# Secondary Analysis Report for the REMAP-CAP Immunoglobulin Domain

Prepared by the ITSC Analysis Committee

August 26, 2021

## Contents

# 1 Introduction

This report summarizes the data and the results for the immunoglobulin domain analyses run by the ITSC analysis committee. The ITSC analysis committee is blinded to all ongoing domains and interventions in REMAP-CAP.

## 1.1 Immunoglobulin domain interventions

There are three interventions in the COVID-19 Immunoglobulin Domain. These are:

1. **Control** (No immunoglobulin against COVID-19)
2. **Convalescent plasma**
3. **Delayed convalescent plasma**

These three interventions are mutually exclusive; patients randomized in this domain are assigned to one of the three interventions. The primary focus of this report is the effect of convalescent plasma relative to control.

## 1.2 Analysis populations

The SAP for the immunoglobulin domain analysis defines five populations in which analyses will be performed. This report includes analysis results for three of the five analysis populations. The analysis results for the **REMAP-CAP COVID-19 severe and moderate state intent-to-treat (ITT)** population are not included in this report since the ITSC analysis committee remains blinded to ongoing domains and interventions. Results for the **Convalescent plasma specific moderate state ITT** population are included in a separate report. In this report, tables and figures summarize data in the **Convalescent plasma specific severe state ITT** population. In this report, we summarize analysis results from the following four analysis populations:

1. The **Unblinded ITT population** is defined as all severe patients randomized in the Immunoglobulin domain or any of the previously reported interventions and domains within the pandemic stratum (Corticosteroid domain, Antiviral domain, and IL-6ra/control interventions within the Immune Modulation Therapy domain) with no prior randomizations in the moderate state. The unblinded ITT population consists of 3472 patients. There are 26 patients within this population that are missing values of OSFD and in-hospital mortality. Below is a breakdown of the randomizations in the Immunoglobulin domain as well as the other unblinded domains in REMAP-CAP.

- 905 patients randomized to **Control** of which 900 have known OSFD outcomes
- 1075 patients randomized to **Convalescent plasma** of which 1072 have known OSFD outcomes

- 11 patients randomized to **Delayed convalescent plasma** of which 11 have known OSFD outcomes
- 386 patients randomized to the Corticosteroid domain of which 379 have known OSFD outcomes
- 1729 patients randomized to control/tocilizumab/sarilumab in the Immune Modulation Therapy domain of which 1717 have known OSFD outcomes.
- 1010 patients randomized to the Anticoagulation domain of which 1006 have known OSFD outcomes.
- 693 patients randomized to the Antiviral domain of which 691 have known OSFD outcomes.

2. The **Convalescent Plasma Specific Severe State ITT population** consists of patients in the severe state that were randomized to the **Control** or **Convalescent plasma** interventions from the immunoglobulin domain within the pandemic stratum. The convalescent plasma specific severe state ITT population consists of 1980 patients. There are 8 patients within this population that are missing values of OSFD and in-hospital mortality. We will refer to this population throughout as the Convalescent Plasma ITT poopulation.

- 905 patients randomized to **Control** of which 900 have known OSFD outcomes
- 1075 patients randomized to **Convalescent plasma** of which 1072 have known OSFD outcomes

3. The **Convalescent Plasma Per Protocol (PP) population** consists of the patients in the Convalescent plasma specific severe state ITT population population who have been treated as per protocol. The Convalescent plasma PP population consists of 1820 patients. There are 7 patients within this population that are missing values of OSFD and in-hospital mortality.

- 900 patients randomized to **Control** of which 895 have known OSFD outcomes
- 920 patients randomized to **Convalescent plasma** of which 918 have known OSFD outcomes

### 1.3 Modeling conventions

- All reported credible intervals (CrIs) are 95% equal-tailed intervals.
- Results from models of ordinal and dichotomous endpoints are reported as odds ratios (ORs). Results from models of time to event endpoints are reported as hazard ratios (HRs). **For consistency of interpretation, all models are parameterized so that an OR/HR greater than 1 indicates patient benefit relative to the reference group and an OR/HR less than 1 indicates patient harm relative to the reference group.**
- The reference group for the age category OR/HRs is the age category from 60-69 years old.
- The reference group for the time epochs OR/HRs is the most recent time epoch consisting of the four-week period preceding Jan 18, 2020. Time epoch 0 is the most recent epoch and the epochs move backwards in time in two-week periods from epoch 1 to 20.

- The reference group for the sex at birth OR/HRs is the male category.
- **Convalescent plasma** and **Delayed convalescent plasma** are compared to the **Control** intervention. A posterior probability of at least 99% that the odds ratio is greater than 1 is used as a statistical trigger for efficacy (or superiority to control) for the comparison of **Convalescent plasma** and **Control**. Similarly, a probability of harm is reported as the probability that the odds ratio is less than 1 relative to control, or 1 minus the probability of efficacy.
- **Convalescent plasma** is compared to **Control** for futility. A 95% probability of a smaller than 1.2 odds ratio for **Convalescent plasma** relative to **Control** is used as a statistical trigger for futility.
- OR/HR effects for **combinations** of interventions from the Immunoglobulin domain with the Antiviral, Immune Modulation Therapy and Anticoagulation domain are reported relative to control. These OR/HRs incorporate the effect of each individual intervention and the interaction term for the combination of interventions.
- OR/HR effects for **interaction effects** are reported relative to an additive effect. For example, if an interaction effect OR/HR is equal to 1, the combination of interventions is additive (equal to the sum of the effects of the two interventions taken separately). If an interaction OR/HR is greater than 1, the effect of the combination of interventions is synergistic (greater than the sum of the effects of the two interventions taken separately). If the interaction OR/HR is less than 1, the effect of the combination is sub-additive (less than the sum of the effects of the two interventions taken separately).
- Interaction effects are reported for interventions from the the Immunoglobulin domain with the unblinded interventions in the Antiviral, Immune Modulation Therapy and Anticoagulation domains.

## 1.4 Overall summaries of OSFD in the Unblinded ITT population

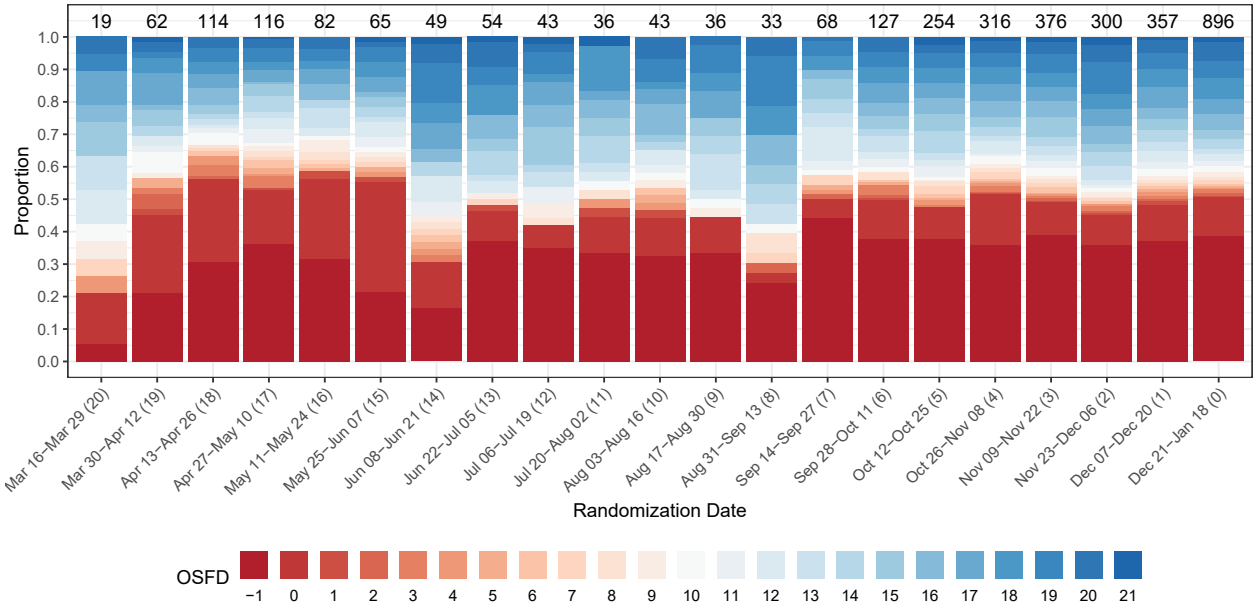


Figure 1: Empirical distribution of organ support free days (OSFD) by time epoch. The Dec 21-Jan 18 category (epoch 0) is the reference time epoch in all models. This plot shows the time epochs defined for the Unblinded ITT population, with the labeled number shown in parentheses. Other analysis populations may have fewer time epochs based on the randomization dates of included patients.

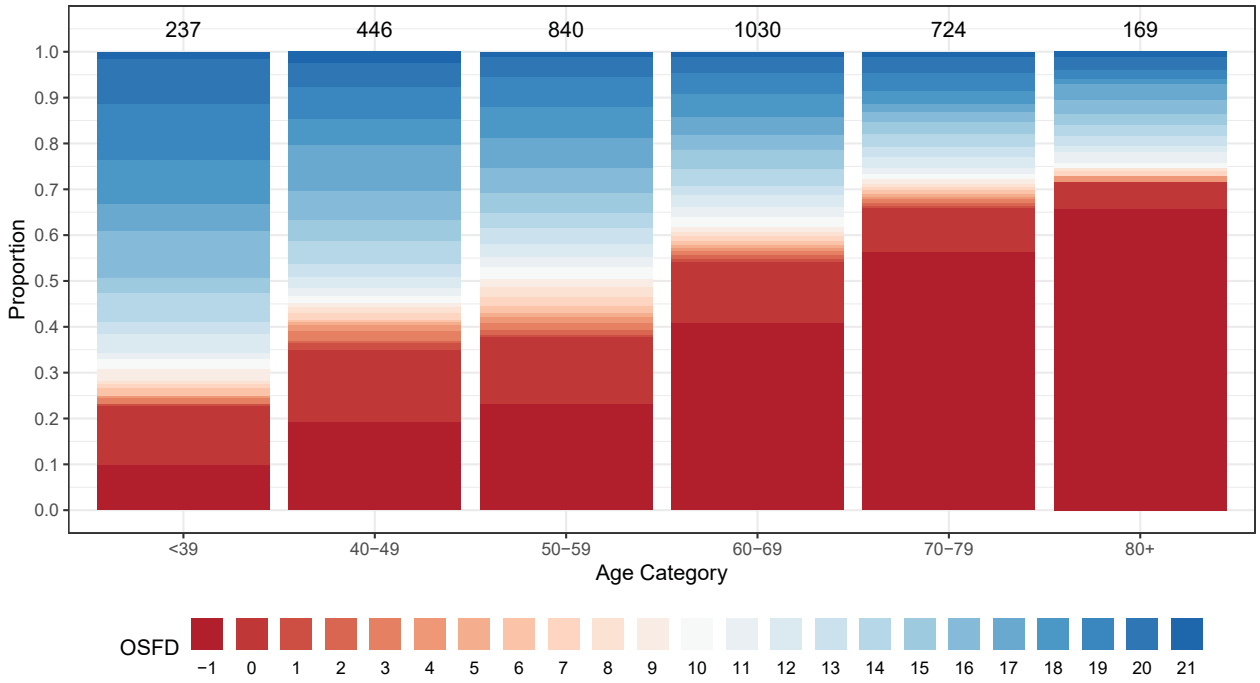


Figure 2: Empirical distribution of organ support free days (OSFD) by age category for the Unblinded ITT population. The 60—69 year age category is the reference group in all models.

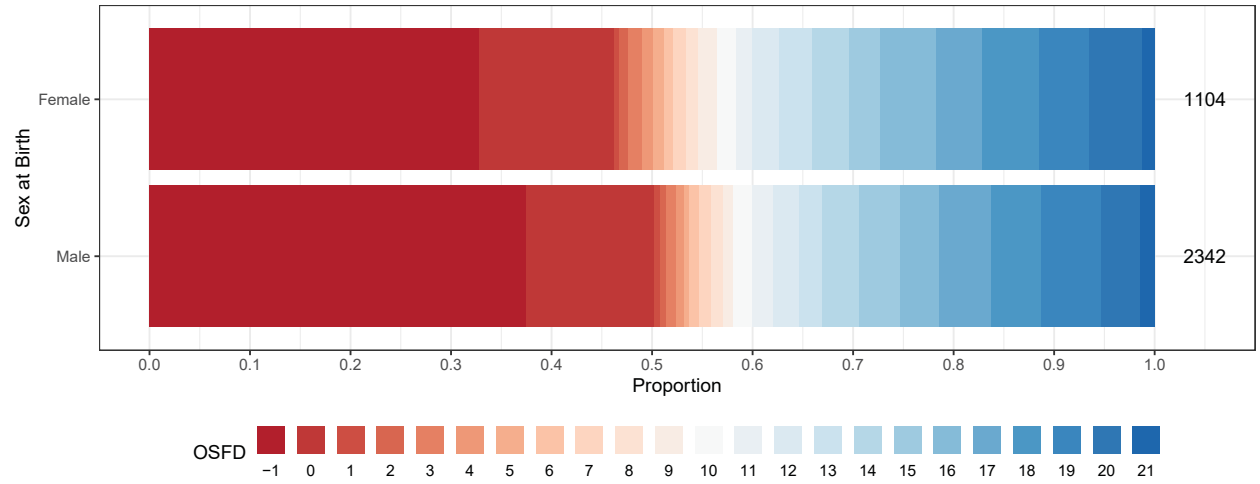


Figure 3: Empirical distribution of organ support free days (OSFD) by sex at birth for the Unblinded ITT population. The male category is the reference group in all models.

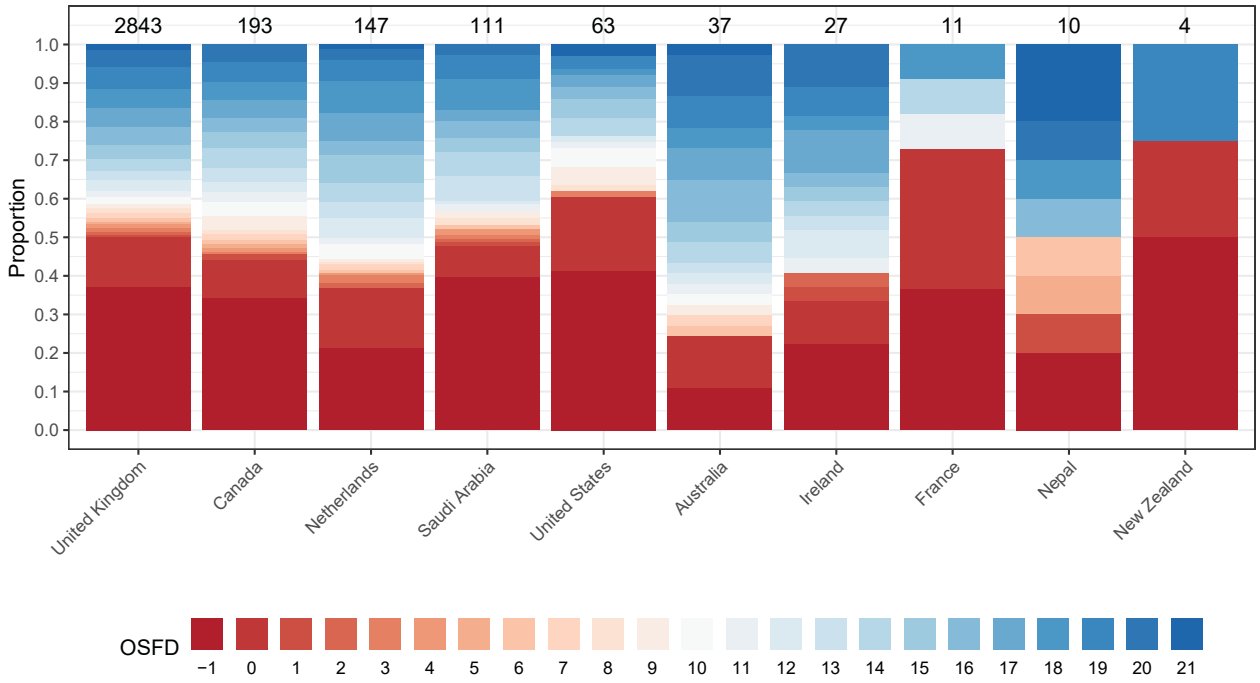


Figure 4: Empirical distribution of organ support free days (OSFD) by country for the Unblinded ITT population.

# 2 Secondary analyses of OSFD

## 2.1 Empirical distribution of OSFD in Convalescent Plasma ITT population

Table 1: Summary of OSFD for the Convalescent Plasma ITT population

| Intervention | # Patients | # Known | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1072 | 0 (-1, 16) | 14 (3, 18) |
| Control | 905 | 900 | 3 (-1, 16) | 14 (7, 18) |

* Days Free of Organ Support in Survivors within 21 days

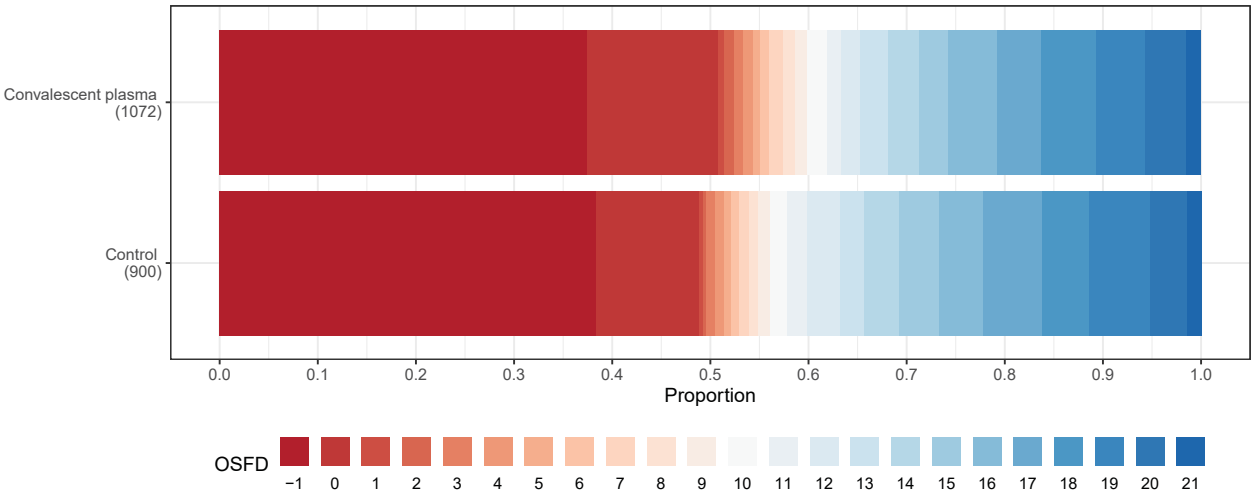


Figure 5: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

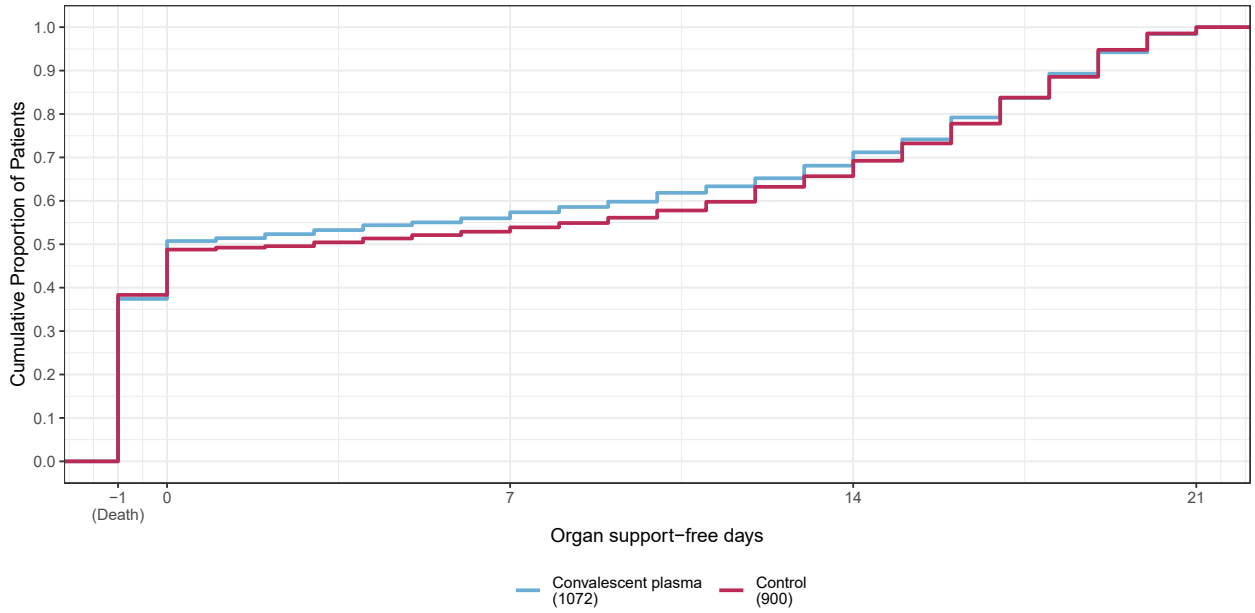


Figure 6: Empirical cumulative distribution of organ support-free days (OSFD) for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

## 2.2 Empirical distribution of OSFD in Unblinded ITT population

Table 2: Summary of OSFD for the Unblinded ITT population

| Intervention | # Patients | # Known | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1072 | 0 (-1, 16) | 14 (3, 18) |
| Delayed convalescent plasma | 11 | 11 | -1 (-1, 0) | 0 (0, 0) |
| Control | 905 | 900 | 3 (-1, 16) | 14 (7, 18) |

* Days Free of Organ Support in Survivors within 21 days

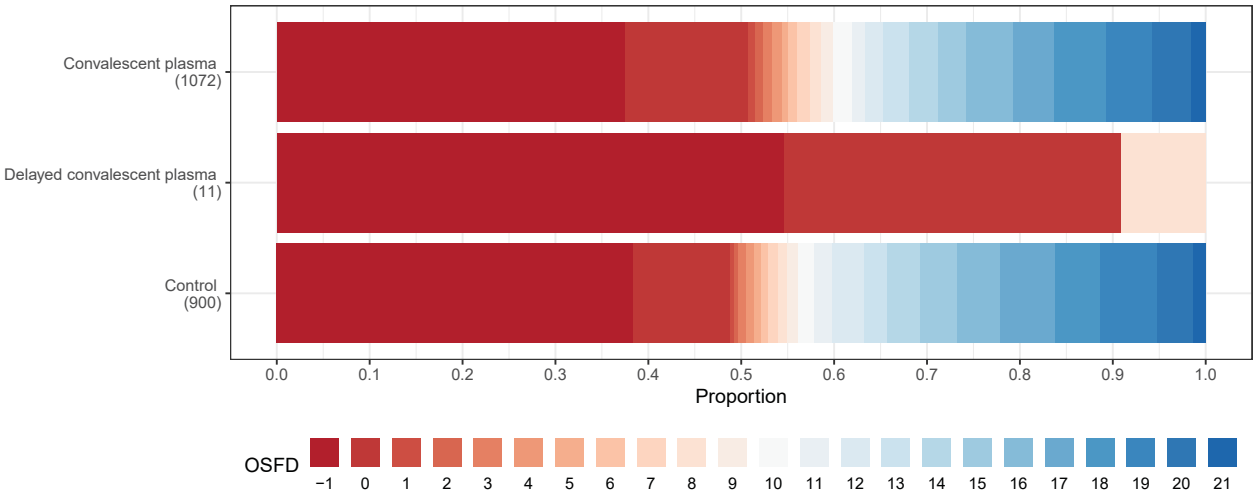


Figure 7: Empirical distribution of organ support free days (OSFD) for convalescent plasma, delayed convalescent plasma, and control. This plot is restricted to patients randomized to one of the three Immunoglobulin domain interventions within the Unblinded ITT population.

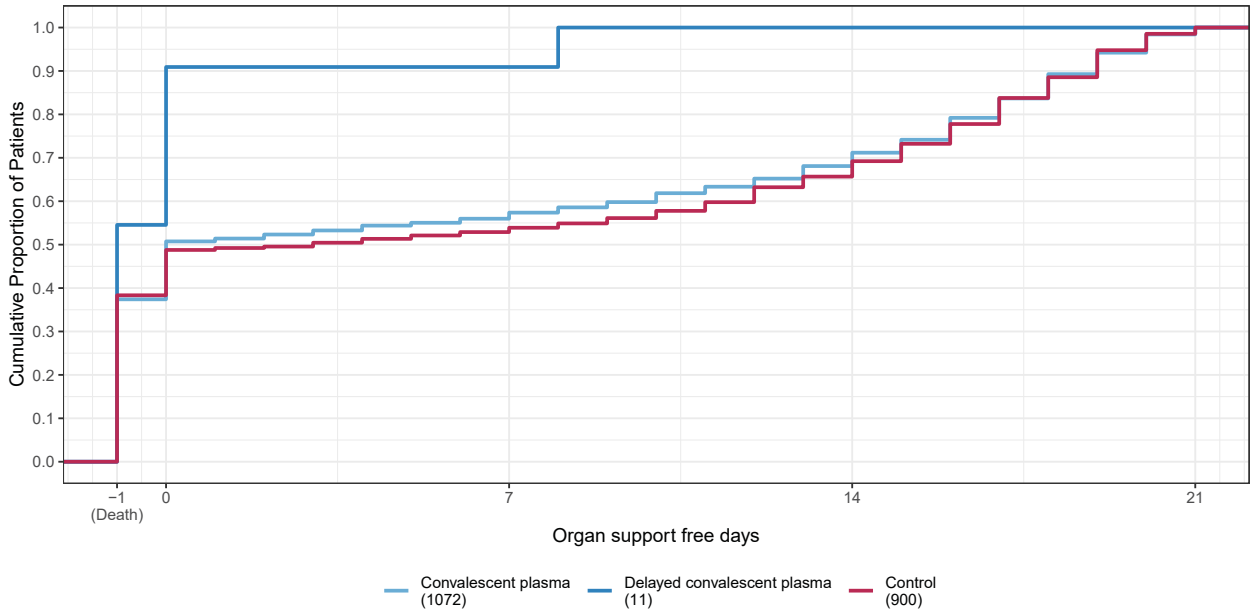


Figure 8: Empirical cumulative distribution of organ support free days (OSFD) for convalescent plasma and control. This plot is restricted to the Unblinded ITT population.

## 2.3 Secondary analysis of OSFD for Unblinded ITT population

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

Table 3: Odds ratio parameters for secondary analysis of OSFD for Unblinded ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.35 | 0.56 | 4.31 | (3.37, 5.56) |
| Age 40-49 | 2.46 | 0.26 | 2.44 | (1.99, 2.99) |
| Age 50-59 | 1.84 | 0.16 | 1.83 | (1.55, 2.16) |
| Age 70-79 | 0.52 | 0.05 | 0.52 | (0.43, 0.62) |
| Age 80+ | 0.33 | 0.06 | 0.32 | (0.23, 0.46) |
| Female | 1.09 | 0.07 | 1.09 | (0.96, 1.24) |
| Time epoch 1 | 1.06 | 0.07 | 1.05 | (0.92, 1.21) |
| Time epoch 2 | 1.13 | 0.12 | 1.12 | (0.92, 1.39) |
| Time epoch 3 | 1.12 | 0.13 | 1.11 | (0.88, 1.39) |
| Time epoch 4 | 1.10 | 0.14 | 1.09 | (0.84, 1.39) |
| Time epoch 5 | 1.10 | 0.15 | 1.10 | (0.83, 1.43) |
| Time epoch 6 | 1.13 | 0.17 | 1.11 | (0.82, 1.49) |
| Time epoch 7 | 1.20 | 0.20 | 1.19 | (0.86, 1.63) |
| Time epoch 8 | 1.34 | 0.25 | 1.31 | (0.93, 1.88) |
| Time epoch 9 | 1.44 | 0.27 | 1.41 | (0.99, 2.05) |
| Time epoch 10 | 1.50 | 0.29 | 1.47 | (1.02, 2.13) |
| Time epoch 11 | 1.54 | 0.29 | 1.51 | (1.04, 2.18) |
| Time epoch 12 | 1.56 | 0.29 | 1.54 | (1.07, 2.22) |
| Time epoch 13 | 1.56 | 0.29 | 1.54 | (1.07, 2.21) |
| Time epoch 14 | 1.52 | 0.29 | 1.49 | (1.04, 2.17) |
| Time epoch 15 | 1.40 | 0.27 | 1.37 | (0.93, 2.00) |
| Time epoch 16 | 1.32 | 0.27 | 1.30 | (0.85, 1.94) |
| Time epoch 17 | 1.34 | 0.28 | 1.31 | (0.85, 1.95) |
| Time epoch 18 | 1.45 | 0.30 | 1.42 | (0.95, 2.10) |
| Time epoch 19 | 1.67 | 0.38 | 1.63 | (1.05, 2.55) |
| Time epoch 20 | 2.01 | 0.66 | 1.90 | (1.07, 3.62) |
| Lopinavir–ritonavir | 0.80 | 0.12 | 0.79 | (0.60, 1.06) |
| Hydroxychloroquine | 0.62 | 0.14 | 0.62 | (0.37, 0.90) |
| Pooled IL-6ra | 1.53 | 0.19 | 1.52 | (1.20, 1.95) |
| Fixed-dose corticosteroids | 1.46 | 0.32 | 1.43 | (0.94, 2.19) |
| Shock-dependent corticosteroids | 1.17 | 0.26 | 1.14 | (0.75, 1.77) |
| Therapeutic anticoagulation | 0.87 | 0.10 | 0.86 | (0.68, 1.09) |
| Convalescent plasma | 0.95 | 0.08 | 0.94 | (0.81, 1.11) |
| Delayed convalescent plasma | 0.52 | 0.30 | 0.46 | (0.16, 1.26) |

Table 4: Posterior probabilities for secondary analysis of OSFD for Unblinded ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.243 |
| Convalescent plasma is futile (OR < 1.2) | 0.998 |
| Convalescent plasma is harmful (OR < 1) | 0.757 |

## 2.4 Secondary analysis of OSFD for Convalescent Plasma ITT population

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control and convalescent plasma.

