                                       | not reported                                                                           | (1) more than 12 days from the onset of respiratory symptoms (2) patients need immediate intubation (3) patients need intubation within 24 hours (4) patients need mechanical ventilation. | (1) receipt of any antimicrobial agent with possible activity against SARS-CoV-2 within 24 hours of randomization (2) duration of IMV of COVID-19 >72 hours (3) patients are not under mechanical ventilation at the time of randomization. | 5 ≤ 12 d                     |
| O’Donnell      | United States and Brazil         | randomized, double-blind, controlled trial | Clinical status at day 28                                                                                   | (1) time to clinical improvement (2) iminophagia (3) death (4) time to discontinuation of supplemental oxygen (5) time to hospital discharge (6) survival and grade 3 and 4 adverse events | not reported                                                                           | (1) hospitalized patients aged 18 years or older with evidence of SARS-CoV-2 infection had been admitted to the hospital within 14 days after admission (2) patients need mechanical ventilation. | (1) receipt of any antimicrobial agent with possible activity against SARS-CoV-2 within 24 hours of randomization (2) duration of IMV of COVID-19 >72 hours (3) patients are not under mechanical ventilation at the time of randomization. | n.a.                           |
| Bennett-Guerrero et al | United States                                           | randomized, double-blind, placebo-controlled trial | ventilator days from randomization to day 28                                                              | (1) all-cause mortality (2) WHO ordinal scale on each day through day 28 (3) immune response     | not reported                                                                           | (1) adult patients hospitalized with a confirmed diagnosis of COVID-19 infection       | (1) contraindication to the use of plasma in patients with a history of prior reactions to blood products (2) receipt of pooled (polyvalent) immunoglobulin or any intravenous polyclonal immunoglobulin in past 30 days (3) female subjects with positive pregnancy test, breastfeeding, or planning to become pregnant. | n.a.                           |
| RECOVERY       | United Kingdom                   | open-label RCT                         | all-cause mortality                                                                                      | (1) time to discharge from hospital (2) receipt of mechanical ventilation (3) death (4) receipt of ventilation (5) time to successful intubation (6) one of renal failure or hemolysis | (1) clinical or radiological advance adumbratons at 72 h following randomization (2) cause-specific mortality (3) major cardiac arrhythmias | (1) hospitalization for COVID-19 proven by a SARS-CoV-2 genotyping in a RT-PCR test in the past 96 h | (1) documented hypoglycemia (2) on mechanical ventilation with <96 h at the time of screening. | n.a.                           |
| CostCOVID      | Netherlands                      | open-label, multicenter                      | all-cause mortality until discharge from hospital or maximum of 60 days after admission                  | (1) oxygenation support-free days up to day 30 (5) hospital survival of ≤7 d (6) patients with SARS-CoV-2 shedding from the airways (4) impact of ComP-f on humoral immunity and inflammation | (1) plasma-related reaction at the 27th day (2) patients need mechanical ventilation. | (1) patients with mild disease not requiring oxygen therapy (2) patients with a normal BMI <70 kg/m² (3) patients without any known active or past medical conditions (4) patients who need mechanical ventilation support (5) a requirement for mechanical ventilation >72 hours (6) patients with a history of allergy to plasma, sodium citrate or multivitamin b, or those with a history of previous reactions or selective IgA deficiency. | (1) patients with mild disease not requiring oxygen therapy (2) patients with a normal BMI <70 kg/m² (3) patients without any known active or past medical conditions (4) patients who need mechanical ventilation support (5) a requirement for mechanical ventilation >72 hours (6) patients with a history of allergy to plasma, sodium citrate or multivitamin b, or those with a history of previous reactions or selective IgA deficiency. | ≤ 14 d                       |
