Natural history, trajectory, and management of mechanically ventilated COVID-19 patients in the United Kingdom

Supplementary Appendix

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STROBE statement

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8-10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	8-10
Study size	10	Explain how the study size was arrived at	8

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-10
		(*b*) Describe any methods used to examine subgroups and interactions	8-10
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	8-10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	8-10
		(c) Consider use of a flow diagram	Fig1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	11-13
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-13

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-13
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	11-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Detailed Methods

Study design. We performed a multicentre, observational cohort study in patients with SARS-CoV-2 infection who required mechanical ventilation for severe Covid-19 infection in the United Kingdom.

Exposure. Adult patients (aged ≥18 years) with laboratory confirmed SARS-CoV-2 infection who required mechanical ventilation in the United Kingdom between March 1st and August 31st 2020.

Ethical approval. Each site registered the protocol as a service evaluation, as approved by the United Kingdom's Health Research Authority. All patients lacked capacity, and the need for individual informed consent was waived for collection of data during routine care, with no breach of privacy or anonymity. The "Strengthening the Reporting of Observational Studies in Epidemiology" statement guidelines were applied (see supplementary appendix pages 4-5) [1].

Data collection and procedures. We set up a data processing pipeline where only routine, anonymised data was collected with no change to clinical care. Patients were identified through daily review of paper or electronic medical records using a standardised case record form (CRF), with retrospective and prospective data collection permitted. Data was extracted from either electronic healthcare records (EHRs) or paper-based records. Sites were given the option to submit their EHRs either in a predetermined format set by the Covid-ICU own secure REDCap database form fields or as a raw dump of data in CSV file format, that was then record-by-record manually screened for data consistency. Paper-based ICU operations sites were able to enter the data directly by the site representative into our REDCap Electronic Data Capture (REDCap v10.0.10; Vanderbilt University, US, local version hosted by Imperial College servers in the UK).

Each site's representative was given a unique username and password for data entering-only access to the database to connect via an encrypted online connection. Confidentiality was protected through a de-identified study number. A range of ICUs were included including secondary and tertiary care organisations (Table S1). In brief, the CRF captured admission demographics, twice daily (8am and 8pm) respiratory physiology and blood gas results, daily ARDS interventions, daily Covid interventions, daily blood results and outcome status. Patients were categorized within 48 hours of invasive mechanical ventilation (IMV) based on their PaO_2/FIO_2 ratio into no ARDS, mild, moderate, and severe ARDS [2].

***ECMO*.** We excluded patients progressing to ECMO. This had a number of reasons: we could not collect timing of ECMO as these data are collected on an online referral system with limited access. Indeed, most patients in the UK were not eligible for ECMO during the pandemic as they did not fall within the acceptance criteria for the national service in the UK (Camporota, L. et al. Consensus on the referral and admission of patients with severe respiratory failure to the NHS ECMO service. Lancet Respir Medicine (2021) doi:10.1016/s2213-2600(20)30581-6). Hence, the exact number of patients placed onto ECMO from the participating ICUs does not provide an accurate reflection of ECMO provision given the commissioned provision of ECMO nationally by five "specialist" centres. We have obtained data from the national commissioners for the time period covered by the study to ensure data transparency. Overall, between March 1st to August 31st, there were 1596 referrals (20% of all ventilated patients) to the service with 306 patients (4% of all ventilated patients) accepted for ECMO in the United Kingdom (data from NHS England commissioned service).

We note, that our deep learning model suggested that PaO2/FiO2, ventilatory ratio and peak pressure to be increasingly predictive of outcome across the first week, in addition to other measures including platelet count, CRP and lactate. ECMO aspects would be worthy of a separate study.

***Resolution of hypoxaemia over first week of IMV*.** Hypoxaemia was categorised as per Berlin definition of ARDS [2]. First week resolvers were defined by moving over the first week of mechanical ventilation to a less severe ARDS hypoxaemia category, and vice-versa for non-resolvers [2,3]. In addition to the patients who resolved, also those who remained mild or got discharged were considered "resolvers" while those who deteriorate, remained moderate or severe, or died, were considered "non-resolvers".

***Responsiveness to prone position*.** We considered the longer-term effect on PaO_2/FiO_2 after prone positioning and defined prone responsiveness as maintenance of a mean PaO_2/FiO_2 >20kPa over 7 days after the first prone episode. Finally, we defined a proning window as a PaO_2/FiO_2<20kPa, with an $FiO_2 \geq 0.6$, a PEEP≥5cmH_2O to assess opportunities to apply the intervention. Prone windows were measured at 8am and 8pm with the ventilator and arterial blood gas evaluation.