Table 5: Odds ratio parameters for sensitivity analysis of OSFD in Convalescent Plasma ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.54 | 0.78 | 4.47 | (3.20, 6.29) |
| Age 40-49 | 2.46 | 0.33 | 2.44 | (1.88, 3.15) |
| Age 50-59 | 1.87 | 0.21 | 1.86 | (1.50, 2.32) |
| Age 70-79 | 0.51 | 0.07 | 0.51 | (0.40, 0.65) |
| Age 80+ | 0.36 | 0.08 | 0.35 | (0.22, 0.54) |
| Female | 1.12 | 0.10 | 1.11 | (0.93, 1.32) |
| Time epoch 1 | 1.08 | 0.07 | 1.08 | (0.95, 1.24) |
| Time epoch 2 | 1.16 | 0.12 | 1.15 | (0.96, 1.42) |
| Time epoch 3 | 1.15 | 0.12 | 1.14 | (0.94, 1.41) |
| Time epoch 4 | 1.13 | 0.12 | 1.12 | (0.91, 1.40) |
| Time epoch 5 | 1.12 | 0.13 | 1.11 | (0.88, 1.41) |
| Time epoch 6 | 1.13 | 0.15 | 1.12 | (0.86, 1.46) |
| Time epoch 7 | 1.18 | 0.19 | 1.17 | (0.86, 1.58) |
| Time epoch 8 | 1.28 | 0.24 | 1.25 | (0.88, 1.83) |
| Time epoch 9 | 1.36 | 0.30 | 1.32 | (0.89, 2.06) |
| Time epoch 10 | 1.41 | 0.35 | 1.36 | (0.89, 2.24) |
| Time epoch 11 | 1.43 | 0.36 | 1.37 | (0.89, 2.31) |
| Time epoch 12 | 1.38 | 0.34 | 1.33 | (0.86, 2.19) |
| Time epoch 13 | 1.28 | 0.29 | 1.24 | (0.81, 1.95) |
| Time epoch 14 | 1.16 | 0.26 | 1.13 | (0.74, 1.73) |
| Time epoch 15 | 1.03 | 0.26 | 1.00 | (0.61, 1.63) |
| Time epoch 16 | 0.93 | 0.32 | 0.89 | (0.44, 1.67) |
| Time epoch 17 | 0.87 | 0.42 | 0.80 | (0.28, 1.90) |
| Convalescent plasma | 0.96 | 0.08 | 0.95 | (0.81, 1.13) |

Table 6: Posterior probabilities for sensitivity analysis of OSFD in Convalescent plasma ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.285 |
| Convalescent plasma is futile (OR < 1.2) | 0.996 |
| Convalescent plasma is harmful (OR < 1) | 0.715 |

## 2.5 Sensitivity analysis of OSFD for Unblinded ITT population with site and time factors removed

- Model: Primary analysis ordinal model
- Factors: Age, sex, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

Table 7: Odds ratio parameters for sensitivity analysis of OSFD with site and time factors removed

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 3.75 | 0.47 | 3.73 | (2.91, 4.74) |
| Age 40-49 | 2.26 | 0.23 | 2.25 | (1.85, 2.74) |
| Age 50-59 | 1.80 | 0.15 | 1.79 | (1.52, 2.10) |
| Age 70-79 | 0.56 | 0.05 | 0.56 | (0.47, 0.67) |
| Age 80+ | 0.40 | 0.07 | 0.39 | (0.28, 0.55) |
| Female | 1.11 | 0.07 | 1.11 | (0.98, 1.26) |
| Lopinavir–ritonavir | 0.82 | 0.12 | 0.81 | (0.61, 1.08) |
| Hydroxychloroquine | 0.53 | 0.12 | 0.52 | (0.32, 0.80) |
| Pooled IL-6ra | 1.40 | 0.17 | 1.39 | (1.10, 1.75) |
| Fixed-dose corticosteroids | 1.27 | 0.22 | 1.25 | (0.90, 1.76) |
| Shock-dependent corticosteroids | 1.21 | 0.26 | 1.18 | (0.79, 1.80) |
| Therapeutic anticoagulation | 0.89 | 0.10 | 0.89 | (0.71, 1.11) |
| Convalescent plasma | 0.96 | 0.08 | 0.96 | (0.82, 1.13) |
| Delayed convalescent plasma | 0.60 | 0.30 | 0.54 | (0.20, 1.34) |

Table 8: Posterior probabilities for sensitivity analysis of OSFD with site and time factors removed

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.309 |
| Convalescent plasma is futile (OR < 1.2) | 0.997 |
| Convalescent plasma is harmful (OR < 1) | 0.691 |

## 2.6 Sensitivity analysis of OSFD for Unblinded ITT population with additional interactions between unblinded domains and interventions

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Additional interactions between convalescent plasma and lopinavir–ritonavir, therapeutic anticoagulation, and pooled IL-6ra interventions are reported below. All interaction effects are estimated using standard normal priors.
- Note: The SAP specified that all interactions between convalescent plasma and unblinded interventions would be explored. The tables below show a breakdown of patients randomized to the Immunoglobulin and other unblinded domains. Due to small sample sizes, interactions between convalescent plasma and corticosteroids and HCQ/combination therapy were not specified. The following model estimates interactions between convalescent plasma and the pooled IL-6ra interventions, lopinavir-ritonavir, and therapeutic-dose anticoagulation.

Table 9: Number of patients randomized in the Immunoglobulin and Immune Modulation Therapy domains

| | No immune modulation | Pooled IL-6ra |
|---|---|---|
| Control | 95 | 327 |
| Convalescent plasma | 108 | 395 |

Table 10: Number of patients randomized in the Immunoglobulin and Antiviral domains

| | No antiviral | Lopinavir-ritonavir | HCQ | Combination therapy |
|---|---|---|---|---|
| Control | 68 | 48 | 2 | 0 |
| Convalescent plasma | 78 | 50 | 0 | 0 |

Table 11: Number of patients randomized in the Immunoglobulin and Anticoagulation domains

| | Venous thromboprophylaxis | Therapeutic dose anticoagulation |
|---|---|---|
| Control | 135 | 143 |
| Convalescent plasma | 169 | 166 |

Table 12: Number of patients randomized in the Immunoglobulin and Corticosteroid domains. Note that this includes patients randomized after the closure of the steroid domain in the fixed-dose corticosteroids intervention

| | No corticosteroid | Fixed-dose corticosteroids | Shock-dependent corticosteroids |
|---|---|---|---|
| Control | 6 | 887 | 2 |
| Convalescent plasma | 4 | 1057 | 3 |

Table 13: Odds ratio parameters for sensitivity analysis of OSFD for Unblinded ITT population with additional interactions for unblinded interventions

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.33 | 0.55 | 4.30 | (3.35, 5.51) |
| Age 40-49 | 2.44 | 0.25 | 2.43 | (2.00, 2.97) |
| Age 50-59 | 1.84 | 0.15 | 1.83 | (1.55, 2.17) |
| Age 70-79 | 0.52 | 0.05 | 0.52 | (0.43, 0.62) |
| Age 80+ | 0.33 | 0.06 | 0.32 | (0.23, 0.46) |
| Female | 1.09 | 0.07 | 1.09 | (0.95, 1.25) |
| Time epoch 1 | 1.05 | 0.07 | 1.05 | (0.92, 1.21) |
| Time epoch 2 | 1.12 | 0.12 | 1.12 | (0.92, 1.39) |
| Time epoch 3 | 1.11 | 0.13 | 1.10 | (0.88, 1.38) |
| Time epoch 4 | 1.08 | 0.14 | 1.07 | (0.83, 1.38) |
| Time epoch 5 | 1.09 | 0.15 | 1.08 | (0.82, 1.42) |
| Time epoch 6 | 1.11 | 0.17 | 1.09 | (0.81, 1.48) |
| Time epoch 7 | 1.18 | 0.20 | 1.17 | (0.85, 1.61) |
| Time epoch 8 | 1.32 | 0.24 | 1.29 | (0.92, 1.87) |

Table 13: Odds ratio parameters for sensitivity analysis of OSFD for Unblinded ITT population with additional interactions for unblinded interventions *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Time epoch 9 | 1.42 | 0.28 | 1.39 | (0.97, 2.06) |
| Time epoch 10 | 1.49 | 0.29 | 1.45 | (1.00, 2.16) |
| Time epoch 11 | 1.53 | 0.30 | 1.49 | (1.03, 2.21) |
| Time epoch 12 | 1.56 | 0.30 | 1.53 | (1.06, 2.23) |
| Time epoch 13 | 1.56 | 0.29 | 1.53 | (1.07, 2.22) |
| Time epoch 14 | 1.52 | 0.29 | 1.49 | (1.04, 2.17) |
| Time epoch 15 | 1.40 | 0.27 | 1.38 | (0.94, 2.00) |
| Time epoch 16 | 1.32 | 0.28 | 1.30 | (0.85, 1.92) |
| Time epoch 17 | 1.33 | 0.28 | 1.31 | (0.85, 1.94) |
| Time epoch 18 | 1.44 | 0.30 | 1.41 | (0.93, 2.09) |
| Time epoch 19 | 1.66 | 0.38 | 1.62 | (1.04, 2.49) |
| Time epoch 20 | 1.99 | 0.65 | 1.87 | (1.05, 3.53) |
| Lopinavir–ritonavir | 0.75 | 0.12 | 0.74 | (0.55, 1.02) |
| Hydroxychloroquine | 0.65 | 0.15 | 0.64 | (0.39, 0.96) |
| Pooled IL-6ra | 1.48 | 0.20 | 1.46 | (1.13, 1.91) |
| Fixed-dose corticosteroids | 1.46 | 0.32 | 1.42 | (0.93, 2.19) |
| Shock-dependent corticosteroids | 1.16 | 0.27 | 1.13 | (0.72, 1.77) |
| Therapeutic anticoagulation | 0.93 | 0.12 | 0.92 | (0.71, 1.20) |
| Convalescent plasma | 0.90 | 0.09 | 0.90 | (0.73, 1.10) |
| Delayed convalescent plasma | 0.52 | 0.29 | 0.45 | (0.15, 1.24) |
| Convalescent plasma*Lopinavir-ritonavir combination | 1.23 | 0.36 | 1.18 | (0.67, 2.07) |
| Convalescent plasma*Pooled IL-6ra combination | 1.53 | 0.25 | 1.51 | (1.10, 2.07) |
| Convalescent plasma*Therapeutic anticoagulation combination | 0.69 | 0.13 | 0.68 | (0.47, 0.98) |
| Convalescent plasma*Lopinavir-ritonavir interaction | 1.84 | 0.55 | 1.76 | (1.00, 3.13) |
| Convalescent plasma*Pooled IL-6ra interaction | 1.16 | 0.17 | 1.15 | (0.87, 1.53) |
| Convalescent plasma*Therapeutic anticoagulation interaction | 0.83 | 0.16 | 0.82 | (0.56, 1.20) |

Table 14: Posterior probabilities for sensitivity analysis of OSFD for Unblinded ITT population with additional interactions with unblinded interventions

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.153 |
| Convalescent plasma is futile (OR < 1.2) | 0.997 |
| Convalescent plasma is harmful (OR < 1) | 0.847 |
| Convalescent plasma*Lopinavir-ritonavir combination OR > 1 | 0.719 |
| Convalescent plasma*Pooled IL-6ra combination OR > 1 | 0.995 |
| Convalescent plasma*Therapeutic Anticoagulation OR > 1 | 0.019 |

# 3 Secondary analyses of in-hospital mortality

For consistency of interpretation, all models are parameterized so that an OR/HR greater than 1 indicates patient benefit relative to the reference group and an OR/HR less than 1 indicates patient harm relative to the reference group. In this section, the ORs can be interpreted for the outcome of in-hospital survival.

## 3.1 Empirical distribution of in-hospital mortality in Convalescent Plasma ITT population

Table 15: Summary of in-hospital mortality for the Convalescent Plasma ITT population

| Intervention | # Patients (N) | # Known (n) | Deaths (y) | Mortality Rate (y/n) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1072 | 401 | 0.374 |
| Control | 905 | 900 | 345 | 0.383 |

## 3.2 Secondary analysis of in-hospital mortality for Unblinded ITT population

- Model: Primary dichotomous model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

Table 16: Odds ratio parameters for secondary analysis of in-hospital mortality for Unblinded ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.55 | 2.04 | 8.31 | (5.36, 13.39) |
| Age 40-49 | 3.58 | 0.50 | 3.54 | (2.71, 4.68) |
| Age 50-59 | 2.43 | 0.27 | 2.41 | (1.94, 3.00) |
| Age 70-79 | 0.46 | 0.05 | 0.46 | (0.37, 0.57) |
| Age 80+ | 0.29 | 0.05 | 0.28 | (0.19, 0.40) |
| Female | 1.20 | 0.11 | 1.20 | (1.01, 1.43) |
| Time epoch 1 | 1.07 | 0.08 | 1.07 | (0.93, 1.24) |
| Time epoch 2 | 1.14 | 0.13 | 1.13 | (0.92, 1.43) |
| Time epoch 3 | 1.18 | 0.16 | 1.17 | (0.90, 1.52) |
| Time epoch 4 | 1.21 | 0.19 | 1.19 | (0.88, 1.60) |
| Time epoch 5 | 1.22 | 0.21 | 1.21 | (0.86, 1.67) |
| Time epoch 6 | 1.24 | 0.23 | 1.22 | (0.84, 1.74) |
| Time epoch 7 | 1.29 | 0.26 | 1.27 | (0.85, 1.86) |
| Time epoch 8 | 1.38 | 0.30 | 1.35 | (0.89, 2.06) |
| Time epoch 9 | 1.48 | 0.34 | 1.44 | (0.93, 2.26) |
| Time epoch 10 | 1.56 | 0.37 | 1.51 | (0.97, 2.40) |
| Time epoch 11 | 1.63 | 0.39 | 1.58 | (1.01, 2.51) |
| Time epoch 12 | 1.71 | 0.40 | 1.66 | (1.06, 2.63) |
| Time epoch 13 | 1.80 | 0.42 | 1.76 | (1.13, 2.77) |
| Time epoch 14 | 1.91 | 0.45 | 1.85 | (1.20, 2.98) |
| Time epoch 15 | 1.97 | 0.47 | 1.91 | (1.22, 3.03) |
| Time epoch 16 | 2.00 | 0.49 | 1.94 | (1.20, 3.10) |
| Time epoch 17 | 2.09 | 0.53 | 2.03 | (1.23, 3.28) |
| Time epoch 18 | 2.31 | 0.62 | 2.23 | (1.34, 3.76) |
| Time epoch 19 | 2.71 | 0.87 | 2.57 | (1.44, 4.83) |
| Time epoch 20 | 3.31 | 1.52 | 2.99 | (1.45, 7.13) |
| Lopinavir−ritonavir | 0.73 | 0.14 | 0.71 | (0.50, 1.04) |
| Hydroxychloroquine | 0.57 | 0.16 | 0.56 | (0.29, 0.89) |
| Pooled IL-6ra | 1.55 | 0.25 | 1.53 | (1.12, 2.09) |
| Fixed-dose corticosteroids | 1.03 | 0.30 | 0.99 | (0.57, 1.71) |
| Shock-dependent corticosteroids | 1.22 | 0.38 | 1.16 | (0.64, 2.14) |
| Therapeutic anticoagulation | 0.83 | 0.12 | 0.82 | (0.62, 1.09) |
| Convalescent plasma | 1.02 | 0.10 | 1.02 | (0.83, 1.24) |
| Delayed convalescent plasma | 0.81 | 0.56 | 0.67 | (0.20, 2.22) |

Table 17: Posterior probabilities for secondary analysis of in-hospital mortality for Unblinded ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.557 |
| Convalescent plasma is futile (OR < 1.2) | 0.949 |
| Convalescent plasma is harmful (OR < 1) | 0.443 |

### 3.3 Secondary analysis of in-hospital mortality for Convalescent Plasma ITT population

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

Table 18: Odds ratio parameters for sensitivity analysis of in hospital mortality in Convalescent Plasma ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.47 | 2.66 | 8.01 | (4.62, 14.83) |
| Age 40-49 | 3.20 | 0.58 | 3.15 | (2.23, 4.47) |
| Age 50-59 | 2.34 | 0.32 | 2.32 | (1.76, 3.04) |
| Age 70-79 | 0.50 | 0.07 | 0.50 | (0.38, 0.65) |
| Age 80+ | 0.34 | 0.08 | 0.33 | (0.21, 0.53) |
| Female | 1.31 | 0.14 | 1.30 | (1.05, 1.61) |
| Time epoch 1 | 1.09 | 0.07 | 1.09 | (0.95, 1.25) |
| Time epoch 2 | 1.18 | 0.12 | 1.17 | (0.97, 1.45) |
| Time epoch 3 | 1.24 | 0.15 | 1.23 | (0.98, 1.57) |
| Time epoch 4 | 1.30 | 0.17 | 1.28 | (1.00, 1.66) |
| Time epoch 5 | 1.32 | 0.19 | 1.31 | (0.99, 1.73) |
| Time epoch 6 | 1.33 | 0.22 | 1.31 | (0.96, 1.79) |
| Time epoch 7 | 1.35 | 0.26 | 1.33 | (0.92, 1.92) |
| Time epoch 8 | 1.41 | 0.31 | 1.38 | (0.91, 2.10) |
| Time epoch 9 | 1.48 | 0.36 | 1.44 | (0.91, 2.31) |
| Time epoch 10 | 1.55 | 0.41 | 1.50 | (0.93, 2.51) |
| Time epoch 11 | 1.62 | 0.44 | 1.56 | (0.95, 2.65) |
| Time epoch 12 | 1.67 | 0.45 | 1.61 | (0.98, 2.72) |
| Time epoch 13 | 1.73 | 0.47 | 1.66 | (1.00, 2.83) |
| Time epoch 14 | 1.81 | 0.53 | 1.73 | (1.00, 3.07) |
| Time epoch 15 | 1.92 | 0.67 | 1.82 | (0.95, 3.50) |
| Time epoch 16 | 2.08 | 0.97 | 1.89 | (0.83, 4.43) |
| Time epoch 17 | 2.33 | 1.62 | 1.97 | (0.69, 6.12) |
| Convalescent plasma | 1.04 | 0.11 | 1.03 | (0.84, 1.27) |

Table 19: Posterior probabilities for sensitivity analysis of in-hospital mortality in Convalescent Plasma ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.619 |
| Convalescent plasma is futile (OR < 1.2) | 0.922 |
| Convalescent plasma is harmful (OR < 1) | 0.381 |

### 3.4 Sensitivity analysis of in-hospital mortality for Unblinded ITT population with site and time factors removed

- Model: Primary dichotomous model

- Factors: Age, sex, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

Table 20: Odds ratio parameters for sensitivity analysis of in-hospital mortality with site and time factors removed

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 6.67 | 1.55 | 6.48 | (4.21, 10.30) |
| Age 40-49 | 3.08 | 0.41 | 3.05 | (2.36, 3.99) |
| Age 50-59 | 2.29 | 0.23 | 2.28 | (1.87, 2.77) |
| Age 70-79 | 0.53 | 0.05 | 0.53 | (0.43, 0.63) |
| Age 80+ | 0.36 | 0.06 | 0.35 | (0.25, 0.49) |
| Female | 1.21 | 0.10 | 1.21 | (1.03, 1.42) |
| Lopinavir–ritonavir | 0.74 | 0.13 | 0.72 | (0.51, 1.04) |
| Hydroxychloroquine | 0.53 | 0.14 | 0.52 | (0.28, 0.84) |
| Pooled IL-6ra | 1.37 | 0.20 | 1.36 | (1.03, 1.80) |
| Fixed-dose corticosteroids | 0.76 | 0.18 | 0.74 | (0.47, 1.15) |
| Shock-dependent corticosteroids | 1.35 | 0.40 | 1.30 | (0.74, 2.29) |
| Therapeutic anticoagulation | 0.86 | 0.12 | 0.85 | (0.64, 1.12) |
| Convalescent plasma | 1.04 | 0.10 | 1.03 | (0.85, 1.25) |
| Delayed convalescent plasma | 1.04 | 0.64 | 0.89 | (0.29, 2.66) |

Table 21: Posterior probabilities for sensitivity analysis of in-hospital mortality with site and time factors removed

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.630 |
| Convalescent plasma is futile (OR < 1.2) | 0.936 |
| Convalescent plasma is harmful (OR < 1) | 0.370 |

### 3.5 Sensitivity analysis of in-hospital mortality endpoint for Unblinded ITT population with additional interactions between unblinded domains and interventions

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain in-

terventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.

- Additional interactions between convalescent plasma and lopinavir−ritonavir, therapeutic anticoagulation, and pooled IL-6ra interventions are reported below. All interaction effects are estimated using standard normal priors.
- Note: An interaction between convalescent plasma and fixed-dose steroids was not specified due to the small number of subjects randomized to convalescent plasma without steroids.

Table 22: Odds ratio parameters for sensitivity analysis of in-hospital mortality endpoint for Unblinded ITT population with additional interactions for unblinded interventions

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.62 | 2.01 | 8.36 | (5.46, 13.23) |
| Age 40-49 | 3.56 | 0.51 | 3.52 | (2.67, 4.68) |
| Age 50-59 | 2.44 | 0.27 | 2.42 | (1.96, 2.99) |
| Age 70-79 | 0.46 | 0.05 | 0.46 | (0.37, 0.57) |
| Age 80+ | 0.29 | 0.05 | 0.28 | (0.19, 0.41) |
| Female | 1.20 | 0.11 | 1.20 | (1.01, 1.43) |
| Time epoch 1 | 1.07 | 0.08 | 1.07 | (0.93, 1.23) |
| Time epoch 2 | 1.14 | 0.13 | 1.13 | (0.91, 1.42) |
| Time epoch 3 | 1.17 | 0.16 | 1.15 | (0.89, 1.51) |
| Time epoch 4 | 1.19 | 0.18 | 1.17 | (0.87, 1.58) |
| Time epoch 5 | 1.20 | 0.20 | 1.18 | (0.86, 1.64) |
| Time epoch 6 | 1.22 | 0.22 | 1.19 | (0.84, 1.71) |
| Time epoch 7 | 1.26 | 0.25 | 1.24 | (0.84, 1.83) |
| Time epoch 8 | 1.36 | 0.29 | 1.33 | (0.88, 2.01) |
| Time epoch 9 | 1.45 | 0.33 | 1.42 | (0.92, 2.20) |
| Time epoch 10 | 1.53 | 0.36 | 1.49 | (0.97, 2.37) |
| Time epoch 11 | 1.61 | 0.38 | 1.57 | (1.01, 2.50) |
| Time epoch 12 | 1.70 | 0.39 | 1.65 | (1.06, 2.58) |
| Time epoch 13 | 1.80 | 0.42 | 1.75 | (1.14, 2.74) |
| Time epoch 14 | 1.92 | 0.45 | 1.87 | (1.21, 2.95) |
| Time epoch 15 | 1.99 | 0.48 | 1.93 | (1.23, 3.07) |
| Time epoch 16 | 2.03 | 0.49 | 1.97 | (1.22, 3.14) |
| Time epoch 17 | 2.12 | 0.54 | 2.06 | (1.26, 3.36) |
| Time epoch 18 | 2.35 | 0.64 | 2.27 | (1.35, 3.84) |
| Time epoch 19 | 2.75 | 0.88 | 2.61 | (1.44, 4.87) |
| Time epoch 20 | 3.35 | 1.55 | 3.02 | (1.43, 7.04) |

Table 22: Odds ratio parameters for sensitivity analysis of in-hospital mortality endpoint for Unblinded ITT population with additional interactions for unblinded interventions *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Lopinavir–ritonavir | 0.71 | 0.14 | 0.70 | (0.47, 1.04) |
| Hydroxychloroquine | 0.63 | 0.18 | 0.62 | (0.32, 1.01) |
| Pooled IL-6ra | 1.51 | 0.25 | 1.49 | (1.06, 2.07) |
| Fixed-dose corticosteroids | 1.03 | 0.30 | 0.99 | (0.56, 1.75) |
| Shock-dependent corticosteroids | 1.20 | 0.38 | 1.14 | (0.63, 2.10) |
| Therapeutic anticoagulation | 0.96 | 0.16 | 0.94 | (0.69, 1.31) |
| Convalescent plasma | 1.01 | 0.13 | 1.00 | (0.78, 1.30) |
| Delayed convalescent plasma | 0.80 | 0.54 | 0.67 | (0.20, 2.21) |
| Convalescent plasma*Lopinavir-ritonavir combination | 1.34 | 0.51 | 1.26 | (0.62, 2.56) |
| Convalescent plasma*Pooled IL-6ra combination | 1.74 | 0.36 | 1.71 | (1.15, 2.54) |
| Convalescent plasma*Therapeutic anticoagulation combination | 0.64 | 0.15 | 0.62 | (0.40, 0.97) |
| Convalescent plasma*Lopinavir-ritonavir interaction | 1.92 | 0.72 | 1.80 | (0.90, 3.71) |
| Convalescent plasma*Pooled IL-6ra interaction | 1.17 | 0.22 | 1.15 | (0.80, 1.64) |
| Convalescent plasma*Therapeutic anticoagulation interaction | 0.68 | 0.16 | 0.66 | (0.41, 1.04) |

Table 23: Posterior probabilities for sensitivity analysis of in-hospital mortality endpoint for Unblinded ITT population with additional interactions with unblinded interventions

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.505 |
| Convalescent plasma is futile (OR < 1.2) | 0.915 |
| Convalescent plasma is harmful (OR < 1) | 0.495 |
| Convalescent plasma*Lopinavir-ritonavir combination OR > 1 | 0.738 |
| Convalescent plasma*Pooled IL-6ra combination OR > 1 | 0.997 |
| Convalescent plasma*Therapeutic Anticoagulation OR > 1 | 0.019 |

# 4 Safety analyses

## 4.1 Serious adverse events

### 4.1.1 Empirical distribution of any serious adverse event in Convalescent Plasma ITT population

Table 24: Summary of any serious adverse event (SAE) for the Convalescent Plasma ITT population. Note that this table shows the number of patients with any serious adverse event rather than the total number of serious adverse events observed.

| Intervention | # Patients (N) | # Known (n) | Any serious adverse event (y) | Rate of any serious adverse event (y/n) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1075 | 32 | 0.030 |
| Control | 905 | 905 | 12 | 0.013 |

### 4.1.2 Primary safety analysis of any serious adverse event in Convalescent Plasma ITT population

- Model: Primary dichotomous model
- Factors: Age, sex, site, control and convalescent plasma

Table 25: Odds ratio parameters for the primary safety analysis of any serious adverse event in the Convalescent Plasma ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 3.38 | 2.84 | 2.57 | (0.75, 10.78) |
| Age 40-49 | 1.12 | 0.55 | 1.00 | (0.43, 2.52) |
| Age 50-59 | 1.82 | 0.82 | 1.67 | (0.75, 3.79) |
| Age 70-79 | 0.97 | 0.39 | 0.90 | (0.43, 1.93) |
| Age 80+ | 1.53 | 1.22 | 1.18 | (0.35, 4.68) |
| Female | 1.56 | 0.58 | 1.45 | (0.76, 2.94) |
| Convalescent plasma | 0.48 | 0.16 | 0.46 | (0.23, 0.86) |

Table 26: Posterior probabilities for the primary safety analysis of any serious adverse event in the Convalescent Plasma ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.008 |

## 4.2 Venous thromboembolic events

### 4.2.1 Empirical distribution of venous thromboembolic events at 90-days

Table 27: Summary of venous thromboembolic event for the Convalescent Plasma ITT population

| Intervention | # Patients (N) | # Known (n) | Venous thromboembolic event (y) | Rate of venous thromboembolic event (y/n) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1075 | 74 | 0.069 |
| Control | 905 | 905 | 61 | 0.067 |

### 4.2.2 Primary safety analysis of venous thromboembolic events at 90-days in Convalescent Plasma ITT population

- Model: Primary dichotomous model
- Factors: Age, sex, site, control and convalescent plasma

Table 28: Odds ratio parameters for the safety analysis of venous thromboembolic events at 90-days in the Convalescent Plasma ITT population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 1.23 | 0.47 | 1.14 | (0.58, 2.40) |
| Age 40-49 | 1.37 | 0.42 | 1.31 | (0.74, 2.40) |
| Age 50-59 | 1.11 | 0.25 | 1.08 | (0.69, 1.68) |
| Age 70-79 | 1.41 | 0.37 | 1.36 | (0.83, 2.28) |
| Age 80+ | 3.63 | 2.54 | 2.97 | (1.06, 9.97) |
| Female | 1.05 | 0.20 | 1.03 | (0.71, 1.51) |
| Convalescent plasma | 1.01 | 0.18 | 0.99 | (0.69, 1.41) |

Table 29: Posterior probabilities for the safety analysis of venous thromboembolic events at 90-days in the Convalescent Plasma ITT population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.479 |

# 5 Per protocol analyses

## 5.1 Data summaries for per protocol analyses

Table 30: Summary of patients treated per protocol by treatment arm

| Intervention | Patients | Known | Treated per protocol |
|---|---|---|---|
| Convalescent plasma | 1075 | 1075 | 920 (85.6%) |
| Control | 905 | 905 | 900 (99.4%) |

Table 31: Summary of OSFD for the Convalescent Plasma Per Protocol population

| Intervention | # Patients | # Known | In-hospital deaths | OSFD median (IQR) | OSFD in survivors* median (IQR) |
|---|---|---|---|---|---|
| Convalescent plasma | 920 | 918 | 335 (36.5%) | 0 (-1, 15) | 13 (3, 17) |
| Control | 900 | 895 | 342 (38.2%) | 3 (-1, 16) | 15 (7, 18) |

* Days free of organ support in survivors within 21 days

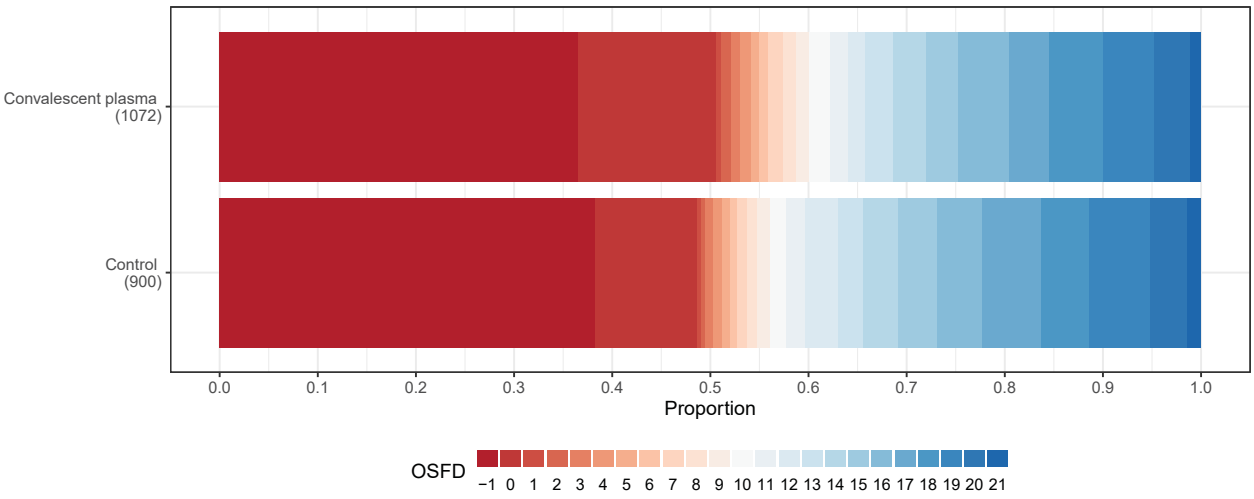


Figure 9: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control. This plot is restricted to the Convalescent Plasma Per Protocol population.