| AlKhawas et al | Bahrain                          | open-label RCT                         | requirement for NIV or MV                                                                                 | (1) C-reactive protein (2) procalcitonin (3) lactate dehydrogenase (4) response (5) lactate (6) D-Dimer (7) brain natriuretic peptide (8) lactate changes (9) 28-day mortality rate | (1) patients are randomized (2) randomized patients (3) patients need oxygen therapy (4) patients are randomized (5) patients are randomized. | (1) COVID-19 patients with domestic COVID-19 pneumonia (2) patients with severe COVID-19 pneumonia (3) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (4) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (5) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (6) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (7) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample. | (1) COVID-19 patients with domestic COVID-19 pneumonia (2) patients with severe COVID-19 pneumonia (3) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (4) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (5) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (6) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample (7) patients with COVID-19 pneumonia and a positive result of an RT-PCR test of a respiratory tract sample. | not reported                   |
| Pradhan et al  | Iran                              | single-blind, parallel-group RCT          | levels of cytokine storm indices                                                                         | (1) length of hospital stay (2) general mortality after admission (3) improvement in the 8-point WHO severity score (4) frequency of CPAP-related catheter-related infections | (1) patients need life support (2) patients need mechanical ventilation (3) patients need mechanical ventilation. | (1) patients with mild disease not requiring oxygen therapy (2) patients with a normal BMI <70 kg/m² (3) patients without any known active or past medical conditions (4) patients who need mechanical ventilation support (5) a requirement for mechanical ventilation >72 hours (6) patients with a history of allergy to plasma, sodium citrate or multivitamin b, or those with a history of previous reactions or selective IgA deficiency. | (1) patients with mild disease not requiring oxygen therapy (2) patients with a normal BMI <70 kg/m² (3) patients without any known active or past medical conditions (4) patients who need mechanical ventilation support (5) a requirement for mechanical ventilation >72 hours (6) patients with a history of allergy to plasma, sodium citrate or multivitamin b, or those with a history of previous reactions or selective IgA deficiency. | ≤ 14 d                       |
| PnumBr         | Argentina                        | double-blind, placebo-controlled RCT         | clinical status at day 30 after intervention                                                             | (1) clinical status on the ordinal scale at day 7 and 14 (2) time to discharge from hospital (3) time to discharge from the ICU (4) time to improvement in at least two categories on the ordinal scale (5) time to death (6) time to death | not reported                                                                           | (1) hospitalized patients admitted to hospital with acute illness due to confirmed COVID-19 (2) patients need mechanical ventilation (3) patients need mechanical ventilation (4) patients need mechanical ventilation (5) patients need mechanical ventilation. | (1) patients need life support (2) patients need mechanical ventilation (3) patients need mechanical ventilation. | ≤ 72 h                        |
| INFANT-COVID-19| Argentina                        | double-blind, placebo-controlled RCT         | development of severe respiratory illness                                                               | (1) time to mechanical ventilation on day 15 and day 28 (2) patients need mechanical ventilation (3) development of severe respiratory illness (4) death associated with COVID-19 | not reported                                                                           | (1) 15 years of age or older (2) hospital admission ≤ 96 h (3) patients with SARS-CoV-2 infection ≤ 96 h (4) patients with COVID-19 infection ≤ 96 h (5) patients with severe respiratory illness ≤ 96 h (6) patients with life-threatening complications ≤ 96 h. | (1) patients need life support (2) patients need mechanical ventilation (3) patients need mechanical ventilation. | not reported                   |