***Interventions periods*.** The incidence and duration of interventions as well as ventilation setting were analysed and reported to current strategies e.g. low tidal volume ventilation and ARDSNet PEEP tables. We defined an intervention period as a daily application of the intervention with a day of no intervention defining the end of the current period and the onset of the next period.

Logistic regression in statistical analysis (details). We ran multivariate logistic regression models, using backward method for variable selection (with screening univariate, $p<0.1$) to each outcome variable to test associations with independent variables. The full list of variables tested for inclusion in these models is shown in Supplementary Table S2. This means that only variables with less than 40% missingness were included in each outcome model (missing value analysis in the relevant time points for each analysis is shown in Table S2). Variables that showed clinical overlap (e.g. SOFA renal and creatinine) had one variable excluded. A data driven approach to collinearity was not taken as many clinical variables were associated with each other due to relationships with severity of illness. A full correlation matrix for each analysis can be found in the Supplementary figures (see Figure SX). For all outcomes, only patients with more than 80% of the variables were included in the models. Accordingly, up to 20% of the data were missing and thus were imputed. Thus, Missing values and imputation were handled according to the following data curation protocol: 1. we removed variables with >40% missingness (deletion of a variable across all patient records); 2. we removed patients which showed >20% missingness on those variables (deletion of patient records if the individual records were too incomplete); 3. Imputing the missing data – which means <20% of the data is imputation. Data imputation was applied using k-nearest neighbours' algorithm. We ran the imputation with a k of 3, 5, and 7 both on the continuous variable and on the quartile categorization. The maximal odds ratio difference between the imputation approaches for each variable was 0.04 (IQR 0.03-0.07) and had no effect on the significance. All reported results are based on 5-nearest neighbours' imputation on the quartile categorization. Data were assumed to be missing at random (MAR) owing to the nature of different personnel at many different sites completing each data entry (the full missing value analysis, by site and by day, is shown in Tables S2, S3 and S4). To enable interpretable and comparable odds ratios, all continuous variables were transformed to categorical by splitting them into quartiles. Accordingly, the odds ratio is the risk increase per quartile increase in the measurement. For age, the odds ratio is the risk increase per decade increase; for SOFA scores, the odds ratio is the risk increase per unit increase in the SOFA score; and for binary variables (e.g., gender, comorbidities) the odds ratio is the risk increase of being positive (e.g. being male, having comorbidity).

Statistical analysis of longitudinal measures (details). The rmANOVA was applied separately to each physiology variable, and for each variable, only patients with more than 80% of the variable's measurements over that week were included in the model. Since this is a univariate analysis over time, here, the missing data points were imputed with a linear interpolation. Variables for which fewer than

30 patients had more than 80% of the measurements were not analysed. To minimise information censuring (due to death or improvement) and resultant bias in longitudinal analyses, only patients with continuous data for the first 7 days were included. To prevent the risk of too many false positive, we accounted for multiple comparisons in the interaction statistic by controlling the false discovery rate (FDR).

Machine Learning models for of daily and weeklong- mortality prediction (details). Imputation for our machine learning models followed the following procedure: We performed advanced statistical inference using Expectation-Maximisation to infer the most likely missing data value based on the overall data correlation structures, performing all imputations simultaneously to maximise the joint probability of the imputed and measured data: Empirical analysis showed that our clinical parameters were either continuously distributed with normal or log-normal distributions or discretely distributed categorical data. We transformed the log-normal values into normal temporary variables. We performed Probabilistic Principal Component Analysis on the variables, without performing dimensionality reduction, so as to reconstruct any missing values in the data tables, encoded as Not a Number (NaN) values [4]. We used the Expectation-Maximisation to iteratively fill in all missing values so that they were most consistent given the data within the clinical parameters, as well as the correlation structure across clinical parameters. We then back-transformed all log-normal distributed values and verified by systematic inspection that the imputed values were self-consistent with the data [SEE Figure S10 in Supplemental].