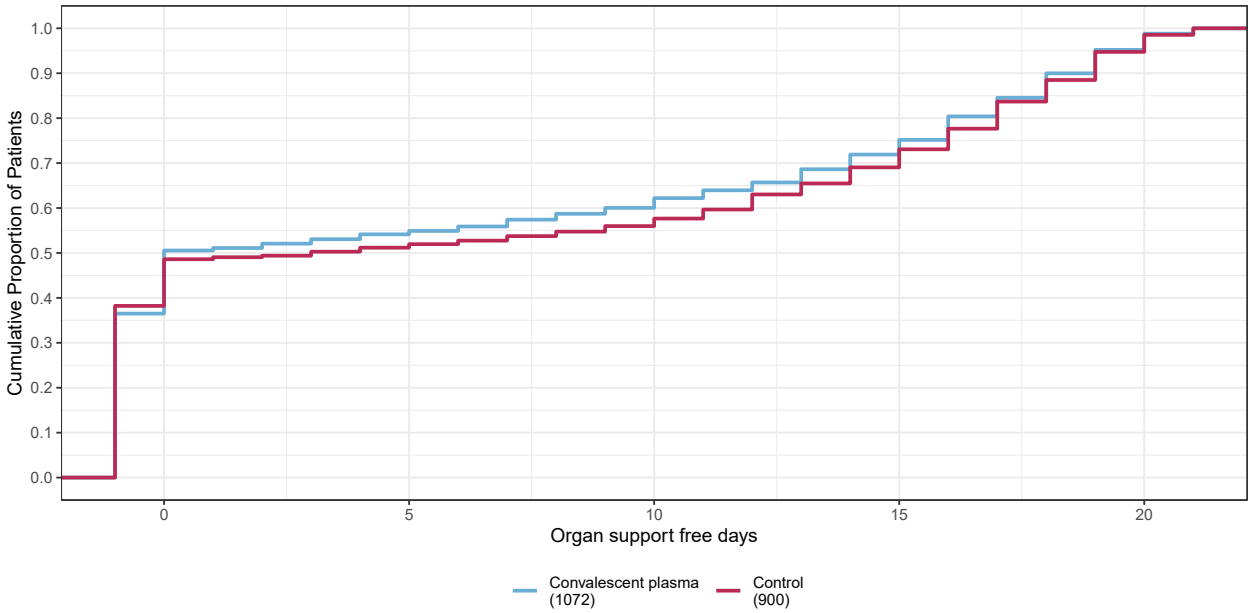


Figure 10: Empirical cumulative distribution of organ support free days (OSFD) for convalescent plasma and control. This plot is restricted to the Convalescent Plasma Per Protocol population.

## 5.2 Sensitivity analysis of OSFD for Convalescent Plasma specific per protocol population

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, convalescent plasma and control interventions
- Population: Convalescent Plasma specific per protocol

Table 32: Odds ratio parameters for sensitivity analysis of OSFD in Convalescent Plasma Per Protocol population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.47 | 0.79 | 4.41 | (3.14, 6.19) |
| Age 40-49 | 2.61 | 0.36 | 2.59 | (1.96, 3.38) |
| Age 50-59 | 1.94 | 0.22 | 1.93 | (1.54, 2.42) |
| Age 70-79 | 0.52 | 0.07 | 0.51 | (0.40, 0.67) |
| Age 80+ | 0.40 | 0.10 | 0.39 | (0.24, 0.63) |
| Female | 1.10 | 0.10 | 1.10 | (0.91, 1.32) |
| Time epoch 1 | 1.09 | 0.08 | 1.09 | (0.95, 1.27) |
| Time epoch 2 | 1.19 | 0.13 | 1.18 | (0.98, 1.50) |
| Time epoch 3 | 1.18 | 0.13 | 1.17 | (0.94, 1.46) |
| Time epoch 4 | 1.14 | 0.13 | 1.13 | (0.90, 1.42) |
| Time epoch 5 | 1.11 | 0.14 | 1.10 | (0.85, 1.40) |
| Time epoch 6 | 1.14 | 0.17 | 1.13 | (0.84, 1.49) |
| Time epoch 7 | 1.23 | 0.21 | 1.21 | (0.87, 1.71) |
| Time epoch 8 | 1.38 | 0.30 | 1.34 | (0.92, 2.07) |
| Time epoch 9 | 1.51 | 0.38 | 1.45 | (0.95, 2.45) |
| Time epoch 10 | 1.61 | 0.45 | 1.53 | (0.96, 2.66) |
| Time epoch 11 | 1.62 | 0.47 | 1.54 | (0.95, 2.75) |
| Time epoch 12 | 1.54 | 0.42 | 1.47 | (0.92, 2.53) |
| Time epoch 13 | 1.38 | 0.34 | 1.34 | (0.86, 2.16) |
| Time epoch 14 | 1.20 | 0.28 | 1.17 | (0.75, 1.83) |
| Time epoch 15 | 1.01 | 0.27 | 0.98 | (0.57, 1.63) |
| Time epoch 16 | 0.86 | 0.34 | 0.81 | (0.35, 1.65) |
| Convalescent plasma | 0.93 | 0.08 | 0.92 | (0.78, 1.10) |

Table 33: Posterior probabilities for sensitivity analysis of OSFD in Convalescent Plasma Per Protocol population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.179 |
| Convalescent plasma is futile (OR < 1.2) | 0.998 |
| Convalescent plasma is harmful (OR < 1) | 0.821 |

## 5.3 Sensitivity analysis of in-hospital mortality for Convalescent Plasma Per Protocol population

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, convalescent plasma and control interventions
- Population: Convalescent Plasma specific per protocol

Table 34: Odds ratio parameters for sensitivity analysis of in-hospital mortality in Convalescent Plasma Per Protocol population

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 7.67 | 2.36 | 7.28 | (4.20, 13.40) |
| Age 40-49 | 3.39 | 0.63 | 3.33 | (2.32, 4.80) |
| Age 50-59 | 2.47 | 0.36 | 2.44 | (1.85, 3.23) |
| Age 70-79 | 0.51 | 0.07 | 0.50 | (0.38, 0.66) |
| Age 80+ | 0.39 | 0.10 | 0.37 | (0.23, 0.62) |
| Female | 1.31 | 0.16 | 1.30 | (1.04, 1.64) |
| Time epoch 1 | 1.09 | 0.08 | 1.08 | (0.95, 1.25) |
| Time epoch 2 | 1.18 | 0.13 | 1.17 | (0.96, 1.46) |
| Time epoch 3 | 1.24 | 0.15 | 1.23 | (0.97, 1.57) |
| Time epoch 4 | 1.29 | 0.17 | 1.28 | (0.99, 1.66) |
| Time epoch 5 | 1.32 | 0.19 | 1.31 | (0.99, 1.73) |
| Time epoch 6 | 1.35 | 0.22 | 1.34 | (0.97, 1.83) |
| Time epoch 7 | 1.41 | 0.27 | 1.39 | (0.95, 2.01) |
| Time epoch 8 | 1.49 | 0.33 | 1.45 | (0.95, 2.24) |
| Time epoch 9 | 1.58 | 0.40 | 1.54 | (0.96, 2.51) |
| Time epoch 10 | 1.67 | 0.46 | 1.60 | (0.98, 2.74) |
| Time epoch 11 | 1.72 | 0.48 | 1.65 | (1.00, 2.87) |
| Time epoch 12 | 1.73 | 0.49 | 1.66 | (1.00, 2.88) |
| Time epoch 13 | 1.75 | 0.49 | 1.67 | (1.00, 2.88) |
| Time epoch 14 | 1.77 | 0.53 | 1.70 | (0.97, 3.03) |
| Time epoch 15 | 1.82 | 0.65 | 1.70 | (0.89, 3.41) |
| Time epoch 16 | 1.89 | 0.88 | 1.70 | (0.73, 4.11) |
| Convalescent plasma | 1.05 | 0.12 | 1.05 | (0.85, 1.30) |

Table 35: Posterior probabilities for sensitivity analysis of in-hospital mortality in Convalescent Plasma Per Protocol population

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.667 |
| Convalescent plasma is futile (OR < 1.2) | 0.894 |
| Convalescent plasma is harmful (OR < 1) | 0.333 |

# 6 Analyses of secondary endpoints

## 6.1 Secondary analysis of 90-day mortality

- Model: Primary TTE model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy, Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

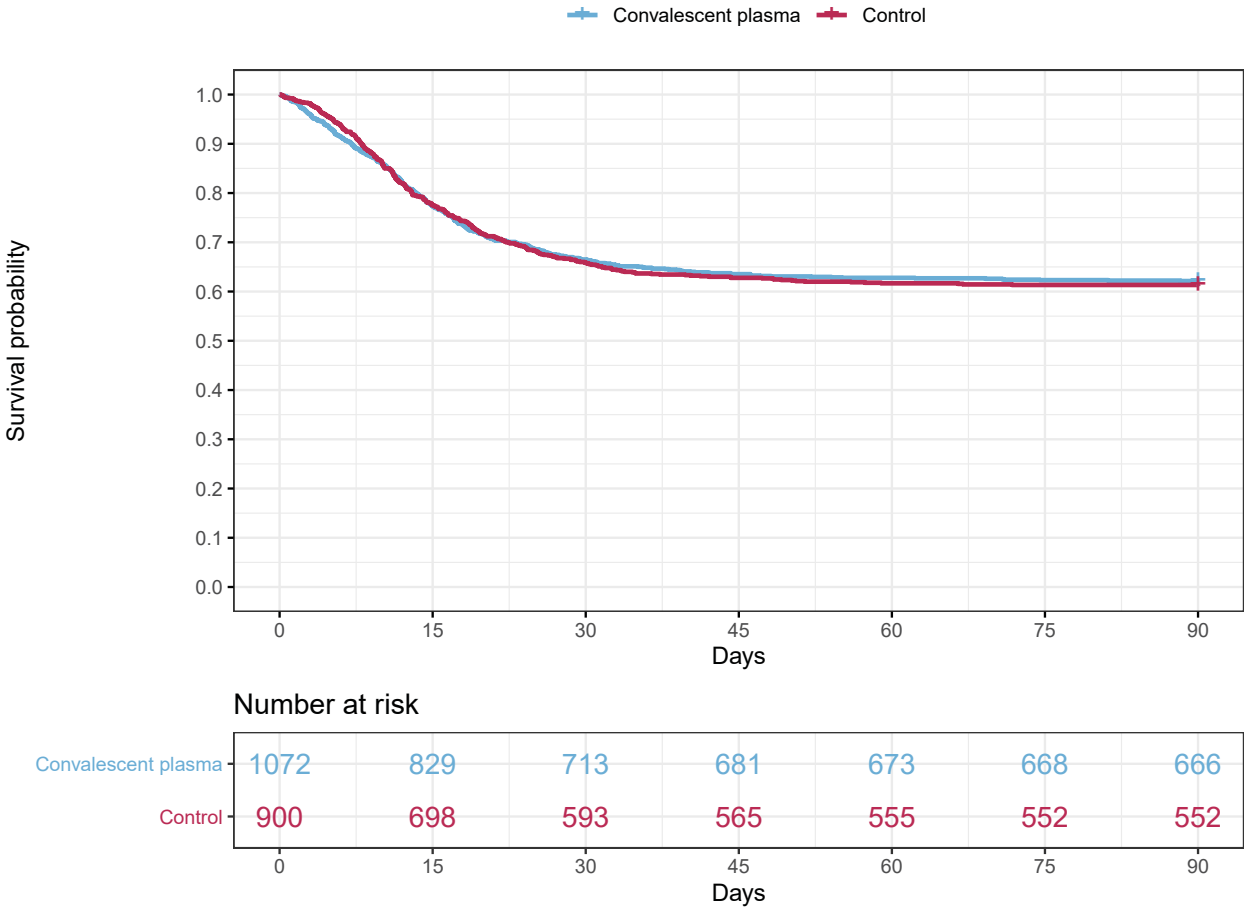


Figure 11: Empirical distribution of 90-day mortality for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 36: Summary of 2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th percentiles from the Kaplan-Meier estimates for mortality (in days). Displaying the observed percentiles for this outcome.

| | 2.5 | 10.0 | 25.0 | 50.0 | 75.0 | 90.0 | 97.5 |
|---|---|---|---|---|---|---|---|
| Convalescent plasma | 2 | 7 | 17 | - | - | - | - |
| Control | 3.5 | 8 | 17.2 | - | - | - | - |

Table 37: Hazard ratio parameters for secondary analysis of 90-day survival

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.88 | 0.97 | 4.77 | (3.34, 7.12) |
| Age 40-49 | 2.50 | 0.29 | 2.48 | (1.98, 3.13) |
| Age 50-59 | 1.95 | 0.17 | 1.94 | (1.64, 2.30) |
| Age 70-79 | 0.55 | 0.04 | 0.55 | (0.48, 0.63) |
| Age 80+ | 0.34 | 0.04 | 0.34 | (0.27, 0.43) |
| Female | 1.11 | 0.07 | 1.11 | (0.98, 1.25) |
| Time epoch 1 | 1.13 | 0.06 | 1.13 | (1.02, 1.27) |
| Time epoch 2 | 1.27 | 0.10 | 1.26 | (1.09, 1.48) |
| Time epoch 3 | 1.34 | 0.11 | 1.34 | (1.14, 1.58) |
| Time epoch 4 | 1.41 | 0.12 | 1.41 | (1.19, 1.68) |
| Time epoch 5 | 1.46 | 0.14 | 1.45 | (1.21, 1.75) |
| Time epoch 6 | 1.49 | 0.16 | 1.48 | (1.20, 1.83) |
| Time epoch 7 | 1.54 | 0.19 | 1.53 | (1.20, 1.96) |
| Time epoch 8 | 1.60 | 0.24 | 1.57 | (1.19, 2.13) |
| Time epoch 9 | 1.62 | 0.26 | 1.59 | (1.19, 2.23) |
| Time epoch 10 | 1.60 | 0.26 | 1.58 | (1.15, 2.19) |
| Time epoch 11 | 1.57 | 0.26 | 1.55 | (1.13, 2.14) |
| Time epoch 12 | 1.55 | 0.25 | 1.53 | (1.12, 2.09) |
| Time epoch 13 | 1.56 | 0.25 | 1.54 | (1.14, 2.11) |
| Time epoch 14 | 1.60 | 0.27 | 1.57 | (1.17, 2.21) |
| Time epoch 15 | 1.56 | 0.26 | 1.53 | (1.14, 2.13) |
| Time epoch 16 | 1.47 | 0.23 | 1.45 | (1.07, 1.99) |
| Time epoch 17 | 1.43 | 0.23 | 1.41 | (1.02, 1.95) |
| Time epoch 18 | 1.50 | 0.26 | 1.48 | (1.06, 2.07) |
| Time epoch 19 | 1.69 | 0.38 | 1.64 | (1.09, 2.59) |
| Time epoch 20 | 1.98 | 0.77 | 1.81 | (1.05, 3.87) |
| Lopinavir–ritonavir | 0.89 | 0.11 | 0.88 | (0.70, 1.12) |
| Hydroxychloroquine | 0.70 | 0.14 | 0.70 | (0.45, 0.99) |
| Pooled IL-6ra | 1.37 | 0.12 | 1.37 | (1.16, 1.61) |
| Fixed-dose corticosteroids | 0.81 | 0.13 | 0.80 | (0.59, 1.09) |
| Shock-dependent corticosteroids | 1.00 | 0.21 | 0.98 | (0.65, 1.48) |
| Therapeutic anticoagulation | 1.00 | 0.09 | 1.00 | (0.84, 1.19) |
| Convalescent plasma | 1.05 | 0.07 | 1.05 | (0.92, 1.19) |
| Delayed convalescent plasma | 1.02 | 0.51 | 0.91 | (0.40, 2.34) |

Table 38: Posterior probabilities for secondary analysis of 90-day survival

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.753 |
| Convalescent plasma is futile (OR < 1.2) | 0.981 |
| Convalescent plasma is harmful (OR < 1) | 0.247 |

## 6.2 Secondary analysis of 28-day mortality

- Model: Primary TTE model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

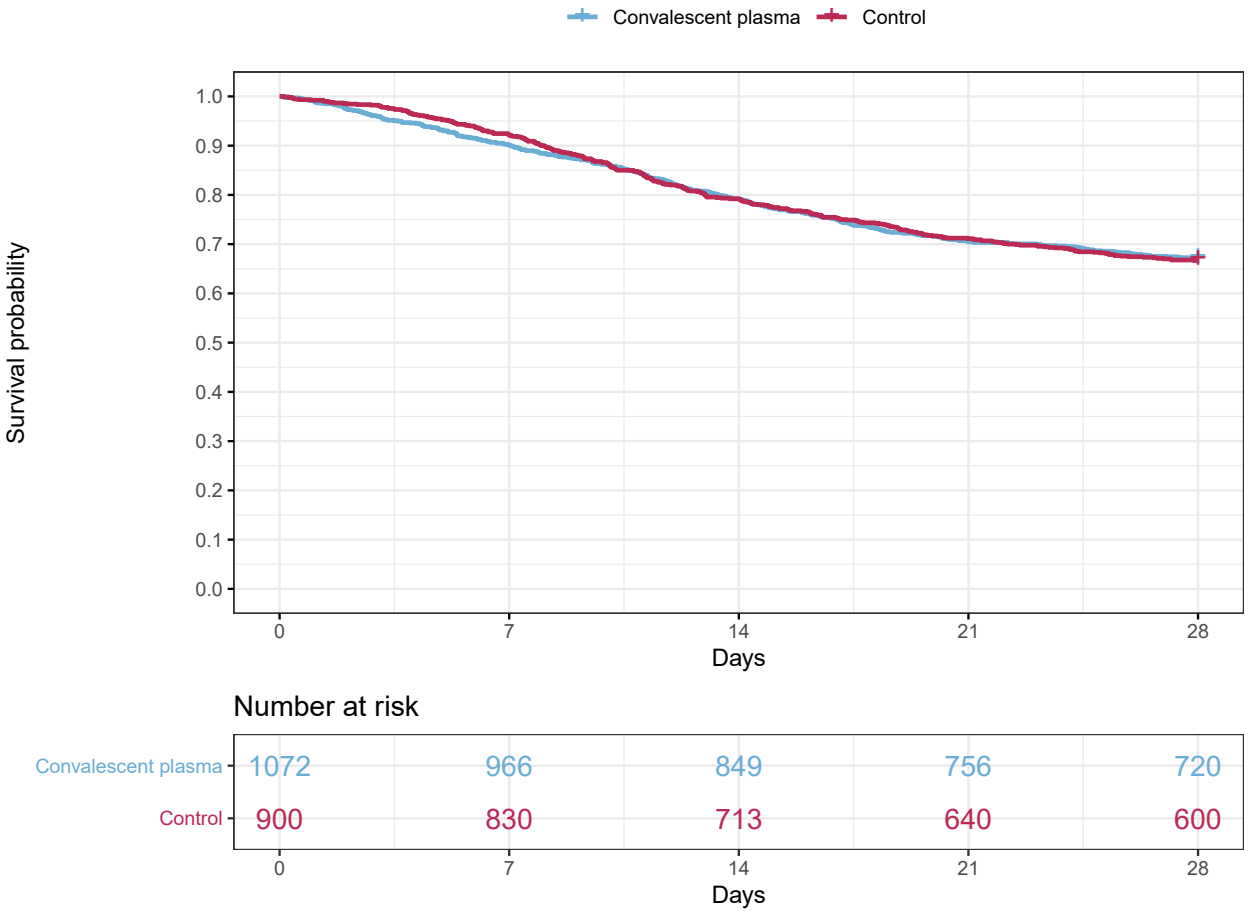


Figure 12: Empirical distribution of 28-day mortality for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 39: Summary of 2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th percentiles from the Kaplan-Meier estimates for mortality (in days). Displaying the observed percentiles for this outcome.

| | 2.5 | 10.0 | 25.0 | 50.0 | 75.0 | 90.0 | 97.5 |
|---|---|---|---|---|---|---|---|
| Convalescent plasma | 2 | 7 | 17 | - | - | - | - |
| Control | 3.5 | 8 | 17.2 | - | - | - | - |

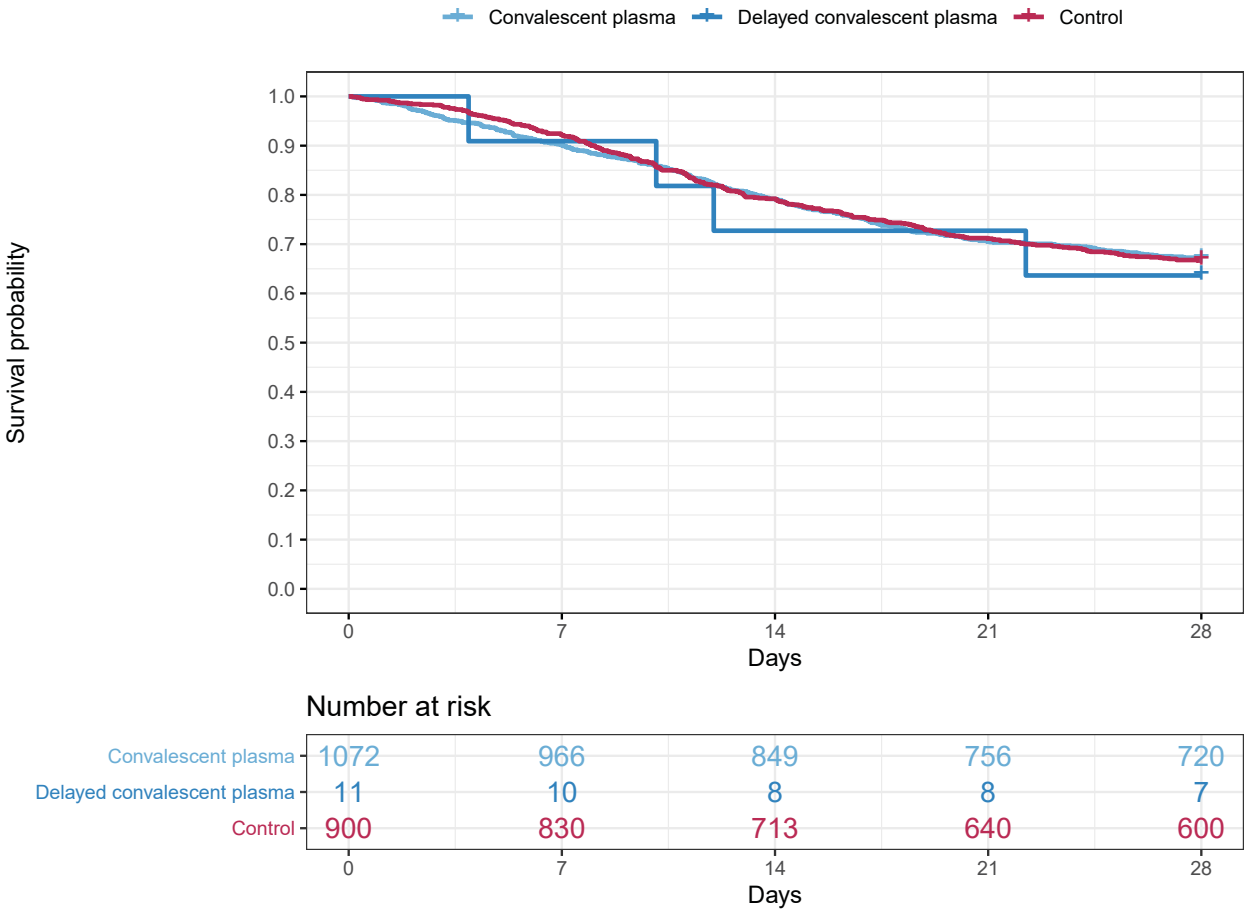


Figure 13: Empirical distribution of 28-day mortality for convalescent plasma and control. This plot is restricted to the Unblinded ITT population.

Table 40: Summary of 2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th percentiles from the Kaplan-Meier estimates for mortality (in days). Displaying the observed percentiles for this outcome.

| | 2.5 | 10.0 | 25.0 | 50.0 | 75.0 | 90.0 | 97.5 |
|---|---|---|---|---|---|---|---|
| Convalescent plasma | 2 | 7 | 17 | - | - | - | - |
| Delayed convalescent plasma | 3.9 | 10.1 | 12 | - | - | - | - |
| Control | 3.5 | 8 | 17.2 | - | - | - | - |

Table 41: Hazard ratio parameters for secondary analysis of 28-day survival

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.57 | 0.98 | 4.43 | (3.01, 6.80) |
| Age 40-49 | 2.44 | 0.31 | 2.41 | (1.89, 3.12) |
| Age 50-59 | 2.04 | 0.20 | 2.03 | (1.68, 2.46) |
| Age 70-79 | 0.54 | 0.04 | 0.53 | (0.46, 0.62) |
| Age 80+ | 0.31 | 0.04 | 0.31 | (0.25, 0.40) |
| Female | 1.11 | 0.08 | 1.10 | (0.97, 1.27) |
| Time epoch 1 | 1.14 | 0.07 | 1.14 | (1.02, 1.28) |
| Time epoch 2 | 1.31 | 0.11 | 1.30 | (1.11, 1.54) |
| Time epoch 3 | 1.42 | 0.13 | 1.41 | (1.18, 1.69) |
| Time epoch 4 | 1.49 | 0.14 | 1.48 | (1.23, 1.79) |
| Time epoch 5 | 1.55 | 0.16 | 1.54 | (1.26, 1.90) |
| Time epoch 6 | 1.62 | 0.19 | 1.60 | (1.28, 2.02) |
| Time epoch 7 | 1.67 | 0.23 | 1.65 | (1.27, 2.17) |
| Time epoch 8 | 1.72 | 0.28 | 1.69 | (1.26, 2.35) |
| Time epoch 9 | 1.72 | 0.30 | 1.68 | (1.23, 2.41) |
| Time epoch 10 | 1.65 | 0.30 | 1.62 | (1.15, 2.33) |
| Time epoch 11 | 1.56 | 0.28 | 1.53 | (1.07, 2.19) |
| Time epoch 12 | 1.50 | 0.26 | 1.48 | (1.04, 2.09) |
| Time epoch 13 | 1.50 | 0.26 | 1.48 | (1.07, 2.07) |
| Time epoch 14 | 1.53 | 0.28 | 1.50 | (1.08, 2.17) |
| Time epoch 15 | 1.50 | 0.28 | 1.46 | (1.04, 2.14) |
| Time epoch 16 | 1.40 | 0.25 | 1.38 | (0.98, 1.94) |
| Time epoch 17 | 1.35 | 0.24 | 1.33 | (0.94, 1.87) |
| Time epoch 18 | 1.42 | 0.27 | 1.39 | (0.97, 2.00) |
| Time epoch 19 | 1.61 | 0.41 | 1.55 | (0.99, 2.58) |
| Time epoch 20 | 1.94 | 0.89 | 1.74 | (0.94, 4.11) |
| Lopinavir–ritonavir | 0.92 | 0.12 | 0.91 | (0.71, 1.19) |
| Hydroxychloroquine | 0.75 | 0.16 | 0.75 | (0.46, 1.07) |
| Pooled IL-6ra | 1.41 | 0.12 | 1.40 | (1.18, 1.67) |
| Fixed-dose corticosteroids | 0.79 | 0.15 | 0.78 | (0.54, 1.11) |
| Shock-dependent corticosteroids | 0.98 | 0.23 | 0.95 | (0.61, 1.49) |
| Therapeutic anticoagulation | 0.99 | 0.09 | 0.99 | (0.82, 1.19) |
| Convalescent plasma | 1.05 | 0.08 | 1.05 | (0.91, 1.20) |
| Delayed convalescent plasma | 1.55 | 0.87 | 1.35 | (0.55, 3.74) |

Table 42: Posterior probabilities for secondary analysis of 28-day survival

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.740 |
| Convalescent plasma is futile (OR < 1.2) | 0.971 |
| Convalescent plasma is harmful (OR < 1) | 0.260 |

## 6.3 Secondary analysis of progression to intubation, ECMO, or death

- Model: Primary dichotomous model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT not on ventilation or ECMO at baseline. There are 1307 patients that meet this criterion.