**Note:** The table provides a summary of the study designs and inclusion/exclusion criteria for the trials included in the analysis. The criteria are based on the primary and secondary efficacy outcomes, safety outcomes, and eligibility criteria specified in the respective studies.
Abbreviations: ECMO extracorporeal membrane oxygenation, ICU intensive care unit, MV mechanical ventilation, NIV non-invasive ventilation, RCT randomized controlled trial
### Appendix Table 3 Risk of bias assessment according to The Cochrane Risk of Bias Tool

| Study                        | Risk of selection bias (random sequence generation) | Risk of selection bias (allocation concealment) | Risk of performance bias | Risk of detection bias | Risk of bias attrition | Risk of reporting bias | Overall risk of bias   |
|------------------------------|-----------------------------------------------------|-----------------------------------------------|--------------------------|------------------------|------------------------|------------------------|------------------------|
| AlQahtani et al., 2021       | Some                                                | Low                                           | Low                      | Low                    | Low                    | Low                    | Some concerns          |
| CONCOR-1, 2021               | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| ConCOVID, 2021               | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| ChiCTR, 2020                 | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| O’Donnell, 2021              | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| PLACHD, 2020                 | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| RECOVERY, 2021               | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| REMAP-CAP, 2021              | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| PlasmAr, 2021                | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| Bennett-Guerrero, 2021       | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| Pouladzadeh et al., 2021     | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| INFANT-COVID-19, 2021        | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| ComPlan-19                   | Some                                                | Low                                           | Low                      | Low                    | Low                    | Low                    | Some concerns          |
| PICP19                       | Some                                                | Some                                          | Low                      | Low                    | Low                    | Low                    | High risk              |
| CAPSID                       | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
| ILBS-COVID-02                | Low                                                 | Low                                           | Low                      | Low                    | Low                    | Low                    | Low risk               |
### Appendix Table 4: Results and definitions of time to clinical improvement

| Study           | Convalescent plasma | Control                  | HR (95% CI) | Definition of clinical improvement | Scale |
|-----------------|---------------------|--------------------------|-------------|------------------------------------|-------|
|                 | Median [IQR] days to clinical improvement | Median [IQR] days to clinical improvement | n= | | |
| O’Donnell, 2021 | 5 (4-6) 150         | 7 (5-8) 73              | 1.20 (0.87–1.64) | Discharge or improvement by 1 point on ordinal outcome scale | WHO scale: |
|                 |                     |                         |             | 1: not hospitalized with resumption of normal activities |       |
|                 |                     |                         |             | 2: not hospitalized, but unable to resume normal activities |       |
|                 |                     |                         |             | 3: hospitalized, not requiring supplemental oxygen |       |
|                 |                     |                         |             | 4: hospitalized, requiring supplemental oxygen |       |
|                 |                     |                         |             | 5: hospitalized, requiring high-flow oxygen therapy or NIMV |       |
|                 |                     |                         |             | 6: hospitalized, requiring ECMO, IMV |       |
|                 |                     |                         |             | 7: death |       |
| PlasmAr, 2021   | 12 (7-29) 228       | 12 (6-ND) 105           | 1.0 (0.76-1.32) | Discharge or improvement by 2 points in ordinal outcome scale | WHO scale (adapted) |
|                 |                     |                         |             | 1: indicated death |       |
|                 |                     |                         |             | 2: IMV |       |
|                 |                     |                         |             | 3: hospitalized with supplemental oxygen requirement |       |
|                 |                     |                         |             | 4: hospitalized without supplemental oxygen requirement |       |
|                 |                     |                         |             | 5: discharged without full return to baseline physical function |       |
|                 |                     |                         |             | 6: discharged with full return to baseline physical function |       |
| ChiCTR, 2020    | 28 (13-ND) 52       | ND (18-ND) 51           | 1.40 (0.79-2.49) | Discharge or improvement by 2 points on ordinal outcome scale |       |
| ConPlas-19, preprint | 6.5 (4-9)*          | 6 (5-8)* 43            | 0.94 (0.59-1.50) | Improvement by 1 point on ordinal outcome scale | WHO scale: |
|                 |                     |                         |             | 1: hospital discharge |       |
|                 |                     |                         |             | 2: hospitalization with no supplemental oxygen |       |
|                 |                     |                         |             | 3: hospitalization plus supplemental oxygen |       |
|                 |                     |                         |             | 4: hospitalization plus NIV or high-flow supplemental oxygen |       |
|                 |                     |                         |             | 5: hospitalization plus ECMO or IMV |       |
|                 |                     |                         |             | 6: death |       |

*median (95% confidence interval)