The deep neural network used fully connected layers consisting of 32 and then 16 neurons, respectively, and an output layer with one neuron (directly encoding mortality). We utilised the rectified linear activation function (ReLU) nonlinearity between each layer. This model comes closest to a generalisation of logistic regression, chosen because of the fixed amount of data, so as to encapsulate a relatively compact, but yet more flexible function approximator than logistic regression. We tried also changes to the neural network architecture with a deeper, 5-layer design, and another architecture with a recurrent LSTM layer to operate on the time series but found that in both cases the more compact 3-layer model performed best. We think of the 3-layer model as a non-linear extension of logistic regression with more expressive power to model the data but a relatively small increase in model complexity.

We utilised 30 epochs for training and a 70-to-30 ratio was used to divide the data into training data (70%) and testing data (30%). Even though the mortality label's distribution in the data was not particularly imbalanced, we nevertheless utilised a Synthetic Minority Oversampling Technique (SMOTE) [5]. The testing data were also randomly sampled to have a balanced distribution of mortality

labels when evaluating and reporting performance. All models were implemented in the PyTorch framework and a single workstation with a GPU was used to train and test all models.

Grouping of dynamic clinical parameter importance through Explainable AI (details). Through interactive data visualisation we were able to identify that the importance of clinical parameters for mortality prediction changed day-by-day over the first week in both the logistic regression and the deep learning model. We grouped the importance of each clinical parameter into 4 categories of 1. increasing, 2. decreasing, 3. constant high and 4. constant low importance for predicting mortality outcome. We utilised a hard thresholding of absolute SHAP values to distinguish between group 1.+3. and 2.+4.: We deemed features with a mean of absolute SHAP value greater than 0.02 to be in the high or rising importance group and the rest to be of low or losing importance group. The threshold was derived from inspection of the empirical histogram of the absolute SHAP suggesting two modes. We then used linear regression coefficients of the SHAP values over the week (giving us a trendline) to distinguish between constant (3.+4.) and changing (1.+2.) variables. In the high or rising group, we considered SHAP curves with linear regression coefficients greater than 0.005 to have rising importance whilst the rest were of high importance. Similarly, in the low or losing collection, we considered SHAP curves with coefficients less than -0.002 to be losing significance whilst the rest were deemed to be of low importance. Again, the threshold was derived from inspection of the empirical histogram of the linear regression coefficients suggesting distinct modes.

References.

1 Elm E von, Altman DG, Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies*. *B World Health Organ* 2007; **85**: 867–72.

2 Acute Respiratory Distress Syndrome: The Berlin Definition. *Jama* 2012; **307**: 2526–33.

3 Bellani G, Laffey JG, Pham T, *et al.* Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *Jama* 2016; **315**: 788–800.

4 Tipping ME, Bishop CM. Probabilistic Principal Component Analysis. *J Royal Statistical Soc Ser B Statistical Methodol* 1999; **61**: 611–22.

5 Chawla NV, Bowyer KW, Hall LO, Kegelmeyer WP. SMOTE: Synthetic Minority Over-sampling Technique. *J Artif Intell Res* 2002; **16**: 321–57.

Supplementary Table Legends

Table S1. Lists of participating sites.

Table S2. Full list of variables for inclusion in models with and percentage missingness per analysis.

Table S3. Percentage of missing values for each parameter in each site.

Table S4. Percentage of missing values for each parameter on each day.

Table S5. Distribution of comorbidities with a) severity on admission and b) ICU outcome

Table S6. Comparison between COVID-ICU and the UK Intensive Care National Audit and Research Centre (ICNARC).

Table S7. Clinical and physiological characteristics, outcomes and interventions according to ICU outcome.

Table S8. ICU admission profiles per quartile of patients admitted across the first surge.

Table S9. Uni- and multivariate model analysis of factors associated with ICU mortality.

Table S10. Time series mixed model ANOVA according to ICU outcome.

Table S11. Progression of hypoxaemia in COVID-19 as compared to pre-COVID ARDS publications. Tables show patient numbers and proportions changing between mild, moderate, and severe hypoxaemia categories from day 1 to day 7 of invasive mechanical ventilation. Table 2a – COVID-ICU database; 2b – LUNG-SAFE study [19]; 2c – Berlin definition study [25].

Table S12. Clinical and physiological characteristics, outcomes, and interventions according to resolution of hypoxaemia over the first week of invasive mechanical ventilation.

Table S13. Time series mixed model ANOVA according to resolution of hypoxaemia over the first week of mechanical ventilation.