Table 43: Summary of progression to intubation, ECMO, or death for the Unblinded ITT population restricted to patients not on mechanical ventilation or ECMO at baseline

| Intervention | # Patients (N) | # Progressors (y) | Progression Rate (y/N) |
|---|---|---|---|
| Convalescent plasma | 701 | 347 | 0.495 |
| Control | 606 | 275 | 0.454 |

Table 44: Summary of progression to intubation, ECMO, or death by component for the Unblinded ITT population restricted to patients not on mechanical ventilation or ECMO at baseline. Note that a patient may progress on more than one component of the composite endpoint, so the sum of events in this table will not match the total number of progressors.

| Intervention | # Patients (N) | Death, n (%) | Intubation, n (%) | ECMO, n (%) |
|---|---|---|---|---|
| Convalescent plasma | 701 | 240 (34.2) | 259 (36.9) | 8 (1.1) |
| Control | 606 | 199 (32.8) | 206 (34) | 6 (1) |

Table 45: Odds ratio parameters for secondary analysis of progression to intubation, ECMO, or death

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 5.19 | 1.20 | 5.05 | (3.25, 7.94) |
| Age 40-49 | 2.45 | 0.38 | 2.42 | (1.79, 3.29) |
| Age 50-59 | 1.80 | 0.23 | 1.78 | (1.38, 2.28) |
| Age 70-79 | 0.67 | 0.09 | 0.66 | (0.51, 0.86) |
| Age 80+ | 0.47 | 0.10 | 0.46 | (0.30, 0.69) |
| Female | 1.04 | 0.11 | 1.03 | (0.85, 1.26) |
| Time epoch 1 | 1.02 | 0.07 | 1.01 | (0.87, 1.17) |
| Time epoch 2 | 1.06 | 0.13 | 1.06 | (0.84, 1.33) |
| Time epoch 3 | 1.10 | 0.17 | 1.09 | (0.82, 1.47) |
| Time epoch 4 | 1.13 | 0.20 | 1.12 | (0.80, 1.57) |
| Time epoch 5 | 1.16 | 0.22 | 1.13 | (0.79, 1.63) |
| Time epoch 6 | 1.14 | 0.23 | 1.12 | (0.75, 1.65) |
| Time epoch 7 | 1.14 | 0.25 | 1.12 | (0.72, 1.71) |
| Time epoch 8 | 1.17 | 0.28 | 1.14 | (0.71, 1.79) |
| Time epoch 9 | 1.21 | 0.30 | 1.18 | (0.72, 1.88) |
| Time epoch 10 | 1.25 | 0.32 | 1.21 | (0.73, 1.98) |
| Time epoch 11 | 1.29 | 0.34 | 1.25 | (0.75, 2.07) |
| Time epoch 12 | 1.33 | 0.35 | 1.30 | (0.78, 2.14) |
| Time epoch 13 | 1.38 | 0.36 | 1.34 | (0.81, 2.22) |
| Time epoch 14 | 1.43 | 0.39 | 1.38 | (0.82, 2.35) |
| Time epoch 15 | 1.45 | 0.42 | 1.40 | (0.80, 2.43) |
| Time epoch 16 | 1.48 | 0.45 | 1.42 | (0.79, 2.54) |
| Time epoch 17 | 1.51 | 0.51 | 1.43 | (0.75, 2.74) |
| Time epoch 18 | 1.59 | 0.62 | 1.49 | (0.71, 3.16) |
| Time epoch 19 | 1.74 | 0.84 | 1.57 | (0.64, 3.84) |
| Lopinavir−ritonavir | 0.75 | 0.16 | 0.73 | (0.49, 1.11) |
| Hydroxychloroquine | 0.49 | 0.19 | 0.48 | (0.17, 0.89) |
| Pooled IL-6ra | 1.63 | 0.29 | 1.61 | (1.15, 2.27) |
| Fixed-dose corticosteroids | 2.87 | 1.15 | 2.66 | (1.27, 5.65) |
| Shock-dependent corticosteroids | 0.90 | 0.43 | 0.81 | (0.32, 1.97) |
| Therapeutic anticoagulation | 0.89 | 0.15 | 0.88 | (0.64, 1.21) |
| Convalescent plasma | 0.83 | 0.10 | 0.82 | (0.65, 1.03) |
| Delayed convalescent plasma | 0.38 | 0.32 | 0.28 | (0.06, 1.25) |

Table 46: Posterior probabilities for secondary analysis of progression to intubation, ECMO, or death

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.047 |
| Convalescent plasma is futile (OR < 1.2) | 0.999 |
| Convalescent plasma is harmful (OR < 1) | 0.953 |

## 6.4 Secondary analysis of cardiovascular support-free days

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

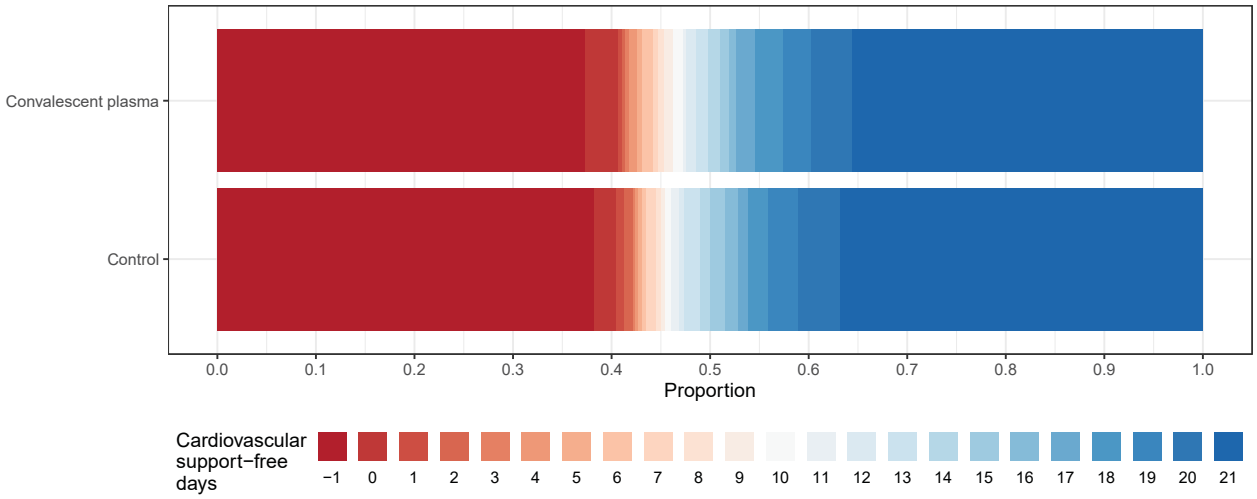


Figure 14: Empirical distribution of days-free of vasopressors and inotropes for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 47: Summary of cardiovascular support-free days for the Convalescent Plasma ITT population

| Intervention | # Patients | # Known | CV support-free days median (IQR) | Days Free of CV support in Survivors* median (IQR) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1074 | 14 (-1, 21) | 21 (17, 21) |
| Control | 905 | 902 | 14.5 (-1, 21) | 21 (17, 21) |

* Days free of cardiovascular support in survivors within 21 days

Table 48: Odds ratio parameters for secondary analysis of cardiovascular support-free days

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.50 | 0.65 | 4.45 | (3.37, 5.92) |
| Age 40-49 | 2.74 | 0.30 | 2.72 | (2.19, 3.38) |
| Age 50-59 | 2.03 | 0.18 | 2.02 | (1.70, 2.41) |
| Age 70-79 | 0.51 | 0.05 | 0.50 | (0.42, 0.61) |
| Age 80+ | 0.30 | 0.06 | 0.29 | (0.20, 0.42) |
| Female | 1.07 | 0.08 | 1.07 | (0.93, 1.22) |
| Time epoch 1 | 1.04 | 0.07 | 1.03 | (0.92, 1.18) |
| Time epoch 2 | 1.07 | 0.10 | 1.06 | (0.89, 1.29) |
| Time epoch 3 | 1.08 | 0.13 | 1.08 | (0.86, 1.35) |
| Time epoch 4 | 1.12 | 0.15 | 1.11 | (0.86, 1.43) |
| Time epoch 5 | 1.17 | 0.17 | 1.16 | (0.88, 1.53) |
| Time epoch 6 | 1.21 | 0.19 | 1.20 | (0.89, 1.63) |
| Time epoch 7 | 1.28 | 0.22 | 1.26 | (0.90, 1.75) |
| Time epoch 8 | 1.36 | 0.25 | 1.33 | (0.94, 1.90) |
| Time epoch 9 | 1.41 | 0.28 | 1.38 | (0.96, 2.05) |
| Time epoch 10 | 1.43 | 0.28 | 1.40 | (0.97, 2.08) |
| Time epoch 11 | 1.43 | 0.28 | 1.39 | (0.97, 2.06) |
| Time epoch 12 | 1.41 | 0.27 | 1.38 | (0.97, 2.01) |
| Time epoch 13 | 1.40 | 0.26 | 1.38 | (0.97, 1.98) |
| Time epoch 14 | 1.39 | 0.26 | 1.36 | (0.95, 1.97) |
| Time epoch 15 | 1.35 | 0.26 | 1.32 | (0.92, 1.92) |
| Time epoch 16 | 1.32 | 0.26 | 1.29 | (0.88, 1.90) |
| Time epoch 17 | 1.30 | 0.26 | 1.27 | (0.86, 1.88) |
| Time epoch 18 | 1.33 | 0.28 | 1.30 | (0.86, 1.96) |
| Time epoch 19 | 1.42 | 0.35 | 1.37 | (0.86, 2.21) |
| Time epoch 20 | 1.56 | 0.51 | 1.47 | (0.81, 2.78) |
| Lopinavir–ritonavir | 0.73 | 0.11 | 0.73 | (0.55, 0.97) |
| Hydroxychloroquine | 0.64 | 0.13 | 0.64 | (0.41, 0.92) |
| Pooled IL-6ra | 1.49 | 0.20 | 1.47 | (1.14, 1.91) |
| Fixed-dose corticosteroids | 1.45 | 0.32 | 1.41 | (0.92, 2.18) |
| Shock-dependent corticosteroids | 1.11 | 0.32 | 1.07 | (0.61, 1.85) |
| Therapeutic anticoagulation | 0.91 | 0.11 | 0.91 | (0.71, 1.15) |
| Convalescent plasma | 0.96 | 0.08 | 0.95 | (0.80, 1.13) |
| Delayed convalescent plasma | 0.91 | 0.55 | 0.78 | (0.25, 2.34) |

Table 49: Posterior probabilities for secondary analysis of cardiovascular support-free days

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.294 |
| Convalescent plasma is futile (OR < 1.2) | 0.996 |
| Convalescent plasma is harmful (OR < 1) | 0.706 |

## 6.5 Secondary analysis of respiratory support-free days

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

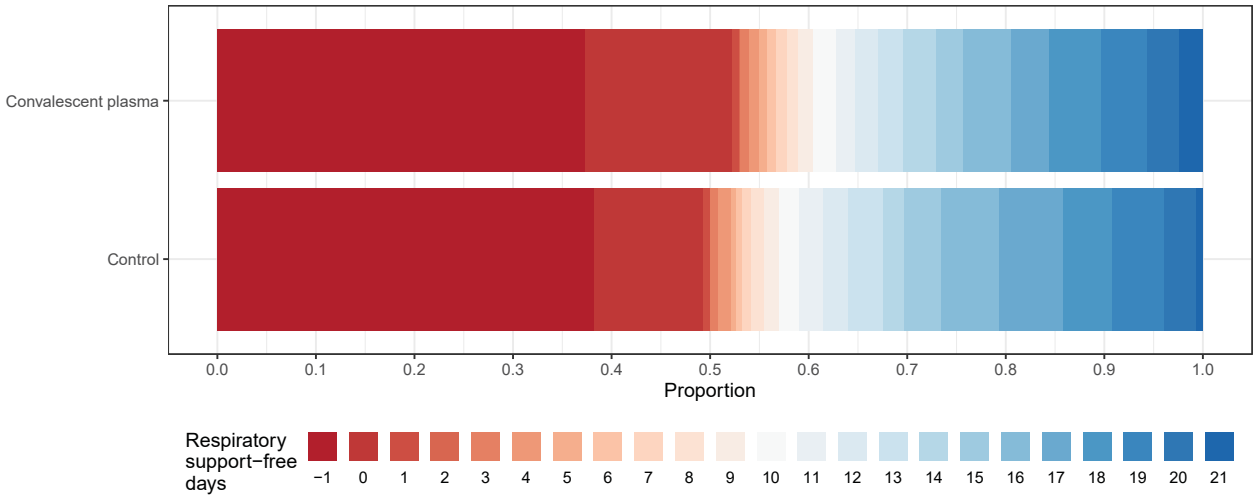


Figure 15: Empirical distribution of respiratory support-free days for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 50: Summary of respiratory support-free days for the Convalescent Plasma ITT population

| Intervention | # Patients | # Known | Resp. support-free days median (IQR) | Days free of resp. support in survivors* median (IQR) |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1074 | 0 (-1, 15) | 13 (2, 17) |
| Control | 905 | 902 | 2 (-1, 16) | 14 (7, 17) |

* Days free of respiratory support in survivors within 21 days

Table 51: Odds ratio parameters for secondary analysis of respiratory support-free days

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.36 | 0.56 | 4.31 | (3.37, 5.58) |
| Age 40-49 | 2.56 | 0.27 | 2.54 | (2.08, 3.12) |
| Age 50-59 | 1.84 | 0.16 | 1.84 | (1.55, 2.17) |
| Age 70-79 | 0.51 | 0.05 | 0.51 | (0.42, 0.62) |
| Age 80+ | 0.32 | 0.06 | 0.32 | (0.22, 0.45) |
| Female | 1.09 | 0.07 | 1.09 | (0.95, 1.25) |
| Time epoch 1 | 1.07 | 0.08 | 1.07 | (0.93, 1.23) |
| Time epoch 2 | 1.18 | 0.13 | 1.17 | (0.96, 1.47) |
| Time epoch 3 | 1.18 | 0.14 | 1.18 | (0.93, 1.49) |
| Time epoch 4 | 1.16 | 0.15 | 1.15 | (0.88, 1.47) |
| Time epoch 5 | 1.17 | 0.17 | 1.16 | (0.87, 1.52) |
| Time epoch 6 | 1.19 | 0.19 | 1.18 | (0.85, 1.58) |
| Time epoch 7 | 1.28 | 0.22 | 1.27 | (0.90, 1.75) |
| Time epoch 8 | 1.44 | 0.27 | 1.42 | (0.99, 2.06) |
| Time epoch 9 | 1.58 | 0.32 | 1.54 | (1.06, 2.31) |
| Time epoch 10 | 1.63 | 0.33 | 1.59 | (1.08, 2.37) |
| Time epoch 11 | 1.66 | 0.33 | 1.62 | (1.11, 2.40) |
| Time epoch 12 | 1.67 | 0.33 | 1.64 | (1.13, 2.40) |
| Time epoch 13 | 1.66 | 0.32 | 1.63 | (1.12, 2.37) |
| Time epoch 14 | 1.59 | 0.31 | 1.56 | (1.07, 2.29) |
| Time epoch 15 | 1.45 | 0.29 | 1.42 | (0.94, 2.07) |
| Time epoch 16 | 1.37 | 0.29 | 1.35 | (0.87, 2.00) |
| Time epoch 17 | 1.38 | 0.30 | 1.36 | (0.87, 2.04) |
| Time epoch 18 | 1.52 | 0.32 | 1.49 | (0.98, 2.25) |
| Time epoch 19 | 1.82 | 0.46 | 1.77 | (1.09, 2.87) |
| Time epoch 20 | 2.33 | 0.95 | 2.13 | (1.11, 4.68) |
| Lopinavir–ritonavir | 0.82 | 0.12 | 0.81 | (0.62, 1.08) |
| Hydroxychloroquine | 0.67 | 0.14 | 0.67 | (0.41, 0.96) |
| Pooled IL-6ra | 1.56 | 0.20 | 1.54 | (1.21, 1.97) |
| Fixed-dose corticosteroids | 1.47 | 0.32 | 1.43 | (0.93, 2.18) |
| Shock-dependent corticosteroids | 1.11 | 0.31 | 1.06 | (0.62, 1.82) |
| Therapeutic anticoagulation | 0.83 | 0.10 | 0.82 | (0.65, 1.03) |
| Convalescent plasma | 0.95 | 0.08 | 0.95 | (0.81, 1.11) |
| Delayed convalescent plasma | 0.60 | 0.35 | 0.52 | (0.18, 1.54) |

Table 52: Posterior probabilities for secondary analysis of respiratory support-free days

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.257 |
| Convalescent plasma is futile (OR < 1.2) | 0.998 |
| Convalescent plasma is harmful (OR < 1) | 0.743 |

## 6.6 Secondary analysis of length of ICU stay

- Model: Primary TTE model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

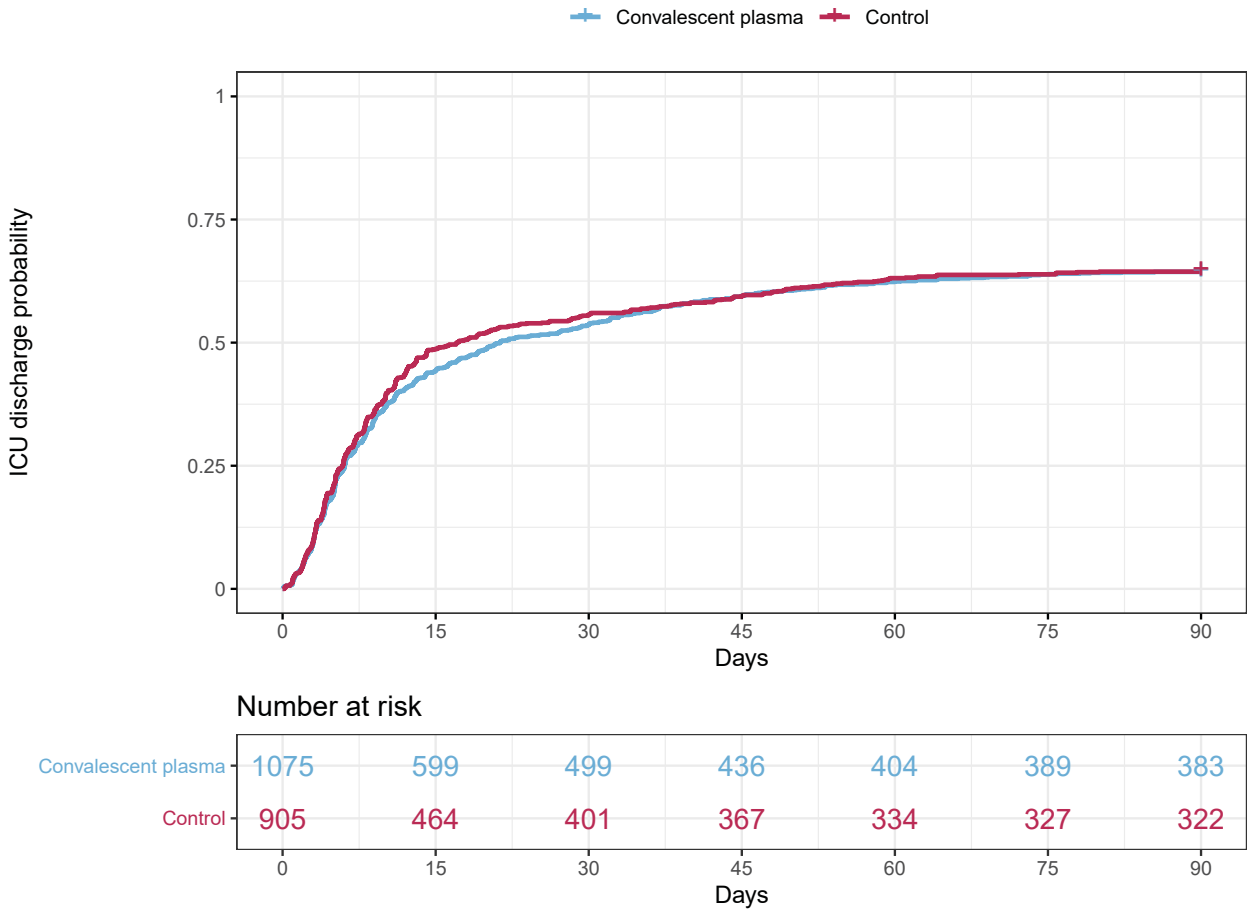


Figure 16: Empirical distribution of length of ICU stay for lopinavir–ritonavir, hydroxychloroquine, combination therapy, and control. This plot is restricted to the Antiviral ITT population.

Table 53: Summary of 2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th percentiles from the Kaplan-Meier estimates for length of ICU stay (in days). Displaying the observed percentiles for this outcome.

| | 2.5 | 10.0 | 25.0 | 50.0 | 75.0 | 90.0 | 97.5 |
|---|---|---|---|---|---|---|---|
| Convalescent plasma | 1.17 | 3.05 | 6.07 | 21.28 | - | - | - |
| Control | 1.1 | 3.07 | 5.9 | 17.09 | - | - | - |

Table 54: Hazard ratio parameters for secondary analysis of length of ICU stay

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 2.73 | 0.23 | 2.71 | (2.31, 3.20) |
| Age 40-49 | 1.82 | 0.12 | 1.82 | (1.59, 2.07) |
| Age 50-59 | 1.59 | 0.09 | 1.59 | (1.42, 1.77) |
| Age 70-79 | 0.67 | 0.05 | 0.67 | (0.58, 0.76) |
| Age 80+ | 0.59 | 0.07 | 0.58 | (0.45, 0.74) |
| Female | 1.08 | 0.05 | 1.07 | (0.98, 1.18) |
| Time epoch 1 | 1.10 | 0.05 | 1.10 | (1.00, 1.22) |
| Time epoch 2 | 1.24 | 0.09 | 1.23 | (1.08, 1.43) |
| Time epoch 3 | 1.24 | 0.08 | 1.23 | (1.08, 1.41) |
| Time epoch 4 | 1.23 | 0.09 | 1.23 | (1.07, 1.41) |
| Time epoch 5 | 1.24 | 0.09 | 1.23 | (1.06, 1.43) |
| Time epoch 6 | 1.24 | 0.11 | 1.23 | (1.04, 1.45) |
| Time epoch 7 | 1.30 | 0.13 | 1.29 | (1.06, 1.58) |
| Time epoch 8 | 1.42 | 0.18 | 1.41 | (1.12, 1.82) |
| Time epoch 9 | 1.48 | 0.20 | 1.46 | (1.14, 1.94) |
| Time epoch 10 | 1.45 | 0.19 | 1.43 | (1.12, 1.86) |
| Time epoch 11 | 1.41 | 0.18 | 1.40 | (1.09, 1.79) |
| Time epoch 12 | 1.37 | 0.17 | 1.36 | (1.06, 1.74) |
| Time epoch 13 | 1.35 | 0.16 | 1.34 | (1.05, 1.70) |
| Time epoch 14 | 1.32 | 0.17 | 1.30 | (1.02, 1.69) |
| Time epoch 15 | 1.23 | 0.15 | 1.22 | (0.96, 1.56) |
| Time epoch 16 | 1.17 | 0.15 | 1.16 | (0.89, 1.48) |
| Time epoch 17 | 1.15 | 0.15 | 1.14 | (0.87, 1.46) |
| Time epoch 18 | 1.22 | 0.16 | 1.22 | (0.94, 1.56) |
| Time epoch 19 | 1.39 | 0.23 | 1.37 | (1.00, 1.90) |
| Time epoch 20 | 1.68 | 0.47 | 1.60 | (0.99, 2.80) |
| Lopinavir–ritonavir | 0.89 | 0.08 | 0.88 | (0.74, 1.06) |
| Hydroxychloroquine | 0.74 | 0.11 | 0.74 | (0.52, 0.96) |
| Pooled IL-6ra | 1.30 | 0.09 | 1.29 | (1.13, 1.48) |
| Fixed-dose corticosteroids | 0.97 | 0.12 | 0.96 | (0.76, 1.22) |
| Shock-dependent corticosteroids | 0.92 | 0.15 | 0.91 | (0.65, 1.25) |
| Therapeutic anticoagulation | 1.01 | 0.07 | 1.00 | (0.88, 1.14) |
| Convalescent plasma | 0.94 | 0.05 | 0.94 | (0.85, 1.04) |
| Delayed convalescent plasma | 0.87 | 0.34 | 0.82 | (0.36, 1.68) |

Table 55: Posterior probabilities for secondary analysis of length of ICU stay

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.101 |
| Convalescent plasma is futile (OR < 1.2) | 1.000 |
| Convalescent plasma is harmful (OR < 1) | 0.899 |

## 6.7 Secondary analysis of length of hospital stay

- Model: Primary TTE model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir–ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT

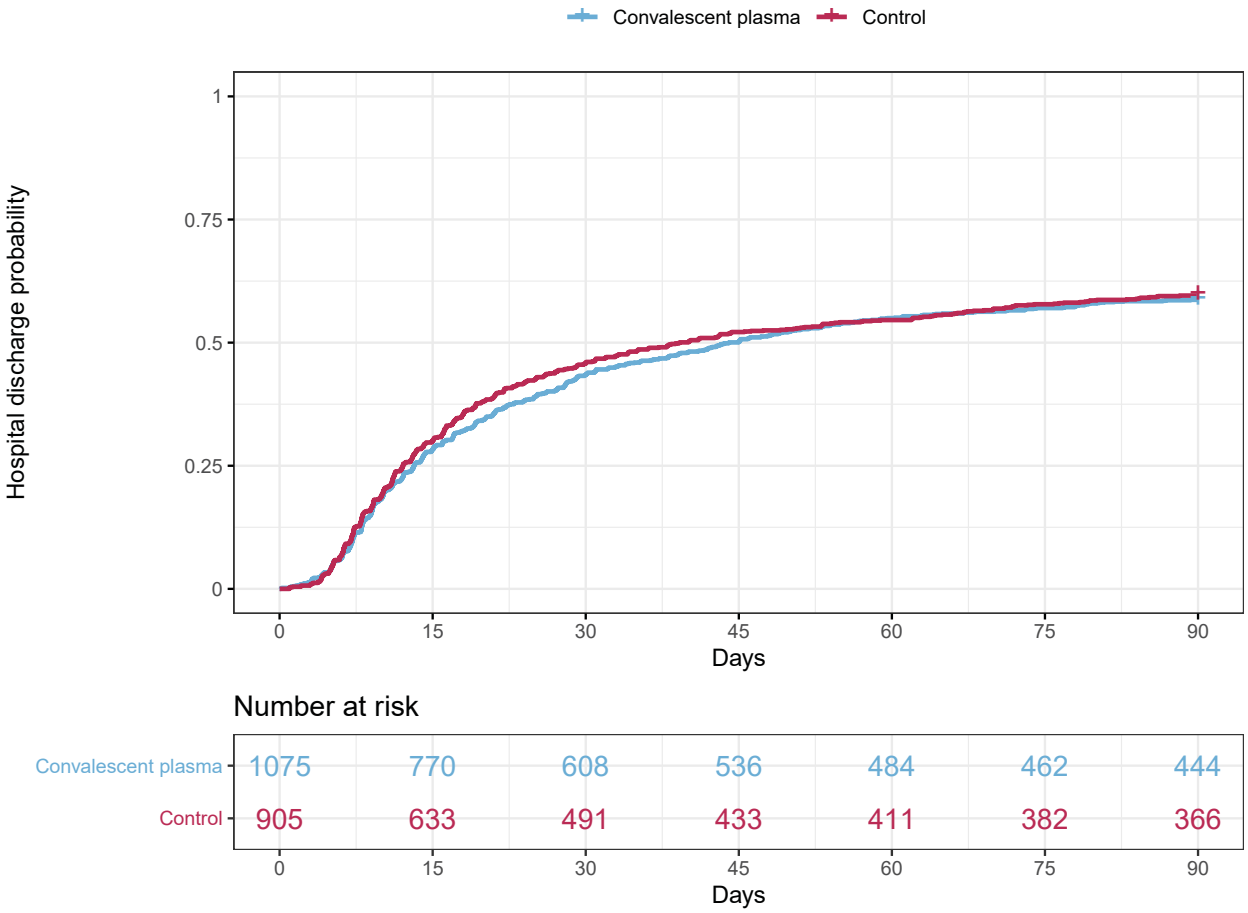


Figure 17: Empirical distribution of length of hospital stay for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 56: Summary of 2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th percentiles from the Kaplan-Meier estimates for length of hospital stay (in days). Displaying the observed percentiles for this outcome.

| | 2.5 | 10.0 | 25.0 | 50.0 | 75.0 | 90.0 | 97.5 |
|---|---|---|---|---|---|---|---|
| Convalescent plasma | 4.03 | 7.17 | 13.17 | 44.07 | - | - | - |
| Control | 4.18 | 7 | 12.09 | 39.25 | - | - | - |

Table 57: Hazard ratio parameters for secondary analysis of length of hospital stay

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 3.19 | 0.27 | 3.18 | (2.68, 3.74) |
| Age 40-49 | 2.02 | 0.14 | 2.01 | (1.74, 2.30) |
| Age 50-59 | 1.73 | 0.10 | 1.73 | (1.54, 1.94) |
| Age 70-79 | 0.61 | 0.04 | 0.61 | (0.53, 0.71) |
| Age 80+ | 0.41 | 0.06 | 0.41 | (0.30, 0.54) |
| Female | 1.10 | 0.05 | 1.10 | (1.00, 1.20) |
| Time epoch 1 | 1.13 | 0.06 | 1.13 | (1.03, 1.25) |
| Time epoch 2 | 1.27 | 0.09 | 1.26 | (1.11, 1.46) |
| Time epoch 3 | 1.31 | 0.09 | 1.30 | (1.14, 1.50) |
| Time epoch 4 | 1.31 | 0.10 | 1.30 | (1.13, 1.50) |
| Time epoch 5 | 1.31 | 0.10 | 1.31 | (1.12, 1.52) |
| Time epoch 6 | 1.31 | 0.12 | 1.31 | (1.10, 1.55) |
| Time epoch 7 | 1.36 | 0.14 | 1.35 | (1.11, 1.65) |
| Time epoch 8 | 1.45 | 0.17 | 1.44 | (1.15, 1.82) |
| Time epoch 9 | 1.52 | 0.19 | 1.50 | (1.18, 1.93) |
| Time epoch 10 | 1.55 | 0.20 | 1.54 | (1.20, 1.99) |
| Time epoch 11 | 1.58 | 0.20 | 1.56 | (1.23, 2.02) |
| Time epoch 12 | 1.60 | 0.20 | 1.58 | (1.25, 2.03) |
| Time epoch 13 | 1.59 | 0.19 | 1.57 | (1.25, 2.01) |
| Time epoch 14 | 1.55 | 0.19 | 1.54 | (1.22, 1.98) |
| Time epoch 15 | 1.46 | 0.18 | 1.45 | (1.14, 1.85) |
| Time epoch 16 | 1.38 | 0.17 | 1.37 | (1.06, 1.74) |
| Time epoch 17 | 1.32 | 0.17 | 1.31 | (1.01, 1.67) |
| Time epoch 18 | 1.32 | 0.18 | 1.31 | (1.00, 1.69) |
| Time epoch 19 | 1.40 | 0.23 | 1.38 | (1.00, 1.90) |
| Time epoch 20 | 1.54 | 0.40 | 1.49 | (0.93, 2.46) |
| Lopinavir–ritonavir | 0.88 | 0.08 | 0.87 | (0.73, 1.05) |
| Hydroxychloroquine | 0.79 | 0.11 | 0.79 | (0.58, 1.01) |
| Pooled IL-6ra | 1.33 | 0.09 | 1.32 | (1.15, 1.52) |
| Fixed-dose corticosteroids | 0.97 | 0.12 | 0.96 | (0.74, 1.22) |
| Shock-dependent corticosteroids | 0.69 | 0.12 | 0.68 | (0.47, 0.94) |
| Therapeutic anticoagulation | 1.00 | 0.07 | 1.00 | (0.87, 1.14) |
| Convalescent plasma | 0.96 | 0.05 | 0.95 | (0.86, 1.06) |
| Delayed convalescent plasma | 0.67 | 0.29 | 0.62 | (0.25, 1.37) |

Table 58: Posterior probabilities for secondary analysis of length of hospital stay

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.185 |
| Convalescent plasma is futile (OR < 1.2) | 1.000 |
| Convalescent plasma is harmful (OR < 1) | 0.815 |

## 6.8 Secondary analysis of WHO scale at 14 days

- Model: Primary analysis ordinal model
- Factors: All interventions and specified interactions, age, sex, site, time, Immunoglobulin Domain interventions: control, convalescent plasma, delayed convalescent plasma, Covid-19 Antiviral Therapy Domain interventions: control, lopinavir−ritonavir, hydroxychloroquine, combination therapy,Corticosteroid Domain interventions: no steroids, fixed-duration corticosteroids, and shock-dependent steroids, reported interventions of the Immune Modulation Therapy Domain: tocilizumab, sarilumab (combined to a single IL-6 arm) and no immune modulation, and interventions of the Anticoagulation Domain: prophylaxis dose anticoagulation, therapeutic anticoagulation.
- Population: Unblinded ITT
- There are 70 missing values of WHO scale at day 14 due to missing daily data. These patients are removed from this analysis.