Abbreviations: ECMO extracorporeal membrane oxygenation, IMV invasive mechanical ventilation, ND not determined, NIMV non-invasive mechanical ventilation.
**Appendix Table 5** Time to hospital discharge in days

| Study                | Convalescent plasma | Control | HR (95% CI) |
|----------------------|---------------------|---------|-------------|
|                      | Days to discharge   | Days to discharge |              |
|                      | median (IQR)        | median (IQR)     | n=           | n=           |             |
| CONCOR-1, 2021       | not reported        | not reported     | 625          | 313          | 0.91        |
|                      |                     |                    |              |              | (0.8-1.04)  |
| ConCOVID, 2021       | not reported        | not reported      | 43           | 43           | 0.88        |
|                      |                     |                    |              |              | (0.49-1.60) |
| ChiCTR, 2020         | 28 (13-ND)          | ND (19-ND)        | 52           | 51           | 1.61        |
|                      |                     |                    |              |              | (0.88-2.95) |
| O’Donnell, 2021      | 9 (6-28)            | 8 (6-22)          | 150          | 73           | 1.02        |
|                      |                     |                    |              |              | (0.75-1.38) |
| REMAP-CAP, 2021      | 44 (not reported)   | 39 (not reported) | 1075         | 905          | 0.95        |
|                      |                     |                    |              |              | (0.86-1.06) |
| PlasmAr, 2021        | 13 (8-30)           | 12 (7-ND)         | 228          | 105          | 1.0         |
|                      |                     |                    |              |              | (0.76-1.32) |
| Pouladzadeh, 2021    | 8.7 ± 3.9*          | 6.7 ± 4.3*        | 30           | 30           | 0.37        |
|                      |                     |                    |              |              | (0.02-6.84) |
| ConPlas-19           | 8.5 (6-13)†         | 9 (6-11)†         | 38           | 43           | 1.14        |
|                      |                     |                    |              |              | (0.71-1.81) |

*mean ± standard deviation

†median (95% confidence interval)

Abbreviation: ND not determined
**Appendix Table 6** Assessment of level of certainty of evidence according to GRADE recommendations

| Outcome                        | All-cause mortality | Mechanical ventilation use | Time to clinical improvement | Time to discharge |
|--------------------------------|---------------------|----------------------------|------------------------------|-------------------|
| Trials                         | 16 RCTs mainly open label | 7 RCTs mainly open label | 4 RCTs mainly open label | 8 RCTs mainly open label |
| Number of patients             | 16,293 (8524 vs. 7769) | 12,229 (6236 vs. 5993) | 740 (468 vs. 272) | 3,807 (2239 vs. 1568) |
| Pooled effect (95% CI)         | RR 0.97 (0.90-1.04)   | RR 0.97 (0.88-1.07)       | HR 1.09 (0.91-1.30)       | HR 0.95 (0.89-1.02) |

### Down-grading factors

- **Risk of bias**
  - low
  - high
  - moderate

- **Imprecision**
  - low
  - high
  - low

- **Inconsistency**
  - low
  - low
  - low

- **Indirectness**
  - very low
  - low
  - moderate
  - low

- **Publication bias**
  - low
  - low
  - low
  - low

### Up-grading factors

- **Large magnitude of effect**
  - no
  - no
  - no
  - no

- **Dose-response gradient**
  - no
  - no
  - no
  - no

- **All residual confounding would decrease magnitude of effect**
  - n.a.
  - n.a.
  - n.a.
  - n.a.

- **Level of certainty**
  - High
  - High
  - Very low
  - Moderate
Appendix Figure 1 Funnel plots depicting the effects estimates of the outcomes of the trials.
Appendix Figure 2 Forrest plot depicting the risk ratio of all-cause mortality between convalescent plasma and control in the subgroups of non-critically and critically ill patients.
Appendix Figure 3 Forrest plot depicting the risk ratio of all-cause mortality between convalescent plasma and control in the subgroups of patients with and without preexisting anti-SARS-CoV-2 antibodies at baseline.
Appendix Figure 4 Forrest plot depicting the risk ratio of requirement of mechanical ventilation after enrollment between convalescent plasma and control.
Appendix Figure 5 Forrest plot depicting the hazard ratio for the time to clinical improvement between convalescent plasma and control.
**Appendix Figure 6** Forrest plot depicting the hazard ratio for the time to hospital discharge between convalescent plasma and control.