Table S14. Uni- and multivariate model analysis of factors associated with progression of hypoxaemia over the first week of invasive mechanical ventilation

Table S15. The application, median start date and duration of the first episode of interventions

Table S16. Clinical and physiological characteristics, outcomes and interventions according to prone responsiveness.

Table S17. Time series mixed model ANOVA according to prone responsiveness.

Table S18. Uni- and multivariate model analysis of pre-pronation factors associated with prone responsiveness.

Table S19. Uni- and multivariate model analysis of post-pronation factors associated with prone responsiveness.

Table S20. Time series mixed model ANOVA according to ARDS severity on admission.

Table S1 - Individual site contributions

ICU site	Number of patients	Proportion of total	Outcome (Mortality rate)	percentage transferred in
A	2	0.3%	100.0%	0.0%
B	1	0.2%	0.0%	100.0%
C	18	2.8%	27.8%	5.6%
D	35	5.5%	31.4%	82.9%
E	49	7.7%	38.8%	79.6%
F	19	3.0%	26.3%	15.8%
G	36	5.7%	47.2%	44.4%
H	57	9.0%	59.6%	7.0%
I	34	5.4%	64.7%	0.0%
J	34	5.4%	29.4%	76.5%
K	3	0.5%	66.7%	0.0%
L	64	10.1%	51.6%	4.7%
M	54	8.5%	48.1%	3.7%
N	5	0.8%	80.0%	40.0%
O	9	1.4%	33.3%	77.8%
P	31	4.9%	35.5%	16.1%
Q	9	1.4%	88.9%	0.0%
R	173	27.3%	32.4%	12.1%
Total	**633**			

Table S2 – Variables included in logistic regression models (with percentage missingness)

	% of Missingness		
FieldLabel	**Admission**	**Before PP**	**After PP**
Age	0%	0%	0%
Male	0%	0%	0%
BMI	17%	11%	11%
Height	23%	16%	16%
symptoms days	36%	33%	33%
Hypertension	0%	0%	0%
Diabetes mellitus	0%	0%	0%
Oxygen saturation	18%	14%	10%
pH	0%	6%	0%
PaCO_2	0%	6%	0%
HCO^-3	1%	6%	0%
Lactate	5%	10%	6%
Peak pressure	5%	13%	5%
PEEP	5%	14%	7%
Minute ventilation	4%	14%	6%
Dynamic Comp	11%	21%	13%
Oxygenation Index	39%	50%	46%
Ventilatory Ratio	26%	27%	20%
Cum fluid balance	7%	14%	19%
Glucose	8%	11%	17%
BUN	21%	31%	33%
Sodium	2%	4%	2%
Potassium	2%	4%	3%
ALP	5%	6%	9%
ALT	6%	9%	13%
Creatinine Kinase	62%	56%	61%
LDH	69%	63%	67%
Haemoglobin	2%	4%	2%
Haematocrit	51%	37%	35%
Neutrophils	2%	4%	2%
Monocytes	3%	4%	3%
Lymphocytes	3%	4%	3%
Basophils	21%	14%	16%
Eosinophils	22%	15%	14%
APTT	37%	31%	37%
PT	37%	31%	36%
Fibrinogen	35%	33%	44%
Ferritin	54%	42%	51%
D-dimer	38%	40%	44%
Triglicerides	70%	69%	77%
CRP	6%	10%	11%
Procalcitonin	80%	77%	82%
High sensitivity Troponin	60%	56%	64%
NT Pro BNP	91%	93%	94%
SOFA Respiratory	1%	6%	0%
SOFA Nervous	20%	33%	27%
SOFA Cardio	9%	11%	9%
SOFA Liver	7%	15%	13%
SOFA Coagulation	2%	4%	2%
SOFA Kidneys	1%	3%	0%
SOFA score	32%	49%	41%
Prone initiation day	-	0%	0%