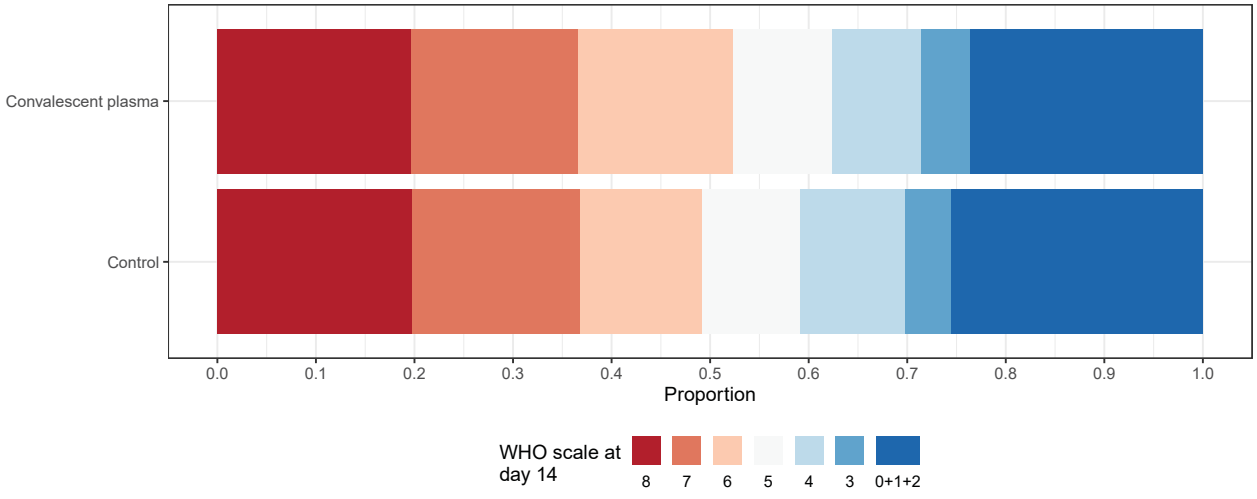


Figure 18: Empirical distribution of modified WHO scale at day 14 for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

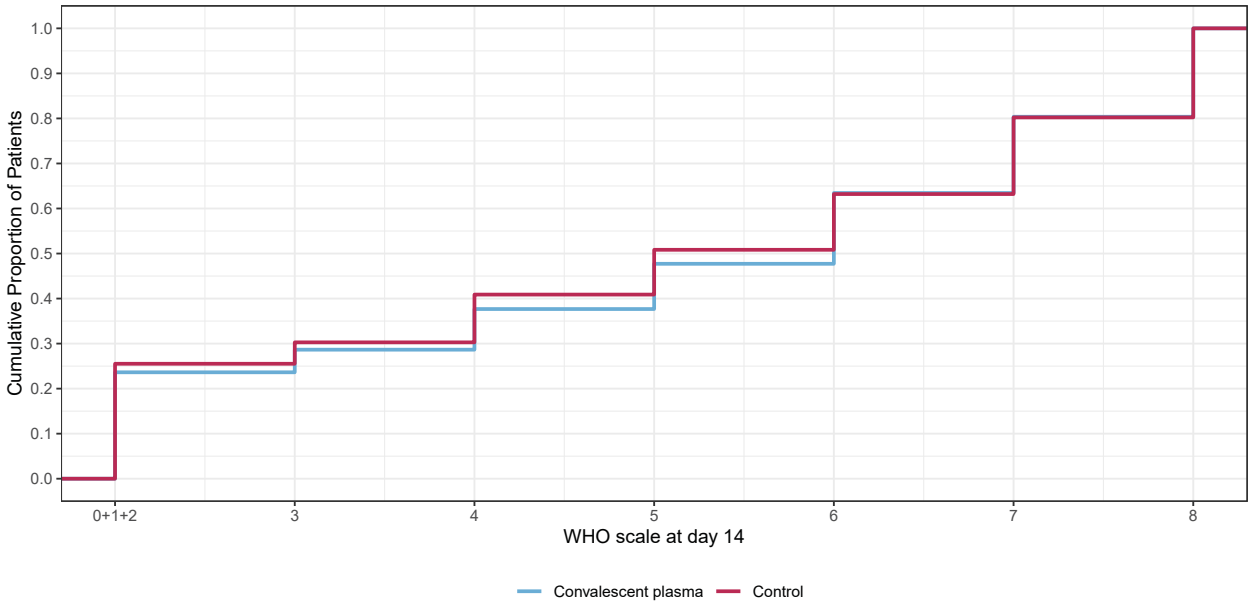


Figure 19: Empirical cumulative distribution of WHO scale for convalescent plasma and control. This plot is restricted to the Convalescent Plasma ITT population.

Table 59: Odds ratio parameters for secondary analysis of WHO scale at day 14

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.44 | 0.62 | 4.39 | (3.36, 5.83) |
| Age 40-49 | 2.44 | 0.26 | 2.42 | (1.97, 3.00) |
| Age 50-59 | 1.77 | 0.15 | 1.76 | (1.50, 2.08) |
| Age 70-79 | 0.55 | 0.05 | 0.55 | (0.46, 0.65) |
| Age 80+ | 0.28 | 0.05 | 0.28 | (0.20, 0.38) |
| Female | 1.00 | 0.07 | 1.00 | (0.87, 1.14) |
| Time epoch 1 | 1.07 | 0.07 | 1.06 | (0.93, 1.21) |
| Time epoch 2 | 1.18 | 0.12 | 1.17 | (0.97, 1.43) |
| Time epoch 3 | 1.25 | 0.14 | 1.24 | (0.99, 1.55) |
| Time epoch 4 | 1.31 | 0.17 | 1.30 | (1.00, 1.67) |
| Time epoch 5 | 1.41 | 0.20 | 1.40 | (1.06, 1.84) |
| Time epoch 6 | 1.52 | 0.23 | 1.51 | (1.12, 2.02) |
| Time epoch 7 | 1.64 | 0.27 | 1.62 | (1.18, 2.22) |
| Time epoch 8 | 1.77 | 0.32 | 1.74 | (1.23, 2.47) |
| Time epoch 9 | 1.81 | 0.35 | 1.78 | (1.24, 2.59) |
| Time epoch 10 | 1.76 | 0.34 | 1.73 | (1.20, 2.51) |
| Time epoch 11 | 1.68 | 0.32 | 1.65 | (1.14, 2.39) |
| Time epoch 12 | 1.58 | 0.29 | 1.56 | (1.09, 2.24) |
| Time epoch 13 | 1.48 | 0.27 | 1.46 | (1.02, 2.09) |
| Time epoch 14 | 1.38 | 0.26 | 1.36 | (0.94, 1.95) |
| Time epoch 15 | 1.29 | 0.26 | 1.27 | (0.85, 1.85) |
| Time epoch 16 | 1.24 | 0.25 | 1.22 | (0.81, 1.80) |
| Time epoch 17 | 1.26 | 0.25 | 1.24 | (0.82, 1.82) |
| Time epoch 18 | 1.34 | 0.28 | 1.31 | (0.88, 1.94) |
| Time epoch 19 | 1.52 | 0.37 | 1.47 | (0.93, 2.34) |
| Time epoch 20 | 1.82 | 0.68 | 1.69 | (0.91, 3.49) |
| Lopinavir–ritonavir | 0.89 | 0.12 | 0.88 | (0.68, 1.16) |
| Hydroxychloroquine | 0.81 | 0.15 | 0.81 | (0.53, 1.14) |
| Pooled IL-6ra | 1.55 | 0.19 | 1.53 | (1.20, 1.96) |
| Fixed-dose corticosteroids | 1.32 | 0.28 | 1.29 | (0.85, 1.94) |
| Shock-dependent corticosteroids | 0.65 | 0.17 | 0.62 | (0.38, 1.05) |
| Therapeutic anticoagulation | 0.79 | 0.09 | 0.79 | (0.62, 0.98) |
| Convalescent plasma | 0.92 | 0.08 | 0.92 | (0.79, 1.08) |
| Delayed convalescent plasma | 0.56 | 0.29 | 0.49 | (0.18, 1.29) |

Table 60: Posterior probabilities for secondary analysis of WHO scale at day 14

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control | 0.155 |
| Convalescent plasma is futile (OR < 1.2) | 1.000 |
| Convalescent plasma is harmful (OR < 1) | 0.845 |

# 7 Subgroup analyses

## 7.1 Subgroup analyses by baseline invasive mechanical ventilation status

### 7.1.1 Data summaries of baseline invasive mechanical ventilation status in the Convalescent Plasma ITT population

Table 61: Summary of baseline invasive mechanical ventilation by intervention

| Intervention | Patients | No IMV at baseline | IMV at baseline |
|---|---|---|---|
| Convalescent plasma | 1075 | 719 (66.9%) | 356 (33.1%) |
| Control | 905 | 617 (68.2%) | 288 (31.8%) |

Table 62: Summary of subjects by baseline invasive mechanical ventilation status in the Convalescent Plasma ITT population

| Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **No invasive mechanical ventilation at baseline** | | | | | |
| Convalescent plasma | 719 | 717 | 243 (33.9%) | 9 (-1, 17) | 16 (9, 18) |
| Control | 617 | 615 | 203 (33%) | 12 (-1, 17) | 16 (12, 18) |
| **Invasive mechanical ventilation at baseline** | | | | | |
| Convalescent plasma | 356 | 355 | 158 (44.5%) | 0 (-1, 8) | 6 (0, 14) |
| Control | 288 | 285 | 142 (49.8%) | 0 (-1, 7) | 7 (0, 13) |

* Days Free of Organ Support in Survivors measured within 21 days.

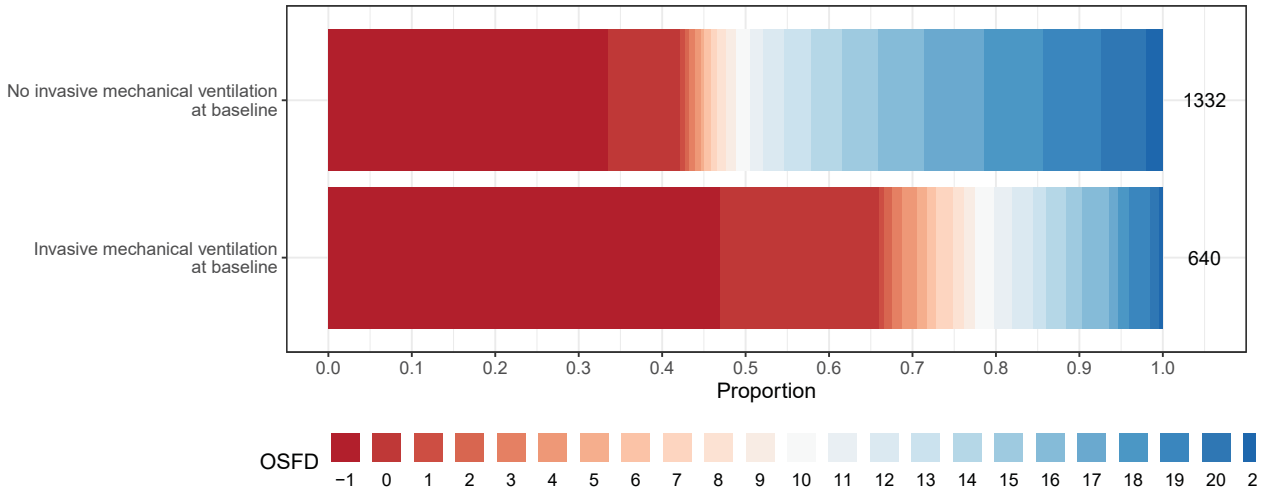


Figure 20: Empirical distribution of organ support free days (OSFD) by baseline invasive mechanical ventilation status. This plot is restricted to the Convalescent Plasma ITT population.

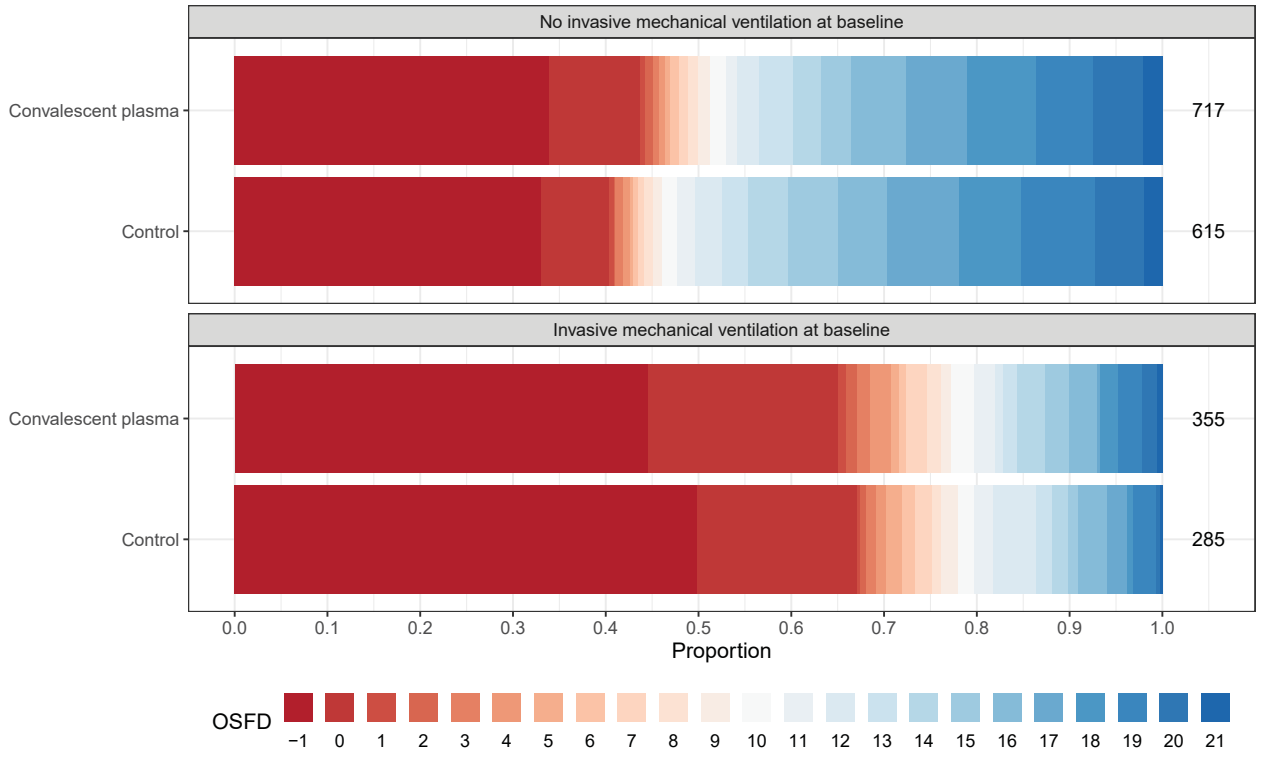


Figure 21: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control by baseline invasive mechanical ventilation status. This plot is restricted to the Convalescent Plasma ITT population.

### 7.1.2 Subgroup analysis with differential effect on OSFD by baseline invasive mechanical ventilation status

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline invasive mechanical ventilation status
- Differential treatment effects for convalescent plasma by baseline invasive mechanical ventilation status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 63: Odds ratio parameters for subgroup analysis with differential effect on OSFD by baseline invasive mechanical ventilation status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.67 | 0.78 | 4.61 | (3.31, 6.35) |
| Age 40-49 | 2.39 | 0.32 | 2.37 | (1.83, 3.08) |
| Age 50-59 | 1.92 | 0.21 | 1.91 | (1.53, 2.38) |
| Age 70-79 | 0.52 | 0.07 | 0.51 | (0.40, 0.66) |
| Age 80+ | 0.32 | 0.07 | 0.31 | (0.20, 0.48) |
| Female | 1.19 | 0.11 | 1.19 | (1.00, 1.42) |
| Time epoch 1 | 1.08 | 0.07 | 1.07 | (0.95, 1.24) |
| Time epoch 2 | 1.15 | 0.12 | 1.14 | (0.96, 1.41) |
| Time epoch 3 | 1.14 | 0.12 | 1.13 | (0.93, 1.41) |
| Time epoch 4 | 1.09 | 0.12 | 1.08 | (0.88, 1.35) |
| Time epoch 5 | 1.04 | 0.13 | 1.03 | (0.81, 1.31) |
| Time epoch 6 | 1.02 | 0.14 | 1.01 | (0.77, 1.31) |
| Time epoch 7 | 1.04 | 0.16 | 1.02 | (0.75, 1.39) |
| Time epoch 8 | 1.09 | 0.20 | 1.07 | (0.75, 1.55) |
| Time epoch 9 | 1.16 | 0.24 | 1.13 | (0.76, 1.72) |
| Time epoch 10 | 1.22 | 0.28 | 1.18 | (0.78, 1.86) |
| Time epoch 11 | 1.27 | 0.30 | 1.23 | (0.80, 1.99) |
| Time epoch 12 | 1.29 | 0.30 | 1.24 | (0.81, 1.99) |
| Time epoch 13 | 1.26 | 0.28 | 1.23 | (0.81, 1.90) |
| Time epoch 14 | 1.23 | 0.27 | 1.20 | (0.79, 1.81) |
| Time epoch 15 | 1.18 | 0.30 | 1.15 | (0.70, 1.86) |
| Time epoch 16 | 1.16 | 0.39 | 1.11 | (0.56, 2.09) |
| Time epoch 17 | 1.18 | 0.56 | 1.08 | (0.41, 2.58) |
| Invasive mechanical ventilation (relative to no IMV) | 0.31 | 0.04 | 0.30 | (0.23, 0.40) |
| Convalescent plasma with IMV at baseline | 1.11 | 0.16 | 1.10 | (0.84, 1.47) |
| Convalescent plasma with no IMV at baseline | 0.92 | 0.09 | 0.91 | (0.75, 1.11) |

Table 64: Posterior probabilities for subgroup analysis with differential effect on OSFD by baseline invasive mechanical ventilation status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with IMV | 0.743 |
| Convalescent plasma is futile with IMV (OR < 1.2) | 0.729 |
| Convalescent plasma is harmful with IMV (OR < 1) | 0.257 |
| Convalescent plasma is superior to control with no IMV | 0.186 |
| Convalescent plasma is futile with no IMV (OR < 1.2) | 0.997 |
| Convalescent plasma is harmful with no IMV (OR < 1) | 0.814 |
| Convalescent plasma with IMV OR > Convalescent Plasma with no IMV OR | 0.856 |

### 7.1.3 Subgroup analysis with differential effect on in-hospital mortality by baseline invasive mechanical ventilation status

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline invasive mechanical ventilation status
- Differential treatment effects for convalescent plasma by baseline invasive mechanical ventilation status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 65: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by baseline invasive mechanical ventilation status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.63 | 2.75 | 8.17 | (4.60, 15.32) |
| Age 40-49 | 3.13 | 0.57 | 3.07 | (2.16, 4.41) |
| Age 50-59 | 2.34 | 0.33 | 2.32 | (1.76, 3.06) |
| Age 70-79 | 0.51 | 0.07 | 0.50 | (0.38, 0.66) |
| Age 80+ | 0.32 | 0.08 | 0.31 | (0.19, 0.50) |
| Female | 1.36 | 0.15 | 1.36 | (1.09, 1.68) |
| Time epoch 1 | 1.08 | 0.07 | 1.08 | (0.95, 1.24) |
| Time epoch 2 | 1.16 | 0.12 | 1.15 | (0.95, 1.42) |
| Time epoch 3 | 1.21 | 0.14 | 1.20 | (0.96, 1.52) |
| Time epoch 4 | 1.25 | 0.16 | 1.24 | (0.96, 1.60) |
| Time epoch 5 | 1.25 | 0.18 | 1.24 | (0.94, 1.63) |
| Time epoch 6 | 1.25 | 0.20 | 1.23 | (0.90, 1.67) |
| Time epoch 7 | 1.26 | 0.23 | 1.24 | (0.86, 1.76) |
| Time epoch 8 | 1.30 | 0.28 | 1.28 | (0.83, 1.91) |

Table 65: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by baseline invasive mechanical ventilation status *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Time epoch 9 | 1.37 | 0.33 | 1.34 | (0.83, 2.11) |
| Time epoch 10 | 1.45 | 0.37 | 1.41 | (0.86, 2.30) |
| Time epoch 11 | 1.53 | 0.41 | 1.49 | (0.89, 2.46) |
| Time epoch 12 | 1.62 | 0.44 | 1.56 | (0.94, 2.64) |
| Time epoch 13 | 1.71 | 0.47 | 1.64 | (0.98, 2.84) |
| Time epoch 14 | 1.84 | 0.54 | 1.76 | (1.03, 3.13) |
| Time epoch 15 | 2.01 | 0.70 | 1.89 | (1.02, 3.71) |
| Time epoch 16 | 2.23 | 1.03 | 2.01 | (0.92, 4.80) |
| Time epoch 17 | 2.56 | 1.70 | 2.16 | (0.76, 6.74) |
| No invasive mechanical ventilation (relative to IMV) | 0.47 | 0.08 | 0.46 | (0.33, 0.64) |
| Convalescent plasma with IMV at baseline | 1.21 | 0.21 | 1.19 | (0.84, 1.69) |
| Convalescent plasma with no IMV at baseline | 0.97 | 0.12 | 0.96 | (0.75, 1.23) |

Table 66: Posterior probabilities for subgroup analysis with differential effect on in-hospital mortality by baseline invasive mechanical ventilation status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with IMV | 0.840 |
| Convalescent plasma is futile with IMV (OR < 1.2) | 0.523 |
| Convalescent plasma is harmful with IMV (OR < 1) | 0.160 |
| Convalescent plasma is superior to control with no IMV | 0.388 |
| Convalescent plasma is futile with no IMV (OR < 1.2) | 0.961 |
| Convalescent plasma is harmful with no IMV (OR < 1) | 0.612 |
| Convalescent plasma with IMV OR > Convalescent Plasma with no IMV OR | 0.838 |

## 7.2 Subgroup analyses by baseline SARS CoV-2 PCR status

This section describes subgroup analyses by SARS CoV-2 PCR status at baseline. The three subgroups are Positive PCR, Negative PCR, and Unknown PCR.

### 7.2.1 Data summaries of baseline SARS CoV-2 PCR status in the Convalescent Plasma ITT population

Table 67: Summary of baseline SARS CoV-2 PCR status for patients randomized to convalescent plasma

| Intervention | Patients | Positive | Negative | Unknown |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 673 (62.6%) | 168 (15.6%) | 234 (21.8%) |
| Control | 905 | 487 (53.8%) | 110 (12.2%) | 308 (34%) |

Table 68: Summary of subjects by baseline SARS CoV PCR status in the Convalescent Plasma ITT population

| Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **PCR Negative** | | | | | |
| Convalescent plasma | 168 | 167 | 38 (22.8%) | 14 (0, 18) | 16 (11, 18) |
| Control | 110 | 109 | 29 (26.6%) | 14 (-1, 18) | 17 (13, 19) |
| **PCR Positive** | | | | | |
| Convalescent plasma | 673 | 672 | 279 (41.5%) | 0 (-1, 14) | 13 (1, 17) |
| Control | 487 | 485 | 206 (42.5%) | 0 (-1, 15) | 14 (4.5, 17) |
| **PCR Unknown** | | | | | |
| Convalescent plasma | 234 | 233 | 84 (36.1%) | 2 (-1, 16) | 15 (4, 18) |
| Control | 308 | 306 | 110 (35.9%) | 6 (-1, 15.75) | 14 (7, 17.25) |

* Days Free of Organ Support in Survivors measured within 21 days.

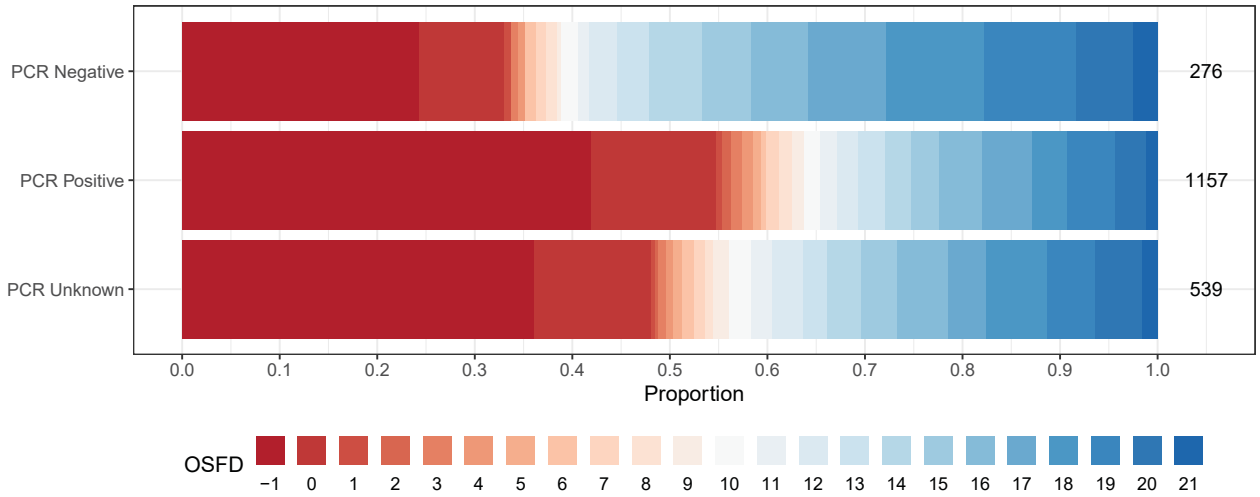


Figure 22: Empirical distribution of organ support free days (OSFD) by baseline SARS CoV PCR status. This plot is restricted to the Antiviral ITT population.

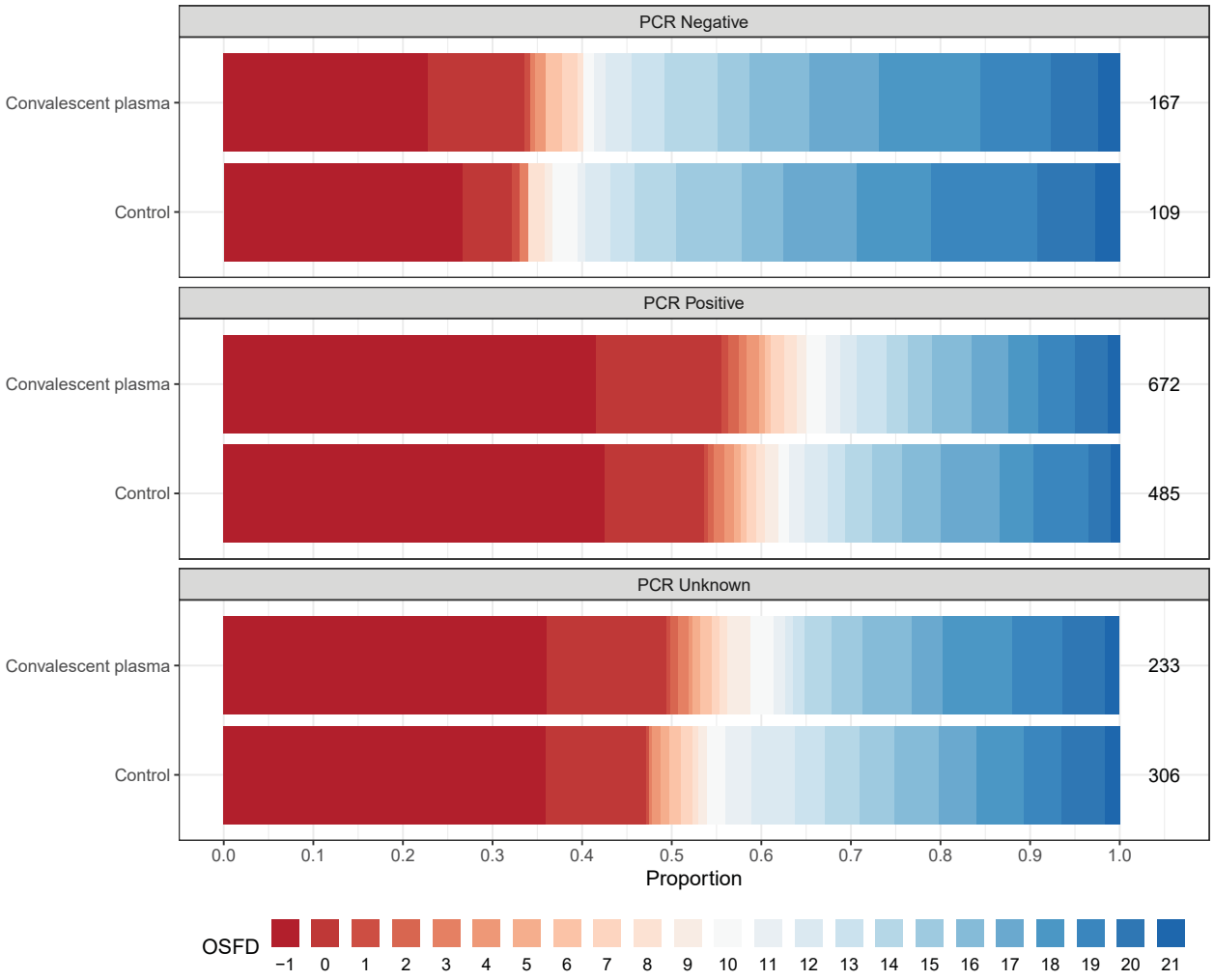


Figure 23: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control by baseline SARS CoV PCR status. This plot is restricted to the Convalescent Plasma ITT population.

### 7.2.2 Subgroup analysis with differential effect on OSFD by baseline SARS CoV-2 PCR status

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline SARS CoV-2 PCR status
- Differential treatment effects for convalescent plasma by baseline SARS CoV-2 PCR status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 69: Odds ratio parameters for subgroup analysis with differential effect on OSFD by SARS CoV PCR status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.49 | 0.76 | 4.42 | (3.18, 6.15) |
| Age 40-49 | 2.32 | 0.31 | 2.30 | (1.78, 2.98) |
| Age 50-59 | 1.80 | 0.20 | 1.79 | (1.45, 2.23) |
| Age 70-79 | 0.51 | 0.06 | 0.50 | (0.39, 0.65) |
| Age 80+ | 0.35 | 0.08 | 0.34 | (0.21, 0.52) |
| Female | 1.11 | 0.10 | 1.10 | (0.93, 1.31) |
| Time epoch 1 | 1.08 | 0.07 | 1.07 | (0.95, 1.23) |
| Time epoch 2 | 1.14 | 0.11 | 1.13 | (0.95, 1.38) |
| Time epoch 3 | 1.12 | 0.12 | 1.12 | (0.92, 1.37) |
| Time epoch 4 | 1.11 | 0.12 | 1.10 | (0.89, 1.37) |
| Time epoch 5 | 1.10 | 0.13 | 1.10 | (0.86, 1.39) |
| Time epoch 6 | 1.11 | 0.15 | 1.10 | (0.84, 1.44) |
| Time epoch 7 | 1.16 | 0.19 | 1.15 | (0.84, 1.57) |
| Time epoch 8 | 1.25 | 0.24 | 1.22 | (0.85, 1.81) |
| Time epoch 9 | 1.31 | 0.29 | 1.27 | (0.86, 2.01) |
| Time epoch 10 | 1.35 | 0.33 | 1.30 | (0.85, 2.11) |
| Time epoch 11 | 1.35 | 0.34 | 1.30 | (0.85, 2.18) |
| Time epoch 12 | 1.30 | 0.32 | 1.26 | (0.82, 2.07) |
| Time epoch 13 | 1.20 | 0.27 | 1.17 | (0.76, 1.83) |
| Time epoch 14 | 1.09 | 0.24 | 1.06 | (0.69, 1.64) |
| Time epoch 15 | 0.97 | 0.25 | 0.94 | (0.57, 1.55) |
| Time epoch 16 | 0.88 | 0.31 | 0.83 | (0.41, 1.63) |
| Time epoch 17 | 0.83 | 0.41 | 0.75 | (0.27, 1.81) |
| Negative PCR (relative to positive PCR) | 2.31 | 0.45 | 2.27 | (1.56, 3.29) |
| Unknown PCR (relative to positive PCR) | 1.17 | 0.17 | 1.16 | (0.88, 1.53) |
| Convalescent plasma with PCR positive | 0.91 | 0.10 | 0.90 | (0.72, 1.12) |
| Convalescent plasma with PCR negative | 0.99 | 0.21 | 0.97 | (0.64, 1.47) |
| Convalescent plasma with PCR unknown | 1.06 | 0.17 | 1.04 | (0.76, 1.43) |

Table 70: Posterior probabilities for subgroup analysis with differential effect on OSFD by SARS CoV PCR status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with PCR positive | 0.176 |
| Convalescent plasma is futile with PCR positive (OR < 1.2) | 0.995 |
| Convalescent plasma is harmful with PCR positive (OR < 1) | 0.824 |
| Convalescent plasma is superior to control with PCR negative | 0.444 |
| Convalescent plasma is futile with PCR negative (OR < 1.2) | 0.839 |
| Convalescent plasma is harmful with PCR negative (OR < 1) | 0.556 |
| Convalescent plasma is superior to control with PCR unknown | 0.603 |
| Convalescent plasma is futile with PCR unknown (OR < 1.2) | 0.808 |

Table 70: Posterior probabilities for subgroup analysis with differential effect on OSFD by SARS CoV PCR status *(continued)*

| | Posterior Probability |
|---|---|
| Convalescent plasma is harmful with PCR unknown (OR < 1) | 0.397 |
| Convalescent plasma with PCR positive OR > Convalescent plasma with PCR negative OR | 0.379 |
| Convalescent plasma with PCR positive OR > Convalescent plasma with PCR unknown OR | 0.231 |
| Convalescent plasma with PCR negative OR > Convalescent plasma with PCR unknown OR | 0.398 |

### 7.2.3 Subgroup analysis with differential effect on in-hospital mortality by baseline SARS CoV-2 PCR status

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline SARS CoV-2 PCR status
- Differential treatment effects for convalescent plasma by baseline SARS CoV-2 PCR status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 71: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by SARS CoV PCR status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.39 | 2.65 | 7.92 | (4.56, 14.83) |
| Age 40-49 | 3.07 | 0.55 | 3.02 | (2.15, 4.29) |
| Age 50-59 | 2.28 | 0.33 | 2.25 | (1.70, 2.98) |
| Age 70-79 | 0.49 | 0.07 | 0.49 | (0.37, 0.64) |
| Age 80+ | 0.33 | 0.08 | 0.32 | (0.20, 0.51) |
| Female | 1.30 | 0.15 | 1.29 | (1.04, 1.61) |
| Time epoch 1 | 1.09 | 0.07 | 1.08 | (0.95, 1.25) |
| Time epoch 2 | 1.17 | 0.12 | 1.16 | (0.96, 1.43) |
| Time epoch 3 | 1.22 | 0.14 | 1.21 | (0.97, 1.53) |
| Time epoch 4 | 1.28 | 0.16 | 1.27 | (0.99, 1.64) |
| Time epoch 5 | 1.31 | 0.19 | 1.30 | (0.99, 1.72) |
| Time epoch 6 | 1.33 | 0.22 | 1.31 | (0.96, 1.80) |
| Time epoch 7 | 1.35 | 0.26 | 1.33 | (0.92, 1.92) |
| Time epoch 8 | 1.41 | 0.31 | 1.37 | (0.90, 2.11) |
| Time epoch 9 | 1.47 | 0.36 | 1.42 | (0.90, 2.32) |
| Time epoch 10 | 1.53 | 0.41 | 1.47 | (0.91, 2.49) |
| Time epoch 11 | 1.58 | 0.43 | 1.51 | (0.92, 2.60) |
| Time epoch 12 | 1.61 | 0.44 | 1.55 | (0.93, 2.65) |

Table 71: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by SARS CoV PCR status *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Time epoch 13 | 1.65 | 0.46 | 1.58 | (0.94, 2.73) |
| Time epoch 14 | 1.71 | 0.51 | 1.62 | (0.94, 2.94) |
| Time epoch 15 | 1.79 | 0.64 | 1.68 | (0.89, 3.38) |
| Time epoch 16 | 1.92 | 0.89 | 1.74 | (0.78, 4.16) |
| Time epoch 17 | 2.12 | 1.37 | 1.79 | (0.64, 5.47) |
| Negative PCR (relative to positive PCR) | 2.12 | 0.54 | 2.05 | (1.27, 3.39) |
| Unknown PCR (relative to positive PCR) | 1.30 | 0.23 | 1.28 | (0.90, 1.78) |
| Convalescent plasma with PCR positive | 1.02 | 0.13 | 1.01 | (0.79, 1.30) |
| Convalescent plasma with PCR negative | 1.19 | 0.36 | 1.14 | (0.64, 2.01) |
| Convalescent plasma with PCR unknown | 1.10 | 0.22 | 1.08 | (0.73, 1.60) |

Table 72: Posterior probabilities for subgroup analysis with differential effect on in-hospital mortality by SARS CoV PCR status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with PCR positive | 0.529 |
| Convalescent plasma is futile with PCR positive (OR < 1.2) | 0.906 |
| Convalescent plasma is harmful with PCR positive (OR < 1) | 0.471 |
| Convalescent plasma is superior to control with PCR negative | 0.664 |
| Convalescent plasma is futile with PCR negative (OR < 1.2) | 0.569 |
| Convalescent plasma is harmful with PCR negative (OR < 1) | 0.336 |
| Convalescent plasma is superior to control with PCR unknown | 0.644 |
| Convalescent plasma is futile with PCR unknown (OR < 1.2) | 0.699 |
| Convalescent plasma is harmful with PCR unknown (OR < 1) | 0.356 |
| Convalescent plasma with PCR positive OR > Convalescent plasma with PCR negative OR | 0.358 |
| Convalescent plasma with PCR positive OR > Convalescent plasma with PCR unknown OR | 0.396 |
| Convalescent plasma with PCR negative OR > Convalescent plasma with PCR unknown OR | 0.556 |

## 7.3 Subgroup analyses by dose of neutralizing antibody received

In this section, the convalescent plasma intervention is divided into three subgroups based on the dose of neutralizing antibody received by the patient. This is estimated as a function of donor plasma antibody titer and volume of plasma infused. There are three possible categories:

- no units received with a Euroimmun $\geq 8$

- one unit received with a Euroimmun $\geq 8$
- two units received with a Euroimmun $\geq 8$

This subgroup is defined only for subjects randomized to convalescent plasma. As a result, there is no main effect for the subgroup variable in this analysis.

### 7.3.1 Data summaries of dose of neutralizing antibody received in the Convalescent Plasma ITT population

Table 73: Summary of number of Convalescent Plasma doses administered

| Intervention | Patients | 0 units EI≥8 | 1 unit EI≥8 | 2 units EI≥8 |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 467 (43.4%) | 418 (38.9%) | 190 (17.7%) |

Table 74: Summary of subjects by dose of neutralizing antibodies received in the Antiviral ITT population

| Subgroup | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **Control** | | | | | |
| | 905 | 900 | 345 (38.3%) | 3 (-1, 16) | 14 (7, 18) |
| **Convalescent plasma** | | | | | |
| One dose | 418 | 417 | 150 (36%) | 0 (-1, 15) | 13 (2, 17) |
| Two doses | 190 | 189 | 67 (35.4%) | 2 (-1, 16) | 14 (3.25, 18) |
| Zero doses | 467 | 466 | 184 (39.5%) | 0 (-1, 16) | 15 (5, 18) |

* Days Free of Organ Support in Survivors measured within 21 days.

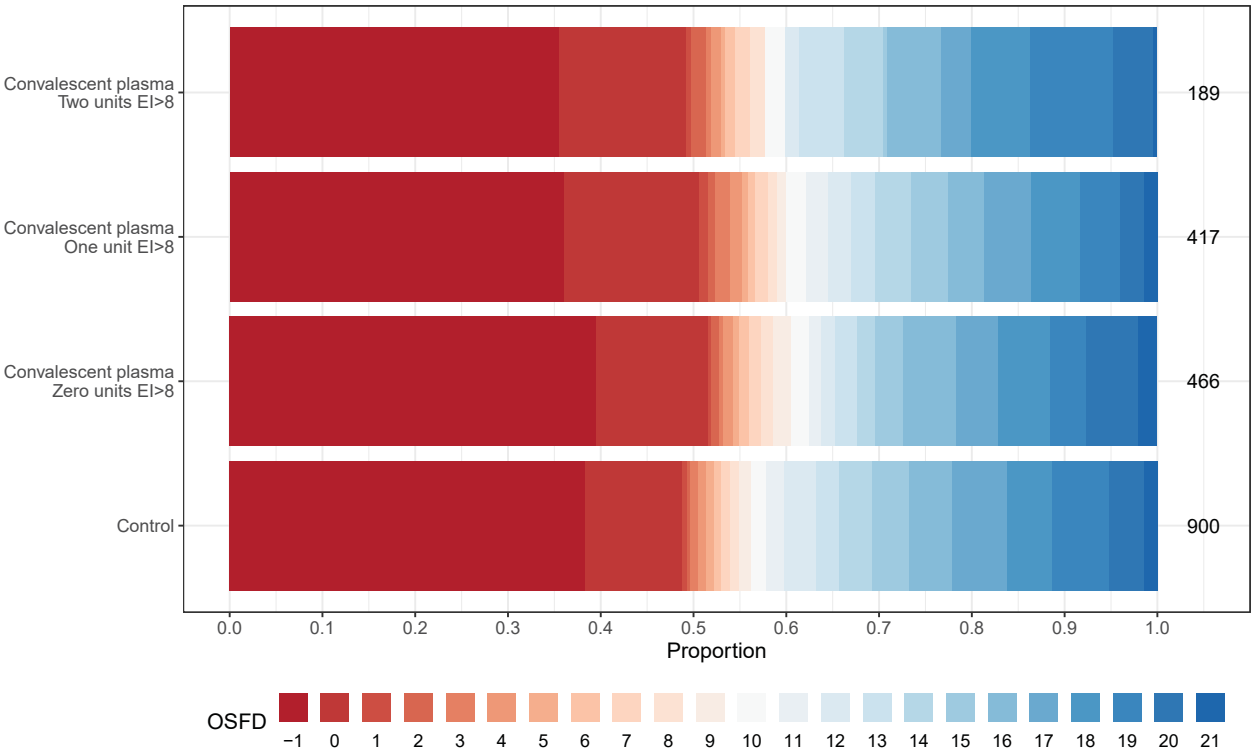


Figure 24: Empirical distribution of organ support free days (OSFD) for control and convalescent plasma (by dose of neutralizing antibodies received). This plot is restricted to the Convalescent Plasma ITT population.

### 7.3.2 Subgroup analysis with differential effect on OSFD by dose of neutralizing antibodies received

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma (by dose of neutralizing antibodies received)
- Differential treatment effects for convalescent plasma by dose of neutralizing antibodies received will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 75: Odds ratio parameters for subgroup analysis with differential effect on OSFD by dose of neutralizing antibodies received

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.53 | 0.76 | 4.46 | (3.19, 6.23) |
| Age 40-49 | 2.45 | 0.33 | 2.43 | (1.87, 3.17) |
| Age 50-59 | 1.87 | 0.21 | 1.85 | (1.49, 2.31) |
| Age 70-79 | 0.51 | 0.06 | 0.51 | (0.40, 0.65) |
| Age 80+ | 0.36 | 0.08 | 0.35 | (0.22, 0.54) |
| Female | 1.12 | 0.10 | 1.11 | (0.93, 1.32) |
| Time epoch 1 | 1.08 | 0.07 | 1.08 | (0.95, 1.24) |
| Time epoch 2 | 1.16 | 0.11 | 1.15 | (0.96, 1.41) |
| Time epoch 3 | 1.15 | 0.12 | 1.14 | (0.93, 1.40) |
| Time epoch 4 | 1.13 | 0.12 | 1.12 | (0.90, 1.39) |
| Time epoch 5 | 1.11 | 0.13 | 1.11 | (0.88, 1.40) |
| Time epoch 6 | 1.12 | 0.15 | 1.11 | (0.84, 1.44) |
| Time epoch 7 | 1.17 | 0.19 | 1.16 | (0.85, 1.57) |
| Time epoch 8 | 1.26 | 0.24 | 1.23 | (0.86, 1.81) |
| Time epoch 9 | 1.34 | 0.30 | 1.30 | (0.88, 2.05) |
| Time epoch 10 | 1.39 | 0.34 | 1.34 | (0.87, 2.22) |
| Time epoch 11 | 1.40 | 0.36 | 1.35 | (0.87, 2.26) |
| Time epoch 12 | 1.36 | 0.34 | 1.31 | (0.85, 2.17) |
| Time epoch 13 | 1.26 | 0.29 | 1.22 | (0.80, 1.95) |
| Time epoch 14 | 1.14 | 0.25 | 1.11 | (0.73, 1.73) |
| Time epoch 15 | 1.02 | 0.26 | 0.99 | (0.59, 1.62) |
| Time epoch 16 | 0.92 | 0.33 | 0.88 | (0.43, 1.68) |
| Time epoch 17 | 0.87 | 0.43 | 0.79 | (0.28, 1.90) |
| Zero units EI≥8 convalescent plasma | 0.95 | 0.10 | 0.95 | (0.77, 1.17) |
| One unit EI≥8 of convalescent plasma | 0.94 | 0.10 | 0.93 | (0.76, 1.15) |
| Two units EI≥8 of convalescent plasma | 1.03 | 0.16 | 1.02 | (0.75, 1.37) |

Table 76: Posterior probabilities for subgroup analysis with differential effect on OSFD by number of convalescent plasma doses

| | Posterior Probability |
|---|---|
| Zero units EI≥8 convalescent plasma is superior to control | 0.308 |
| Zero units EI≥8 convalescent plasma is futile (OR < 1.2) | 0.985 |
| Zero units EI≥8 convalescent plasma is harmful (OR < 1) | 0.692 |
| One unit EI≥8 convalescent plasma is superior to control | 0.261 |
| One unit EI≥8 convalescent plasma is futile (OR < 1.2) | 0.991 |
| One unit EI≥8 convalescent plasma is harmful (OR < 1) | 0.739 |
| Two units EI≥8 convalescent plasma is superior to control | 0.543 |
| Two units EI≥8 convalescent plasma is futile (OR < 1.2) | 0.861 |
| Two units EI≥8 convalescent plasma is harmful (OR < 1) | 0.457 |
| Zero units EI≥8 convalescent plasma OR > One unit EI≥8 convalescent plasma OR | 0.544 |
| Zero units EI≥8 convalescent plasma OR > Two units EI≥8 convalescent plasma OR | 0.338 |
| One unit EI≥8 convalescent plasma > Two units EI≥8 convalescent plasma OR | 0.303 |

### 7.3.3 Subgroup analysis with differential effect on in-hospital mortality by dose of neutralizing antibodies received

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, control and convalescent plasma (by dose of neutralizing antibodies received)
- Differential treatment effects for convalescent plasma by dose of neutralizing antibodies received will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 77: Odds ratio parameters for subgroup analysis with differential effect on OSFD by dose of neutralizing antibodies received

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.50 | 2.67 | 8.06 | (4.66, 14.89) |
| Age 40-49 | 3.20 | 0.57 | 3.14 | (2.24, 4.48) |
| Age 50-59 | 2.34 | 0.32 | 2.32 | (1.77, 3.02) |
| Age 70-79 | 0.50 | 0.07 | 0.50 | (0.38, 0.65) |
| Age 80+ | 0.34 | 0.08 | 0.33 | (0.21, 0.53) |
| Female | 1.31 | 0.15 | 1.31 | (1.05, 1.63) |
| Time epoch 1 | 1.09 | 0.07 | 1.09 | (0.96, 1.25) |
| Time epoch 2 | 1.18 | 0.12 | 1.17 | (0.97, 1.44) |
| Time epoch 3 | 1.24 | 0.15 | 1.22 | (0.97, 1.55) |
| Time epoch 4 | 1.29 | 0.17 | 1.27 | (0.98, 1.65) |
| Time epoch 5 | 1.31 | 0.19 | 1.30 | (0.98, 1.71) |
| Time epoch 6 | 1.32 | 0.22 | 1.30 | (0.94, 1.79) |
| Time epoch 7 | 1.34 | 0.26 | 1.31 | (0.90, 1.91) |
| Time epoch 8 | 1.39 | 0.31 | 1.36 | (0.88, 2.09) |
| Time epoch 9 | 1.47 | 0.37 | 1.42 | (0.88, 2.29) |
| Time epoch 10 | 1.54 | 0.42 | 1.49 | (0.90, 2.50) |
| Time epoch 11 | 1.61 | 0.45 | 1.54 | (0.92, 2.66) |
| Time epoch 12 | 1.66 | 0.47 | 1.59 | (0.94, 2.76) |
| Time epoch 13 | 1.72 | 0.48 | 1.65 | (0.97, 2.86) |
| Time epoch 14 | 1.80 | 0.54 | 1.71 | (0.97, 3.09) |
| Time epoch 15 | 1.91 | 0.69 | 1.79 | (0.92, 3.52) |
| Time epoch 16 | 2.06 | 0.97 | 1.86 | (0.81, 4.44) |
| Time epoch 17 | 2.31 | 1.55 | 1.94 | (0.64, 6.18) |
| Zero units EI≥8 convalescent plasma | 0.97 | 0.13 | 0.97 | (0.75, 1.25) |
| One unit EI≥8 of convalescent plasma | 1.12 | 0.15 | 1.11 | (0.85, 1.45) |
| Two units EI≥8 of convalescent plasma | 1.06 | 0.20 | 1.04 | (0.73, 1.51) |

Table 78: Posterior probabilities for subgroup analysis with differential effect on OSFD by number of convalescent plasma doses

| | Posterior Probability |
|---|---|
| Zero units EI≥8 convalescent plasma is superior to control | 0.398 |
| Zero units EI≥8 convalescent plasma is futile (OR < 1.2) | 0.950 |
| Zero units EI≥8 convalescent plasma is harmful (OR < 1) | 0.602 |
| One unit EI≥8 convalescent plasma is superior to control | 0.775 |
| One unit EI≥8 convalescent plasma is futile (OR < 1.2) | 0.720 |
| One unit EI≥8 convalescent plasma is harmful (OR < 1) | 0.225 |
| Two units EI≥8 convalescent plasma is superior to control | 0.584 |
| Two units EI≥8 convalescent plasma is futile (OR < 1.2) | 0.785 |
| Two units EI≥8 convalescent plasma is harmful (OR < 1) | 0.416 |
| Zero units EI≥8 convalescent plasma OR > One unit EI≥8 convalescent plasma OR | 0.187 |
| Zero units EI≥8 convalescent plasma OR > Two units EI≥8 convalescent plasma OR | 0.362 |
| One unit EI≥8 convalescent plasma > Two units EI≥8 convalescent plasma OR | 0.621 |

## 7.4 Subgroup analyses by time from hospitalization to randomization

This section describes subgroup analyses defined by the time from hospitalization to randomization. The three pre-defined subgroups are (1) randomized within 3 days; (2) randomized within 3-7 days; (3) randomized after 7 days.

### 7.4.1 Data summaries of time from hospitalization to randomization in the Convalescent Plasma ITT population

Table 79: Summary of time from hospitalization to randomization subgroup

| Intervention | Patients | Randomized within 3 days | Randomized within 3-7 days | Randomized after >7 days |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 781 (72.7%) | 226 (21%) | 68 (6.3%) |
| Control | 905 | 654 (72.3%) | 193 (21.3%) | 58 (6.4%) |
| Overall | 1980 | 1435 (72.5%) | 419 (21.2%) | 126 (6.4%) |

Table 80: Summary of subjects by time from hospitalization to randomization subgroup

| Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **Randomized within 3 days** | | | | | |
| Convalescent plasma | 781 | 780 | 255 (32.7%) | 4 (-1, 16) | 14 (4, 18) |
| Control | 654 | 654 | 232 (35.5%) | 7 (-1, 16) | 14.5 (9, 18) |
| Overall | 1435 | 1434 | 487 (34%) | 5 (-1, 16) | 14 (6, 18) |
| **Randomized in 3 to 7 days** | | | | | |
| Convalescent plasma | 226 | 225 | 101 (44.9%) | 0 (-1, 16) | 14.5 (4.75, 18) |
| Control | 193 | 189 | 81 (42.9%) | 0 (-1, 16) | 15 (6, 18) |
| Overall | 419 | 414 | 182 (44%) | 0 (-1, 16) | 15 (6, 18) |
| **Randomized after >7 days** | | | | | |
| Convalescent plasma | 68 | 67 | 45 (67.2%) | -1 (-1, 0) | 6 (0, 15.25) |
| Control | 58 | 57 | 32 (56.1%) | -1 (-1, 4) | 9 (0, 18) |
| Overall | 126 | 124 | 77 (62.1%) | -1 (-1, 0.25) | 8 (0, 17) |

* Days Free of Organ Support in Survivors measured within 21 days.

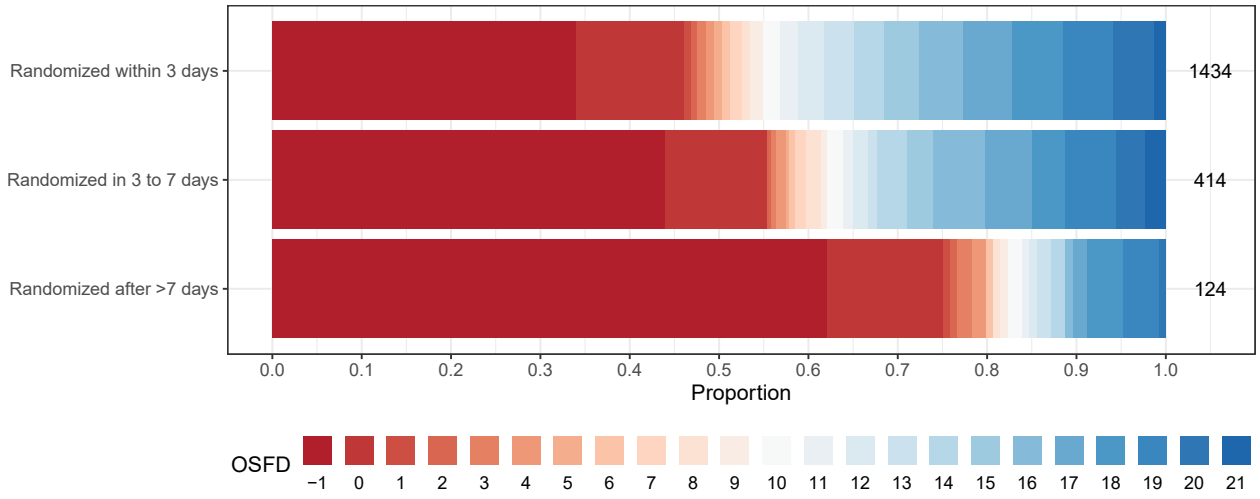


Figure 25: Empirical distribution of organ support free days (OSFD) by time from hospitalization to randomization subgroup. This plot is restricted to the Convalescent Plasma ITT population.

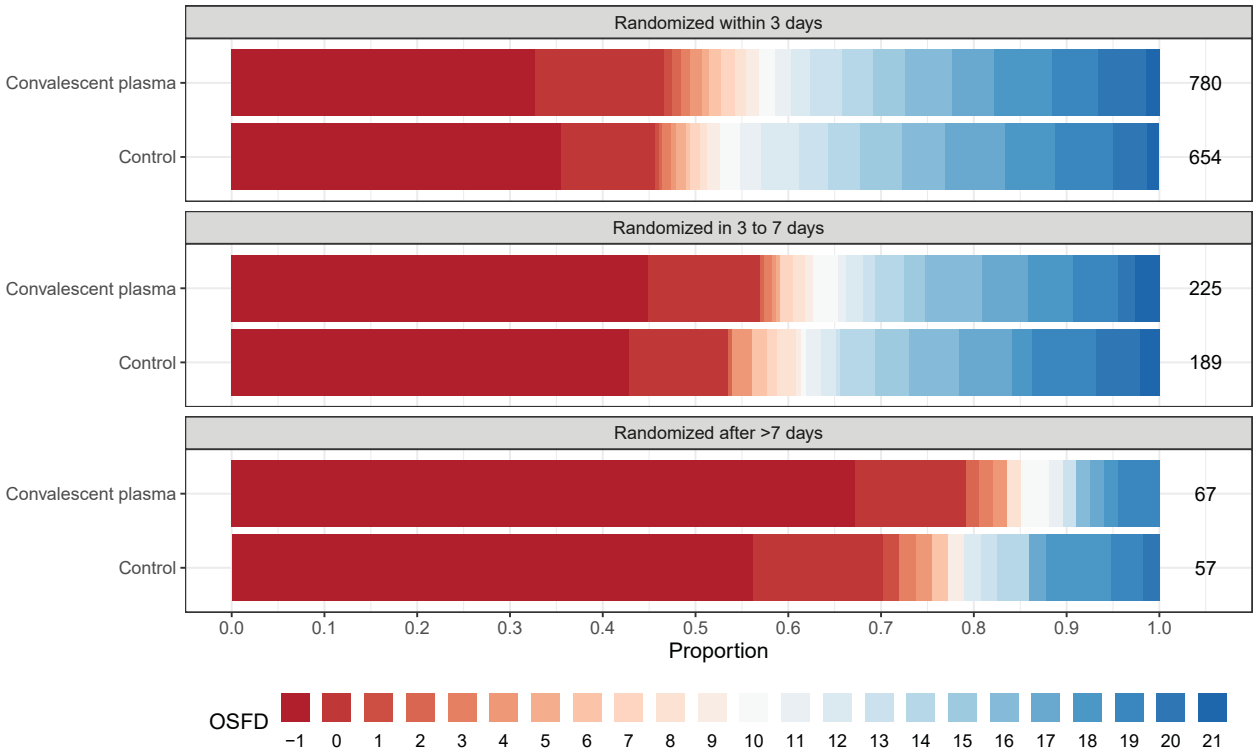


Figure 26: Empirical distribution of organ support free days (OSFD) for Lopinavir−ritonavir, Hydroxychloroquine, combination therapy, and control by time from hospitalization to randomization subgroup. This plot is restricted to the Convalescent Plasma ITT population.

### 7.4.2 Subgroup analysis with differential effect on OSFD by time from hospitalization to randomization

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma, time from hospitalization to randomization
- Differential treatment effects for convalescent plasma by time from hospitalization to randomization will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 81: Odds ratio parameters for subgroup analysis with differential effect on OSFD by time from hospitalization to randomization

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.35 | 0.72 | 4.29 | (3.10, 5.93) |
| Age 40-49 | 2.42 | 0.32 | 2.41 | (1.86, 3.10) |

Table 81: Odds ratio parameters for subgroup analysis with differential effect on OSFD by time from hospitalization to randomization *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age 50-59 | 1.82 | 0.20 | 1.81 | (1.46, 2.24) |
| Age 70-79 | 0.52 | 0.07 | 0.51 | (0.40, 0.66) |
| Age 80+ | 0.36 | 0.08 | 0.35 | (0.22, 0.55) |
| Female | 1.11 | 0.10 | 1.11 | (0.93, 1.32) |
| Time epoch 1 | 1.06 | 0.07 | 1.06 | (0.94, 1.21) |
| Time epoch 2 | 1.13 | 0.11 | 1.12 | (0.94, 1.37) |
| Time epoch 3 | 1.11 | 0.11 | 1.10 | (0.90, 1.35) |
| Time epoch 4 | 1.09 | 0.12 | 1.08 | (0.87, 1.33) |
| Time epoch 5 | 1.07 | 0.13 | 1.07 | (0.84, 1.34) |
| Time epoch 6 | 1.08 | 0.14 | 1.07 | (0.82, 1.38) |
| Time epoch 7 | 1.12 | 0.18 | 1.11 | (0.81, 1.50) |
| Time epoch 8 | 1.20 | 0.23 | 1.17 | (0.83, 1.72) |
| Time epoch 9 | 1.26 | 0.28 | 1.22 | (0.83, 1.93) |
| Time epoch 10 | 1.31 | 0.32 | 1.26 | (0.82, 2.06) |
| Time epoch 11 | 1.32 | 0.34 | 1.27 | (0.82, 2.14) |
| Time epoch 12 | 1.28 | 0.32 | 1.24 | (0.80, 2.06) |
| Time epoch 13 | 1.19 | 0.28 | 1.16 | (0.76, 1.83) |
| Time epoch 14 | 1.08 | 0.24 | 1.06 | (0.69, 1.63) |
| Time epoch 15 | 0.96 | 0.25 | 0.94 | (0.57, 1.53) |
| Time epoch 16 | 0.87 | 0.30 | 0.83 | (0.42, 1.57) |
| Time epoch 17 | 0.82 | 0.40 | 0.75 | (0.27, 1.78) |
| Randomized after 3-7 days (relative to <3) | 0.89 | 0.14 | 0.88 | (0.65, 1.19) |
| Randomized after 7 days (relative to <3) | 0.50 | 0.13 | 0.49 | (0.29, 0.81) |
| Convalescent plasma when randomized within 3 days | 1.00 | 0.10 | 0.99 | (0.82, 1.20) |
| Convalescent plasma when randomized between 3-7 days | 0.93 | 0.18 | 0.92 | (0.64, 1.32) |
| Convalescent plasma when randomized after 7 days | 0.67 | 0.24 | 0.63 | (0.32, 1.25) |

Table 82: Posterior probabilities for subgroup analysis with differential effect on OSFD by time from hospitalization to randomization

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control in <3 day subgroup | 0.463 |
| Convalescent plasma is futile in <3 day subgroup (OR < 1.2) | 0.975 |
| Convalescent plasma is harmful in <3 day subgroup (OR < 1) | 0.537 |
| Convalescent plasma is superior to control in 3-7 day subgroup | 0.325 |
| Convalescent plasma is futile in 3-7 day subgroup (OR < 1.2) | 0.927 |
| Convalescent plasma is harmful in 3-7 day subgroup (OR < 1) | 0.675 |
| Convalescent plasma is superior to control in >7 day subgroup | 0.097 |
| Convalescent plasma is futile in >7 day subgroup (OR < 1.2) | 0.967 |
| Convalescent plasma is harmful in >7 day subgroup (OR < 1) | 0.903 |

Table 82: Posterior probabilities for subgroup analysis with differential effect on OSFD by time from hospitalization to randomization *(continued)*

| | Posterior Probability |
|---|---|
| Convalescent plasma in <3 day subgroup OR > Convalescent plasma 3-7 day subgroup OR | 0.642 |
| Convalescent plasma <3 day subgroup OR > Convalescent plasma in >7 day subgroup OR | 0.894 |
| Convalescent plasma 3-7 day subgroup OR > Convalescent plasma in >7 day subgroup OR | 0.825 |

### 7.4.3 Subgroup analysis with differential effect on in-hospital mortality by time from hospitalization to randomization

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, control and convalescent plasma, time from hospitalization to randomization
- Differential treatment effects for convalescent plasma by time from hospitalization to randomization will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 83: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by time from hospitalization to randomization

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.10 | 2.51 | 7.70 | (4.48, 14.20) |
| Age 40-49 | 3.17 | 0.57 | 3.11 | (2.21, 4.46) |
| Age 50-59 | 2.28 | 0.32 | 2.25 | (1.72, 2.99) |
| Age 70-79 | 0.52 | 0.07 | 0.51 | (0.39, 0.67) |
| Age 80+ | 0.35 | 0.08 | 0.34 | (0.21, 0.54) |
| Female | 1.30 | 0.14 | 1.29 | (1.04, 1.60) |
| Time epoch 1 | 1.07 | 0.07 | 1.07 | (0.94, 1.23) |
| Time epoch 2 | 1.14 | 0.12 | 1.14 | (0.94, 1.40) |
| Time epoch 3 | 1.19 | 0.14 | 1.18 | (0.93, 1.49) |
| Time epoch 4 | 1.23 | 0.16 | 1.22 | (0.95, 1.57) |
| Time epoch 5 | 1.25 | 0.18 | 1.24 | (0.94, 1.64) |
| Time epoch 6 | 1.25 | 0.20 | 1.24 | (0.90, 1.68) |
| Time epoch 7 | 1.26 | 0.23 | 1.24 | (0.86, 1.77) |
| Time epoch 8 | 1.31 | 0.28 | 1.28 | (0.83, 1.92) |
| Time epoch 9 | 1.36 | 0.33 | 1.33 | (0.83, 2.11) |

Table 83: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by time from hospitalization to randomization *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Time epoch 10 | 1.43 | 0.37 | 1.38 | (0.84, 2.29) |
| Time epoch 11 | 1.49 | 0.40 | 1.44 | (0.87, 2.42) |
| Time epoch 12 | 1.55 | 0.42 | 1.49 | (0.89, 2.50) |
| Time epoch 13 | 1.60 | 0.44 | 1.54 | (0.92, 2.63) |
| Time epoch 14 | 1.68 | 0.50 | 1.60 | (0.93, 2.85) |
| Time epoch 15 | 1.78 | 0.62 | 1.68 | (0.89, 3.29) |
| Time epoch 16 | 1.92 | 0.87 | 1.74 | (0.79, 4.10) |
| Time epoch 17 | 2.14 | 1.33 | 1.81 | (0.64, 5.56) |
| Randomized after 3-7 days (relative to <3) | 0.81 | 0.15 | 0.80 | (0.56, 1.15) |
| Randomized after 7 days (relative to <3) | 0.53 | 0.16 | 0.51 | (0.29, 0.89) |
| Convalescent plasma when randomized within 3 days | 1.13 | 0.14 | 1.12 | (0.88, 1.41) |
| Convalescent plasma when randomized between 3-7 days | 0.97 | 0.21 | 0.95 | (0.63, 1.45) |
| Convalescent plasma when randomized after 7 days | 0.69 | 0.26 | 0.65 | (0.32, 1.34) |

Table 84: Posterior probabilities for subgroup analysis with differential effect on in-hospital mortality by time from hospitalization to randomization

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control in <3 day subgroup | 0.824 |
| Convalescent plasma is futile in <3 day subgroup (OR < 1.2) | 0.721 |
| Convalescent plasma is harmful in <3 day subgroup (OR < 1) | 0.176 |
| Convalescent plasma is superior to control in 3-7 day subgroup | 0.406 |
| Convalescent plasma is futile in 3-7 day subgroup (OR < 1.2) | 0.861 |
| Convalescent plasma is harmful in 3-7 day subgroup (OR < 1) | 0.594 |
| Convalescent plasma is superior to control in >7 day subgroup | 0.118 |
| Convalescent plasma is futile in >7 day subgroup (OR < 1.2) | 0.952 |
| Convalescent plasma is harmful in >7 day subgroup (OR < 1) | 0.882 |
| Convalescent plasma in <3 day subgroup OR > Convalescent plasma 3-7 day subgroup OR | 0.746 |
| Convalescent plasma <3 day subgroup OR > Convalescent plasma in >7 day subgroup OR | 0.920 |
| Convalescent plasma 3-7 day subgroup OR > Convalescent plasma in >7 day subgroup OR | 0.816 |

## 7.5 Subgroup analyses by presence/absence of immunodeficiency

This section describes subgroup analyses based on the presence or absence of immunodeficiency. Presence of immunodeficiency is defined as on immunosuppressive drugs or underlying disease causing immune deficiency.

### 7.5.1 Data summaries of presence/absence of immunodeficiency in the Convalescent Plasma ITT population

Table 85: Summary of immunodeficiency by intervention

| Intervention | Patients | Known | No immunodeficiency | Immunodeficiency |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 1063 | 997 (93.8%) | 66 (6.2%) |
| Control | 905 | 903 | 843 (93.4%) | 60 (6.6%) |

Table 86: Summary of subjects by presence/abscence of immunodeficiency in the Convalescent Plasma ITT population

| Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **No immunodeficiency** | | | | | |
| Convalescent plasma | 997 | 994 | 366 (36.8%) | 0 (-1, 16) | 14 (3, 18) |
| Control | 843 | 840 | 308 (36.7%) | 5 (-1, 16) | 15 (8, 18) |
| **Immunodeficiency** | | | | | |
| Convalescent plasma | 66 | 66 | 31 (47%) | 0 (-1, 13) | 13 (3, 15.5) |
| Control | 60 | 60 | 37 (61.7%) | -1 (-1, 3.25) | 8 (0, 13) |

* Days Free of Organ Support in Survivors measured within 21 days.

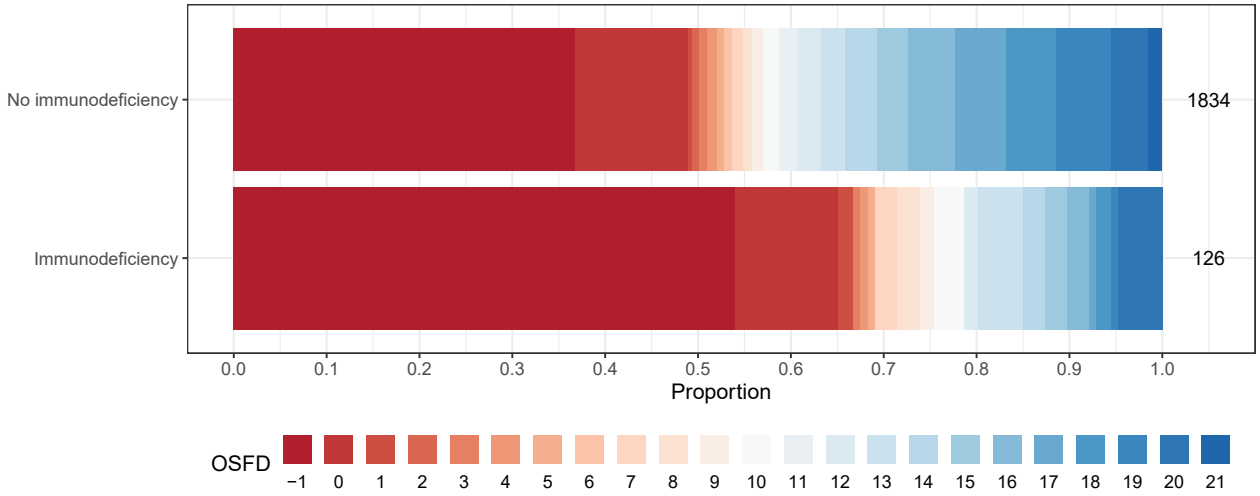


Figure 27: Empirical distribution of organ support free days (OSFD) by presence/abscence of immunodefiency. This plot is restricted to the Convalescent Plasma ITT population.

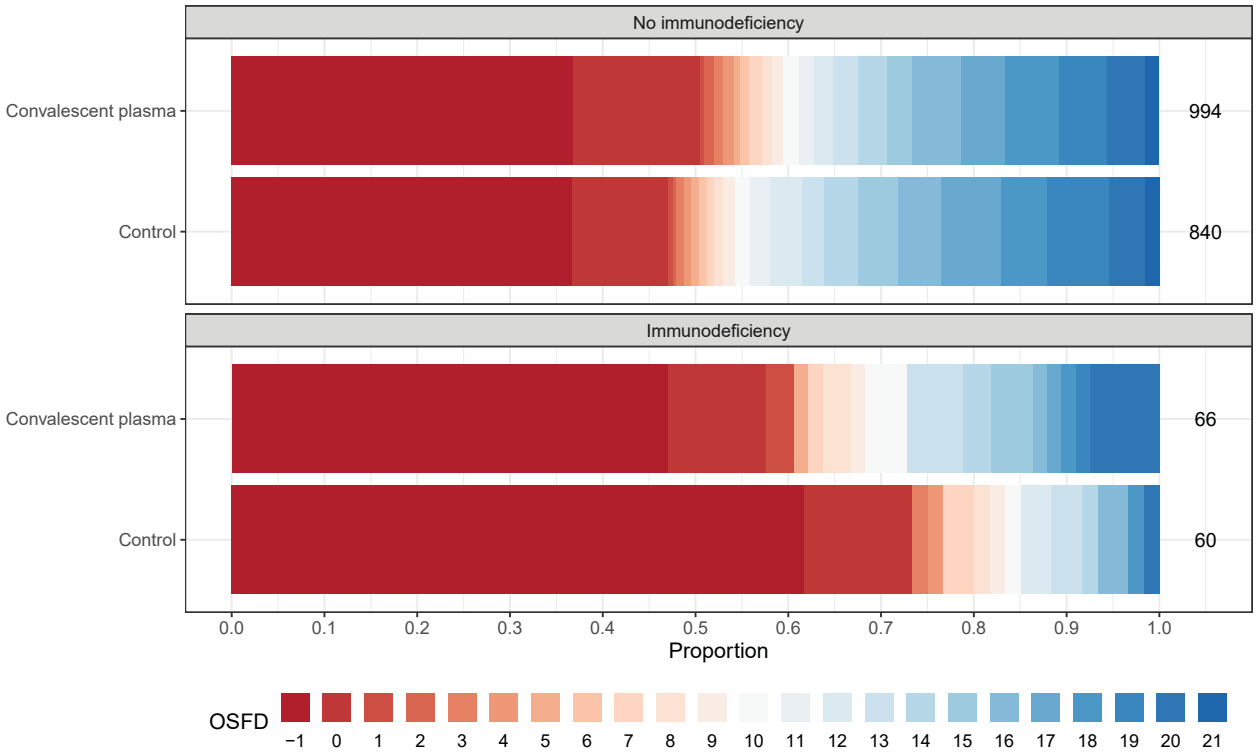


Figure 28: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control by presence/abscence of immunodefiency. This plot is restricted to the Convalescent Plasma ITT population.

### 7.5.2 Subgroup analysis with differential effect on OSFD by presence/abscence of immunodeficiency

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma, presence/absence of immunodeficiency
- Differential treatment effects for convalescent plasma by presence/absence of immunodeficiency will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 87: Odds ratio parameters for subgroup analysis with differential effect on OSFD by presence/abscence of immunodeficiency

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.42 | 0.77 | 4.35 | (3.12, 6.12) |
| Age 40-49 | 2.39 | 0.32 | 2.37 | (1.83, 3.09) |
| Age 50-59 | 1.84 | 0.21 | 1.83 | (1.47, 2.28) |

Table 87: Odds ratio parameters for subgroup analysis with differential effect on OSFD by presence/abscence of immunodeficiency *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age 70-79 | 0.52 | 0.07 | 0.51 | (0.40, 0.66) |
| Age 80+ | 0.36 | 0.08 | 0.35 | (0.22, 0.54) |
| Female | 1.15 | 0.10 | 1.15 | (0.96, 1.37) |
| Time epoch 1 | 1.09 | 0.07 | 1.08 | (0.96, 1.25) |
| Time epoch 2 | 1.16 | 0.12 | 1.15 | (0.96, 1.42) |
| Time epoch 3 | 1.15 | 0.12 | 1.14 | (0.94, 1.41) |
| Time epoch 4 | 1.14 | 0.12 | 1.13 | (0.91, 1.39) |
| Time epoch 5 | 1.13 | 0.14 | 1.13 | (0.89, 1.42) |
| Time epoch 6 | 1.15 | 0.16 | 1.15 | (0.87, 1.49) |
| Time epoch 7 | 1.23 | 0.20 | 1.21 | (0.89, 1.65) |
| Time epoch 8 | 1.34 | 0.27 | 1.31 | (0.91, 1.98) |
| Time epoch 9 | 1.44 | 0.34 | 1.39 | (0.93, 2.25) |
| Time epoch 10 | 1.49 | 0.38 | 1.43 | (0.93, 2.42) |
| Time epoch 11 | 1.48 | 0.39 | 1.42 | (0.91, 2.43) |
| Time epoch 12 | 1.41 | 0.35 | 1.35 | (0.88, 2.23) |
| Time epoch 13 | 1.29 | 0.29 | 1.26 | (0.82, 1.97) |
| Time epoch 14 | 1.17 | 0.27 | 1.15 | (0.74, 1.78) |
| Time epoch 15 | 1.05 | 0.28 | 1.02 | (0.62, 1.69) |
| Time epoch 16 | 0.96 | 0.34 | 0.91 | (0.44, 1.78) |
| Time epoch 17 | 0.92 | 0.46 | 0.83 | (0.29, 2.06) |
| Immunodeficient (relative to not immunodeficient) | 0.36 | 0.09 | 0.35 | (0.21, 0.56) |
| Convalescent plasma in immunodeficient patients | 1.60 | 0.55 | 1.51 | (0.80, 2.92) |
| Convalescent plasma in non-immunodeficient patients | 0.92 | 0.08 | 0.92 | (0.78, 1.08) |

Table 88: Posterior probabilities for subgroup analysis with differential effect on OSFD by presence/abscence of immunodeficiency

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior in immunodeficient subgroup | 0.898 |
| Convalescent plasma is futile in immunodeficient subgroup (OR < 1.2) | 0.238 |
| Convalescent plasma is harmful in immunodeficient subgroup (OR < 1) | 0.102 |
| Convalescent plasma is superior to control in non-immunodeficient subgroup | 0.163 |
| Convalescent plasma is futile in non-immunodeficient subgroup (OR < 1.2) | 0.999 |
| Convalescent plasma is harmful in non-immunodeficient subgroup (OR < 1) | 0.837 |
| Convalescent plasma immunodeficient subgroup OR > Convalescent Plasma non-immunodeficient subgroup OR | 0.929 |

### 7.5.3 Subgroup analysis with differential effect on OSFD by presence/abscence of immunodeficiency

- Model: Primary analysis ordinal model

- Factors: Age, sex, site, time, control and convalescent plasma, presence/absence of immunodeficiency
- Differential treatment effects for convalescent plasma by presence/absence of immunodeficiency will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 89: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by presence/abscence of immunodeficiency

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.41 | 2.70 | 7.93 | (4.50, 15.04) |
| Age 40-49 | 3.11 | 0.57 | 3.06 | (2.15, 4.41) |
| Age 50-59 | 2.30 | 0.33 | 2.27 | (1.73, 2.99) |
| Age 70-79 | 0.50 | 0.07 | 0.49 | (0.38, 0.65) |
| Age 80+ | 0.34 | 0.08 | 0.33 | (0.20, 0.52) |
| Female | 1.35 | 0.15 | 1.34 | (1.07, 1.68) |
| Time epoch 1 | 1.10 | 0.07 | 1.09 | (0.96, 1.25) |
| Time epoch 2 | 1.19 | 0.12 | 1.18 | (0.97, 1.45) |
| Time epoch 3 | 1.25 | 0.15 | 1.24 | (0.98, 1.57) |
| Time epoch 4 | 1.31 | 0.17 | 1.30 | (1.00, 1.68) |
| Time epoch 5 | 1.34 | 0.19 | 1.33 | (1.01, 1.76) |
| Time epoch 6 | 1.37 | 0.22 | 1.35 | (0.98, 1.85) |
| Time epoch 7 | 1.41 | 0.27 | 1.38 | (0.95, 1.99) |
| Time epoch 8 | 1.48 | 0.32 | 1.45 | (0.94, 2.20) |
| Time epoch 9 | 1.57 | 0.39 | 1.52 | (0.95, 2.48) |
| Time epoch 10 | 1.65 | 0.45 | 1.58 | (0.96, 2.70) |
| Time epoch 11 | 1.69 | 0.48 | 1.62 | (0.97, 2.82) |
| Time epoch 12 | 1.72 | 0.48 | 1.66 | (0.98, 2.84) |
| Time epoch 13 | 1.76 | 0.49 | 1.70 | (0.98, 2.92) |
| Time epoch 14 | 1.84 | 0.55 | 1.75 | (1.01, 3.15) |
| Time epoch 15 | 1.95 | 0.69 | 1.83 | (0.96, 3.61) |
| Time epoch 16 | 2.12 | 0.97 | 1.92 | (0.86, 4.50) |
| Time epoch 17 | 2.39 | 1.59 | 2.00 | (0.71, 6.13) |
| Immunodeficient (relative to not immunodeficient) | 0.36 | 0.10 | 0.35 | (0.20, 0.60) |
| Convalescent plasma in immunodeficient patients | 1.57 | 0.60 | 1.47 | (0.72, 3.06) |
| Convalescent plasma in non-immunodeficient patients | 1.00 | 0.11 | 1.00 | (0.81, 1.24) |

Table 90: Posterior probabilities for subgroup analysis with differential effect on in-hospital mortality by presence/abscence of immunodeficiency

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior in immunodeficient subgroup | 0.850 |
| Convalescent plasma is futile in immunodeficient subgroup (OR < 1.2) | 0.295 |
| Convalescent plasma is harmful in immunodeficient subgroup (OR < 1) | 0.150 |
| Convalescent plasma is superior to control in non-immunodeficient subgroup | 0.489 |
| Convalescent plasma is futile in non-immunodeficient subgroup (OR < 1.2) | 0.956 |
| Convalescent plasma is harmful in non-immunodeficient subgroup (OR < 1) | 0.511 |
| Convalescent plasma immunodeficient subgroup OR > Convalescent Plasma non-immunodeficient subgroup OR | 0.839 |

## 7.6 Subgroup analyses by SARS CoV-2 antibody status

This section describes subgroup analyses based on the baseline SARS CoV-2 recipient antibody status. The two subgroups are baseline antibody positive and baseline antibody negative.

### 7.6.1 Data summaries of SARS CoV-2 antibody status in the Convalescent Plasma ITT population

Table 91: Summary of baseline SARS CoV-2 antibody status for patients randomized to convalescent plasma

| Intervention | Patients | Antibodies detected | Antibodies not detected | Unknown |
|---|---|---|---|---|
| Convalescent plasma | 1075 | 599 (55.7%) | 271 (25.2%) | 205 (19.1%) |
| Control | 905 | 409 (45.2%) | 148 (16.4%) | 348 (38.5%) |

Table 92: Summary of subjects by baseline SARS CoV antibody status in the Convalescent Plasma ITT population

| Antibody Subgroup | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **Antibodies detected** | | | | | |
| Convalescent plasma | 599 | 597 | 190 (31.8%) | 8 (-1, 17) | 15 (7, 18) |
| Control | 409 | 405 | 135 (33.3%) | 10 (-1, 17) | 15 (10, 18) |
| **Antibodies not detected** | | | | | |
| Convalescent plasma | 271 | 270 | 130 (48.1%) | 0 (-1, 10) | 10 (0, 15) |
| Control | 148 | 148 | 78 (52.7%) | -1 (-1, 10) | 11 (0, 16) |
| **Unknown** | | | | | |
| Convalescent plasma | 205 | 205 | 81 (39.5%) | 0 (-1, 15) | 13 (0, 18) |
| Control | 348 | 347 | 132 (38%) | 3 (-1, 16) | 14 (7, 17) |

* Days Free of Organ Support in Survivors measured within 21 days.

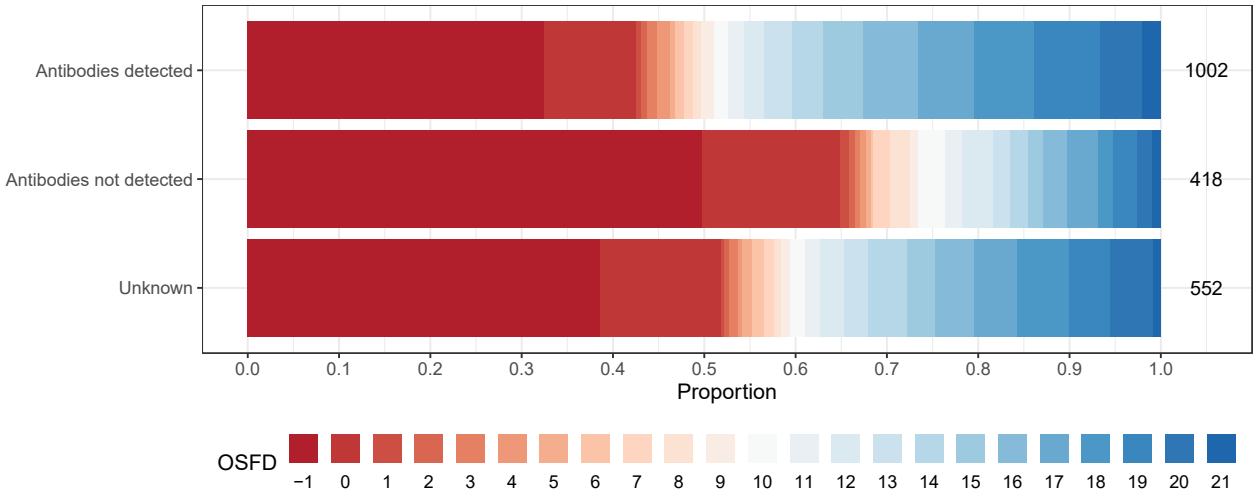


Figure 29: Empirical distribution of organ support free days (OSFD) by baseline SARS CoV antibody status. This plot is restricted to the Convalescent Plasma ITT population.

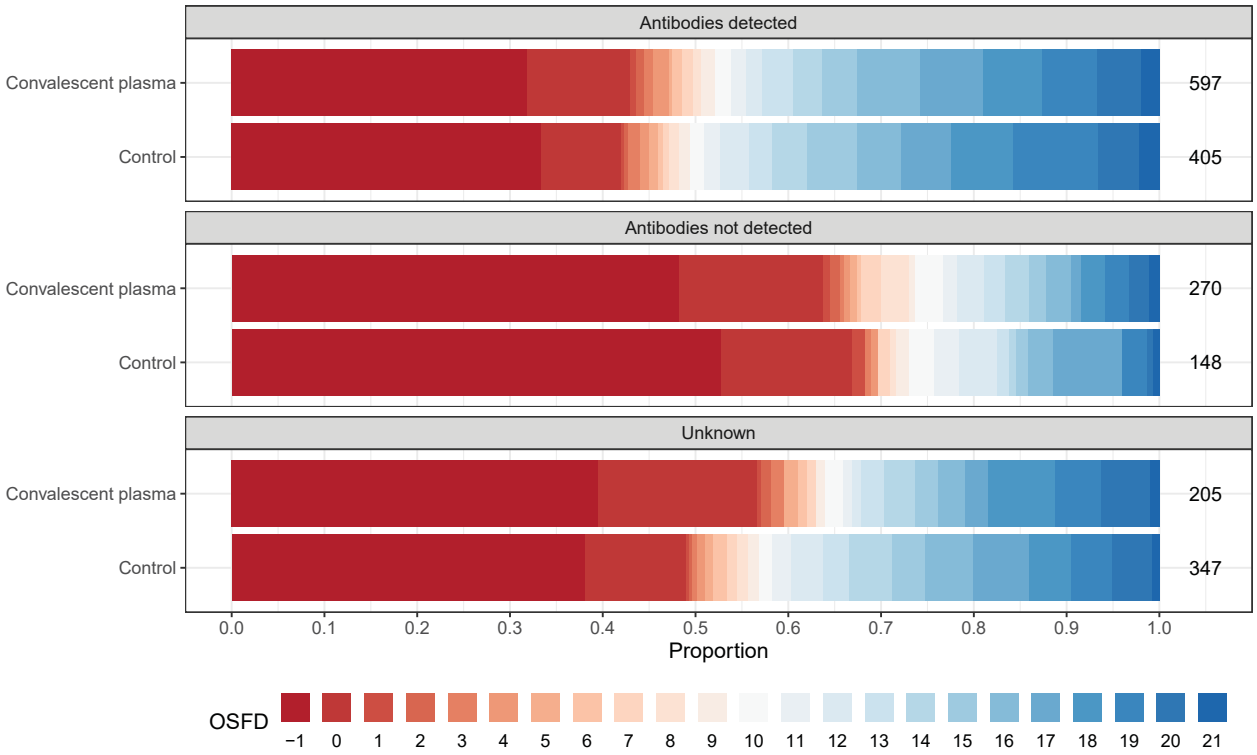


Figure 30: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control by baseline SARS CoV antibody status. This plot is restricted to the Convalescent Plasma ITT population.

### 7.6.2 Subgroup analysis with differential effect on OSFD by baseline SARS CoV-2 antibody status

- Model: Primary analysis ordinal model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline SARS CoV-2 antibody status
- Differential treatment effects for convalescent plasma by baseline SARS CoV-2 antibody status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 93: Odds ratio parameters for subgroup analysis with differential effect on OSFD by SARS CoV antibody status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 4.55 | 0.76 | 4.49 | (3.24, 6.21) |
| Age 40-49 | 2.47 | 0.33 | 2.45 | (1.88, 3.17) |

Table 93: Odds ratio parameters for subgroup analysis with differential effect on OSFD by SARS CoV antibody status *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age 50-59 | 1.81 | 0.20 | 1.80 | (1.44, 2.23) |
| Age 70-79 | 0.52 | 0.07 | 0.52 | (0.40, 0.66) |
| Age 80+ | 0.35 | 0.08 | 0.34 | (0.21, 0.52) |
| Female | 1.18 | 0.10 | 1.18 | (0.99, 1.39) |
| Time epoch 1 | 1.09 | 0.07 | 1.09 | (0.96, 1.25) |
| Time epoch 2 | 1.16 | 0.11 | 1.15 | (0.96, 1.42) |
| Time epoch 3 | 1.14 | 0.12 | 1.13 | (0.93, 1.40) |
| Time epoch 4 | 1.12 | 0.12 | 1.12 | (0.90, 1.38) |
| Time epoch 5 | 1.13 | 0.13 | 1.12 | (0.88, 1.41) |
| Time epoch 6 | 1.15 | 0.16 | 1.15 | (0.87, 1.50) |
| Time epoch 7 | 1.23 | 0.20 | 1.22 | (0.89, 1.67) |
| Time epoch 8 | 1.35 | 0.27 | 1.32 | (0.92, 1.98) |
| Time epoch 9 | 1.45 | 0.34 | 1.40 | (0.93, 2.24) |
| Time epoch 10 | 1.51 | 0.38 | 1.44 | (0.93, 2.41) |
| Time epoch 11 | 1.51 | 0.40 | 1.45 | (0.92, 2.47) |
| Time epoch 12 | 1.45 | 0.37 | 1.39 | (0.90, 2.33) |
| Time epoch 13 | 1.32 | 0.31 | 1.28 | (0.84, 2.03) |
| Time epoch 14 | 1.18 | 0.27 | 1.15 | (0.74, 1.79) |
| Time epoch 15 | 1.03 | 0.27 | 1.00 | (0.60, 1.66) |
| Time epoch 16 | 0.92 | 0.33 | 0.87 | (0.42, 1.70) |
| Time epoch 17 | 0.85 | 0.42 | 0.76 | (0.28, 1.88) |
| Antibodies not detected (relative to detected) | 0.36 | 0.07 | 0.36 | (0.25, 0.51) |
| Unknown antibody status (relative to detected) | 0.65 | 0.09 | 0.64 | (0.49, 0.86) |
| Convalescent plasma with antibodies detected | 0.92 | 0.11 | 0.92 | (0.73, 1.15) |
| Convalescent plasma with antibodies not detected | 1.09 | 0.22 | 1.07 | (0.73, 1.57) |
| Convalescent plasma with unknown antibody status | 0.97 | 0.16 | 0.96 | (0.69, 1.33) |

Table 94: Posterior probabilities for subgroup analysis with differential effect on OSFD by SARS CoV Antibody status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with antibodies detected | 0.230 |
| Convalescent plasma is futile with antibodies detected (OR < 1.2) | 0.989 |
| Convalescent plasma is harmful with antibodies detected (OR < 1) | 0.770 |
| Convalescent plasma is superior to control with antibodies not detected | 0.626 |
| Convalescent plasma is futile with antibodies not detected (OR < 1.2) | 0.723 |
| Convalescent plasma is harmful with antibodies not detected (OR < 1) | 0.374 |
| Convalescent plasma is superior to control with unknown antibodies | 0.403 |
| Convalescent plasma is futile with unknown antibodies (OR < 1.2) | 0.911 |
| Convalescent plasma is harmful with unknown antibodies (OR < 1) | 0.597 |

Table 94: Posterior probabilities for subgroup analysis with differential effect on OSFD by SARS CoV Antibody status *(continued)*

| | Posterior Probability |
|---|---|
| Convalescent plasma with antibodies detected OR > Convalescent plasma with antibodies not detected OR | 0.247 |
| Convalescent plasma with antibodies detected OR > Convalescent plasma with unknown antibodies OR | 0.410 |
| Convalescent plasma with antibodies not detected OR > Convalescent plasma with unknown antibodies OR | 0.658 |

### 7.6.3 Subgroup analysis with differential effect on in-hospital mortality by baseline SARS CoV-2 antibody status

- Model: Primary dichotomous model
- Factors: Age, sex, site, time, control and convalescent plasma interventions, baseline SARS CoV-2 antibody status
- Differential treatment effects for convalescent plasma by baseline SARS CoV-2 antibody status will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 95: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by SARS CoV antibody status

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 8.59 | 2.71 | 8.13 | (4.66, 15.03) |
| Age 40-49 | 3.24 | 0.59 | 3.19 | (2.24, 4.56) |
| Age 50-59 | 2.30 | 0.33 | 2.27 | (1.73, 3.02) |
| Age 70-79 | 0.51 | 0.07 | 0.50 | (0.38, 0.66) |
| Age 80+ | 0.34 | 0.09 | 0.33 | (0.20, 0.53) |
| Female | 1.37 | 0.16 | 1.36 | (1.09, 1.71) |
| Time epoch 1 | 1.10 | 0.08 | 1.09 | (0.96, 1.26) |
| Time epoch 2 | 1.19 | 0.12 | 1.18 | (0.97, 1.46) |
| Time epoch 3 | 1.25 | 0.15 | 1.24 | (0.98, 1.57) |
| Time epoch 4 | 1.31 | 0.17 | 1.30 | (1.01, 1.68) |
| Time epoch 5 | 1.36 | 0.20 | 1.34 | (1.02, 1.78) |
| Time epoch 6 | 1.39 | 0.23 | 1.38 | (0.99, 1.88) |
| Time epoch 7 | 1.44 | 0.27 | 1.41 | (0.97, 2.04) |
| Time epoch 8 | 1.52 | 0.33 | 1.48 | (0.96, 2.27) |
| Time epoch 9 | 1.61 | 0.39 | 1.56 | (0.98, 2.54) |
| Time epoch 10 | 1.69 | 0.45 | 1.63 | (1.00, 2.75) |
| Time epoch 11 | 1.76 | 0.49 | 1.70 | (1.03, 2.93) |

Table 95: Odds ratio parameters for subgroup analysis with differential effect on in-hospital mortality by SARS CoV antibody status *(continued)*

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Time epoch 12 | 1.82 | 0.50 | 1.74 | (1.04, 2.99) |
| Time epoch 13 | 1.87 | 0.52 | 1.79 | (1.06, 3.11) |
| Time epoch 14 | 1.94 | 0.59 | 1.85 | (1.06, 3.34) |
| Time epoch 15 | 2.05 | 0.74 | 1.91 | (1.01, 3.86) |
| Time epoch 16 | 2.19 | 1.04 | 1.97 | (0.87, 4.77) |
| Time epoch 17 | 2.43 | 1.64 | 2.04 | (0.70, 6.32) |
| Antibodies not detected (relative to detected) | 0.43 | 0.09 | 0.42 | (0.28, 0.64) |
| Unknown antibody status (relative to detected) | 0.71 | 0.13 | 0.70 | (0.49, 0.99) |
| Convalescent plasma with antibodies detected | 1.00 | 0.15 | 0.99 | (0.74, 1.33) |
| Convalescent plasma with antibodies not detected | 1.16 | 0.26 | 1.12 | (0.73, 1.76) |
| Convalescent plasma with unknown antibody status | 1.07 | 0.22 | 1.05 | (0.72, 1.55) |

Table 96: Posterior probabilities for subgroup analysis with differential effect on in-hospital mortality by SARS CoV antibody status

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with antibodies detected | 0.482 |
| Convalescent plasma is futile with antibodies detected (OR < 1.2) | 0.894 |
| Convalescent plasma is harmful with antibodies detected (OR < 1) | 0.518 |
| Convalescent plasma is superior to control with antibodies not detected | 0.706 |
| Convalescent plasma is futile with antibodies not detected (OR < 1.2) | 0.612 |
| Convalescent plasma is harmful with antibodies not detected (OR < 1) | 0.294 |
| Convalescent plasma is superior to control with unknown antibodies | 0.600 |
| Convalescent plasma is futile with unknown antibodies (OR < 1.2) | 0.748 |
| Convalescent plasma is harmful with unknown antibodies (OR < 1) | 0.400 |
| Convalescent plasma with antibodies detected OR > Convalescent plasma with antibodies not detected OR | 0.317 |
| Convalescent plasma with antibodies detected OR > Convalescent plasma with unknown antibodies OR | 0.411 |
| Convalescent plasma with antibodies not detected OR > Convalescent plasma with unknown antibodies OR | 0.589 |

## 7.7 Posthoc subgroup analysis of viral load

In response to reviewers, we have included this additional subgroup analysis looking at treatment effect results of Convalescent Plasma compared to control based on baseline viral load (grouped by Negative, 100-1000, 1000-10,000, 10,000-100,000, >100,000). Only patients from UK sites had viral load data available. Therefore, the summaries and analysis are estimated only on patients from the UK sites with this information available.

### 7.7.1 Data summaries of viral load levels in the UK patients in the Convalescent Plasma ITT population

Table 97: Summary of baseline viral load for UK patients

| Intervention | Patients | Negative | 100-1000 | 1000-10,000 | 10,000-100,000 | >100,000 |
|---|---|---|---|---|---|---|
| Convalescent plasma | 701 | 61 (8.7%) | 53 (7.6%) | 110 (15.7%) | 53 (17.8%) | 110 (50.2%) |
| Control | 458 | 52 (11.4%) | 37 (8.1%) | 69 (15.1%) | 37 (17%) | 69 (48.5%) |

Table 98: Summary of subjects by viral load grouping in the UK patients of the Convalescent Plasma ITT population

| Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|
| **Negative** | | | | | |
| Convalescent plasma | 61 | 61 | 17 (27.9%) | 13 (-1, 16) | 15 (12, 17.25) |
| Control | 52 | 52 | 17 (32.7%) | 10 (-1, 17) | 16 (10, 18) |
| **100-1000** | | | | | |
| Convalescent plasma | 53 | 53 | 12 (22.6%) | 12 (0, 18) | 16 (7, 19) |
| Control | 37 | 36 | 7 (19.4%) | 15.5 (6, 18.25) | 17 (14, 19) |
| **1000-10,000** | | | | | |
| Convalescent plasma | 110 | 110 | 29 (26.4%) | 13 (-1, 18) | 16 (10, 18) |
| Control | 69 | 68 | 21 (30.9%) | 14.5 (-1, 18) | 17 (13.5, 19) |
| **10,000-100,000** | | | | | |
| Convalescent plasma | 125 | 125 | 51 (40.8%) | 0 (-1, 15) | 14 (1.25, 17) |
| Control | 78 | 78 | 36 (46.2%) | 0 (-1, 15) | 15 (5.5, 18.75) |
| **>100,000** | | | | | |
| Convalescent plasma | 352 | 351 | 156 (44.4%) | 0 (-1, 12.5) | 11 (0, 16) |
| Control | 222 | 221 | 106 (48%) | 0 (-1, 13) | 12 (2.5, 17) |

* Days Free of Organ Support in Survivors measured within 21 days.

Table 99: Summary of subjects by viral load grouping and immunodeficiency status in the UK patients of the Convalescent Plasma ITT population

| Immunodeficiency Subgroup | Intervention | Patients | Known | Deaths (%) | OSFD median (IQR) | OSFD in Survivors* median (IQR) |
|---|---|---|---|---|---|---|
| **Negative** | | | | | | |
| No immunodeficiency | Convalescent plasma | 57 | 57 | 15 (26.3%) | 13 (-1, 17) | 15.5 (12, 17.75) |
| | Control | 49 | 49 | 15 (30.6%) | 11 (-1, 17) | 16 (10.25, 18) |
| Immunodeficiency | Convalescent plasma | 4 | 4 | 2 (50%) | -0.5 (-1, 3.25) | 6.5 (3.25, 9.75) |
| | Control | 3 | 3 | 2 (66.7%) | -1 (-1, 1) | 3 (3, 3) |
| **100-1000** | | | | | | |
| No immunodeficiency | Convalescent plasma | 51 | 51 | 11 (21.6%) | 14 (0, 18) | 16 (7, 19) |
| | Control | 36 | 36 | 7 (19.4%) | 15.5 (6, 18.25) | 17 (14, 19) |
| Immunodeficiency | Convalescent plasma | 2 | 2 | 1 (50%) | 3.5 (1.25, 5.75) | 8 (8, 8) |
| **1000-10,000** | | | | | | |
| No immunodeficiency | Convalescent plasma | 104 | 104 | 28 (26.9%) | 12.5 (-1, 18) | 16.5 (9.25, 18) |
| | Control | 65 | 65 | 19 (29.2%) | 15 (-1, 18) | 17 (14.25, 19) |
| Immunodeficiency | Convalescent plasma | 6 | 6 | 1 (16.7%) | 15 (10.5, 16.5) | 15 (15, 17) |
| | Control | 3 | 3 | 2 (66.7%) | -1 (-1, 3) | 7 (7, 7) |
| **10,000-100,000** | | | | | | |
| No immunodeficiency | Convalescent plasma | 118 | 118 | 47 (39.8%) | 0 (-1, 15) | 15 (1, 17.5) |
| | Control | 72 | 72 | 32 (44.4%) | 0 (-1, 15) | 15 (4.5, 19) |
| Immunodeficiency | Convalescent plasma | 7 | 7 | 4 (57.1%) | -1 (-1, 9) | 10 (9, 12) |
| | Control | 6 | 6 | 4 (66.7%) | -1 (-1, 5) | 12.5 (9.75, 15.25) |
| **>100,000** | | | | | | |
| No immunodeficiency | Convalescent plasma | 325 | 324 | 142 (43.8%) | 0 (-1, 12) | 10 (0, 16) |
| | Control | 202 | 201 | 93 (46.3%) | 0 (-1, 14) | 12.5 (2.75, 17) |
| Immunodeficiency | Convalescent plasma | 27 | 27 | 14 (51.9%) | -1 (-1, 13.5) | 14 (10, 18) |
| | Control | 20 | 20 | 13 (65%) | -1 (-1, 2.25) | 12 (4.5, 13.5) |

* Days Free of Organ Support in Survivors measured within 21 days.

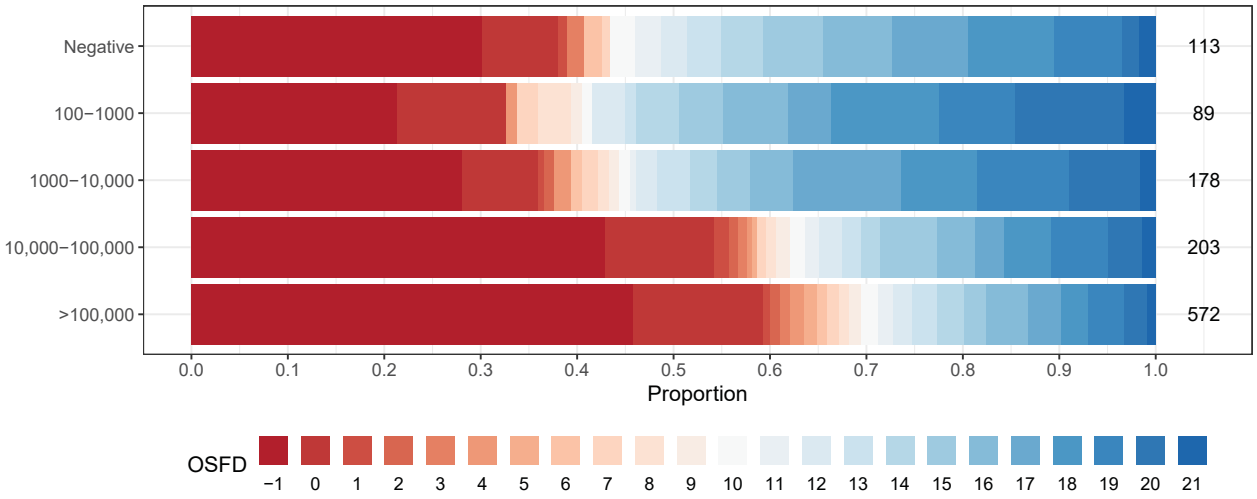


Figure 31: Empirical distribution of organ support free days (OSFD) by baseline viral load. This plot is restricted to the UK patients from the CP ITT population.

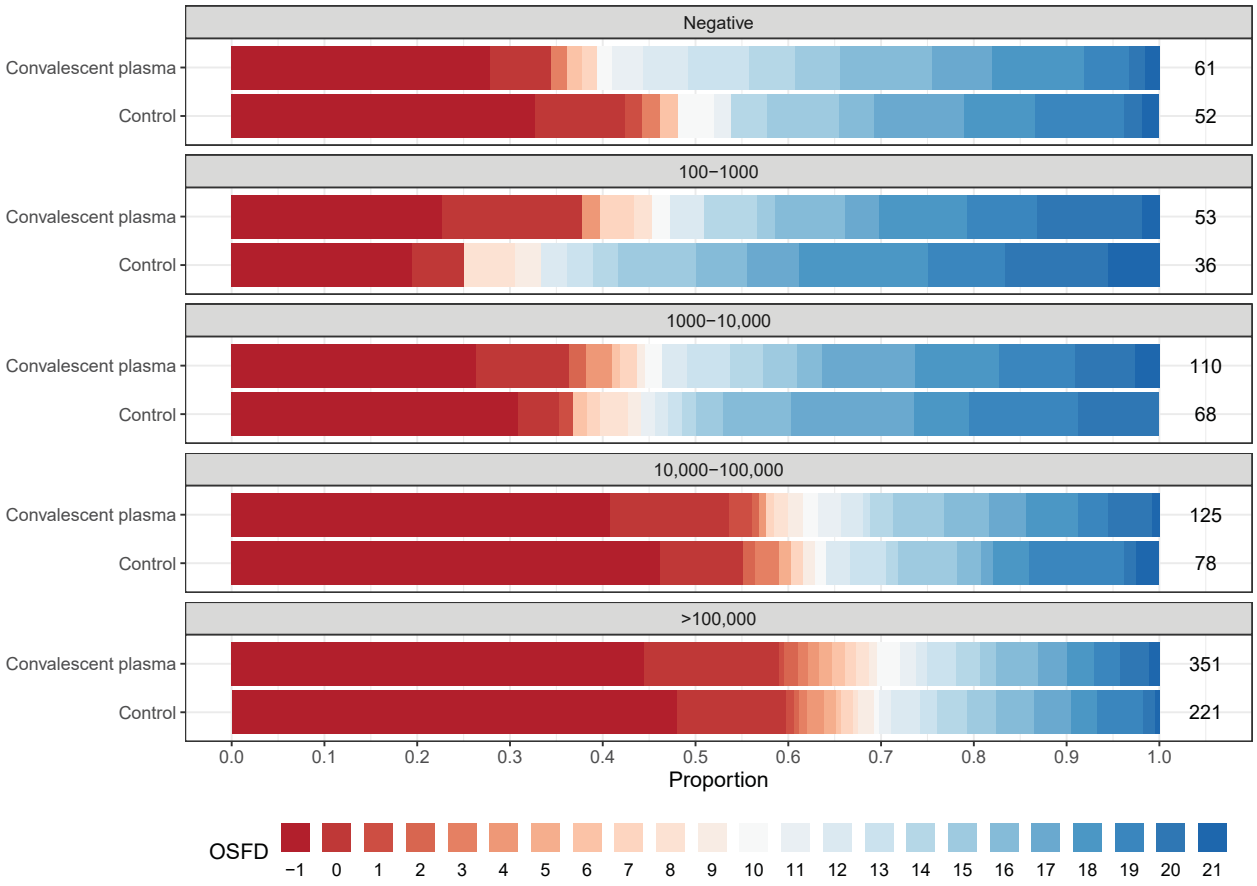


Figure 32: Empirical distribution of organ support free days (OSFD) for convalescent plasma and control by baseline viral load. This plot is restricted to the UK patients from the Convalescent Plasma ITT population.

### 7.7.2 Subgroup analysis with differential effect on OSFD by viral load levels

- Model: Primary ordinal model
- Factors: Age, sex, time, control and convalescent plasma interventions, baseline viral load (grouped by Negative, 100-1000, 1000-10,000, 10,000-100,000, >100,000)
- Differential treatment effects for convalescent plasma by baseline viral load will be compared to the control arm. A posterior probability of superiority of 99% will be used as a statistical trigger for efficacy for each subgroup.
- Population: Convalescent Plasma ITT

Table 100: Odds ratio parameters for subgroup analysis with differential effect on OSFD by viral load

| | Mean | SD | Median | CrI |
|---|---|---|---|---|
| Age<39 | 2.93 | 0.66 | 2.86 | (1.87, 4.40) |
| Age 40-49 | 2.26 | 0.39 | 2.23 | (1.59, 3.10) |
| Age 50-59 | 1.94 | 0.28 | 1.92 | (1.46, 2.55) |
| Age 70-79 | 0.59 | 0.10 | 0.58 | (0.42, 0.79) |
| Age 80+ | 0.61 | 0.18 | 0.59 | (0.33, 1.02) |
| Female | 1.18 | 0.13 | 1.17 | (0.94, 1.46) |
| Time epoch 1 | 1.07 | 0.08 | 1.07 | (0.93, 1.26) |
| Time epoch 2 | 1.11 | 0.13 | 1.10 | (0.90, 1.40) |
| Time epoch 3 | 1.07 | 0.13 | 1.06 | (0.84, 1.35) |
| Time epoch 4 | 1.04 | 0.14 | 1.03 | (0.80, 1.33) |
| Time epoch 5 | 0.99 | 0.14 | 0.98 | (0.74, 1.29) |
| Time epoch 6 | 0.96 | 0.16 | 0.95 | (0.68, 1.30) |
| Time epoch 7 | 0.95 | 0.18 | 0.94 | (0.63, 1.34) |
| Time epoch 8 | 1.00 | 0.23 | 0.98 | (0.62, 1.51) |
| Time epoch 9 | 1.07 | 0.30 | 1.03 | (0.62, 1.78) |
| Time epoch 10 | 1.15 | 0.37 | 1.09 | (0.63, 2.05) |
| Time epoch 11 | 1.21 | 0.42 | 1.14 | (0.65, 2.27) |
| Time epoch 12 | 1.24 | 0.43 | 1.16 | (0.66, 2.30) |
| Time epoch 13 | 1.23 | 0.39 | 1.17 | (0.65, 2.18) |
| Time epoch 14 | 1.21 | 0.39 | 1.16 | (0.63, 2.12) |
| Time epoch 15 | 1.23 | 0.46 | 1.15 | (0.56, 2.34) |
| Time epoch 16 | 1.31 | 0.66 | 1.17 | (0.45, 2.96) |
| Time epoch 17 | 1.48 | 1.22 | 1.21 | (0.34, 4.16) |
| 100-1000 viral load (relative to negative) | 2.16 | 0.76 | 2.04 | (1.04, 4.02) |
| 1000-10,000 viral load (relative to negative) | 1.51 | 0.47 | 1.44 | (0.81, 2.59) |
| 10,000-100,000 viral load (relative to negative) | 0.68 | 0.20 | 0.65 | (0.37, 1.16) |
| >100,000 viral load (relative to negative) | 0.56 | 0.14 | 0.54 | (0.34, 0.88) |
| Convalescent plasma with negative viral load | 1.06 | 0.33 | 1.01 | (0.56, 1.84) |
| Convalescent plasma with 100-1000 viral load | 0.74 | 0.28 | 0.70 | (0.34, 1.41) |
| Convalescent plasma with 1000-10,000 viral load | 0.93 | 0.25 | 0.90 | (0.54, 1.51) |
| Convalescent plasma with 10,00-100,000 viral load | 1.09 | 0.28 | 1.06 | (0.64, 1.74) |
| Convalescent plasma with >100,000 viral load | 1.01 | 0.16 | 0.99 | (0.74, 1.36) |

Table 101: Posterior probabilities for subgroup analysis with differential effect on OSFD by viral load

| | Posterior Probability |
|---|---|
| Convalescent plasma is superior to control with negative viral load | 0.510 |
| Convalescent plasma is futile with negative viral load (OR < 1.2) | 0.715 |
| Convalescent plasma is harmful with negative viral load (OR < 1) | 0.490 |
| Convalescent plasma is superior to control with 100-1000 viral load | 0.156 |

Table 101: Posterior probabilities for subgroup analysis with differential effect on OSFD by viral load *(continued)*

| | Posterior Probability |
|---|---|
| Convalescent plasma is futile with 100-1000 viral load (OR < 1.2) | 0.936 |
| Convalescent plasma is harmful with 100-1000 viral load (OR < 1) | 0.844 |
| Convalescent plasma is superior to control with 1000-10,000 viral load | 0.340 |
| Convalescent plasma is futile with 1000-10,000 viral load (OR < 1.2) | 0.867 |
| Convalescent plasma is harmful with 1000-10,000 viral load (OR < 1) | 0.660 |
| Convalescent plasma is superior to control with 10,000-100,000 viral load | 0.585 |
| Convalescent plasma is futile with 10,000-100,000 viral load (OR < 1.2) | 0.695 |
| Convalescent plasma is harmful with 10,000-100,000 viral load (OR < 1) | 0.415 |
| Convalescent plasma is superior to control with >100,000 viral load | 0.484 |
| Convalescent plasma is futile with >100,000 viral load (OR < 1.2) | 0.890 |
| Convalescent plasma is harmful with >100,000 viral load (OR < 1) | 0.515 |

# 8 Report production and data sources

All analyses in this report are based on the following documents:

- Statistical Analysis Appendix for REMAP-COVID, version 1, dated August 18, 2020;
- Statistical Analysis Plan for the Immunoglobulin Domain for Patients with COVID-19 Pandemic Infection Suspected Or Proven (PISOP), version 1.1, dated February 23, 2021;
- Current State of the Statistical Model: Pandemic Model, version 3.1, dated March 1, 2021

The blinded ITSC analysis team at Berry Consultants performed the analyses in this report using data received from multiple sources. The OSFD outcomes and treatment assignments for patients in unblinded domains were sent from the unblinded Statistical Analysis Committee (SAC) with all blinded information removed. The baseline/discharge, daily, and medication data for patients randomized in unblinded domains were sent from an unblinded data coordination team at Monash University. The table below shows the file names for the data exports from each data source and the date each file was received by the blinded ITSC analysis committee. All merging and summarization of data was done using the R statistical computing environment. This report was generated from an Rmarkdown document in the Rstudio software.

Table 102: Summary of data sources

| Filename | Date received | Description |
|---|---|---|
| merged_REMAP_PISOPSevere_CP_2021-04-22.csv | April 22, 2021 | OSFD and treatment assignments from unblinded SAC |
| Immunoglobulin baseline discharge data_April19_withH_Designteam.csv | May 6, 2021 | Baseline and discharge data for unblinded ITT |
| Immunoglobulin_additionalPCRdata.csv | May 12, 2021 | Additional data on PCR and antibody status for control patients |
| Immunoglobulin daily_April19_withH_Designteam.csv | May 6, 2021 | Daily ICU data for unblinded ITT |
| Immunoglobulin cpdata_April19.csv | April 23, 2021 | Convalescent plasma medication data |