Table S3 - Missing values for each parameter – by site

Site	All	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
N	**633**	**2**	**1**	**18**	**35**	**49**	**19**	**36**	**57**	**34**	**34**	**3**	**64**	**54**	**5**	**9**	**31**	**9**	**173**
% of Missing Data																			
PaO_2 / FiO_2	6%	0%	2%	5%	3%	8%	7%	1%	10%	4%	22%	0%	1%	6%	0%	0%	5%	5%	5%
Oxygen saturation	21%	7%	0%	7%	0%	1%	100%	100%	100%	0%	2%	0%	1%	0%	0%	0%	0%	0%	0%
pH	5%	0%	2%	4%	1%	2%	6%	1%	10%	4%	13%	0%	1%	6%	0%	0%	3%	6%	4%
PaCO_2	5%	0%	2%	4%	1%	2%	6%	1%	10%	4%	13%	0%	1%	6%	0%	0%	3%	6%	4%
Base excess	6%	0%	2%	5%	2%	3%	17%	2%	12%	4%	14%	0%	2%	7%	0%	0%	3%	6%	4%
HCO^-3	5%	0%	2%	4%	2%	2%	13%	1%	10%	5%	13%	0%	1%	6%	0%	0%	3%	6%	5%
Lactate	9%	0%	100%	4%	3%	2%	6%	1%	10%	5%	13%	0%	1%	7%	0%	0%	90%	6%	5%
Peak pressure	13%	0%	4%	12%	14%	12%	7%	7%	4%	11%	17%	8%	4%	6%	0%	1%	10%	3%	21%
PEEP	14%	0%	2%	16%	20%	9%	0%	2%	0%	6%	18%	0%	2%	4%	0%	1%	4%	2%	30%
Mean airway pressure	41%	0%	25%	100%	22%	14%	82%	28%	12%	96%	20%	32%	100%	97%	0%	22%	58%	100%	32%
Tidal Volume per Kg	30%	100%	8%	51%	14%	28%	8%	22%	89%	6%	14%	0%	15%	37%	67%	97%	47%	86%	21%
Respiratory rate	12%	0%	57%	11%	13%	34%	0%	0%	0%	0%	10%	0%	0%	0%	0%	0%	5%	0%	20%
Minute ventilation	15%	0%	62%	34%	14%	37%	8%	6%	3%	2%	16%	0%	4%	4%	0%	1%	21%	2%	22%
Dynamic Compliance	19%	0%	9%	37%	20%	14%	13%	9%	5%	16%	20%	0%	6%	4%	3%	1%	26%	5%	31%
Oxygenation Index	43%	0%	25%	100%	22%	16%	82%	29%	20%	96%	25%	32%	100%	97%	0%	22%	59%	100%	32%
Ventilatory Ratio	34%	100%	62%	54%	15%	48%	14%	23%	90%	9%	20%	0%	16%	39%	67%	97%	48%	86%	22%
SOFA Score	47%	13%	96%	21%	22%	17%	65%	54%	68%	58%	81%	84%	76%	55%	6%	47%	80%	59%	31%
Non-Respiratory SOFA	44%	13%	96%	18%	18%	8%	63%	52%	59%	56%	78%	84%	76%	52%	6%	47%	79%	55%	29%
Cumulative fluid balance	11%	7%	100%	5%	4%	7%	3%	4%	28%	0%	10%	4%	3%	2%	3%	1%	83%	0%	4%
Glucose	12%	13%	100%	10%	1%	3%	6%	1%	3%	8%	21%	12%	4%	61%	6%	4%	90%	2%	2%
BUN	26%	0%	100%	19%	10%	100%	8%	4%	5%	4%	100%	8%	7%	3%	3%	10%	100%	8%	11%
Creatinine	6%	0%	4%	6%	6%	3%	8%	4%	5%	4%	6%	8%	4%	3%	3%	6%	6%	8%	7%
Sodium	5%	0%	4%	7%	7%	1%	5%	1%	3%	4%	6%	8%	3%	3%	3%	3%	6%	8%	7%
Potassium	5%	0%	4%	6%	7%	4%	5%	1%	3%	4%	6%	8%	4%	3%	6%	3%	6%	9%	8%
Bilirubin	16%	13%	11%	6%	14%	2%	19%	5%	21%	8%	6%	12%	3%	37%	6%	46%	60%	47%	14%
Alkaline Phosphatase	11%	0%	11%	10%	9%	2%	8%	4%	5%	11%	6%	12%	2%	32%	6%	27%	61%	33%	8%
AST	92%	13%	100%	97%	100%	100%	100%	100%	100%	16%	98%	76%	22%	100%	78%	99%	97%	100%	100%
ALT	13%	13%	11%	6%	11%	2%	9%	9%	6%	7%	6%	12%	3%	38%	3%	46%	60%	68%	10%
Creatinine Kinase	71%	100%	98%	99%	100%	8%	83%	40%	71%	14%	26%	48%	8%	99%	33%	100%	87%	91%	100%
LDH	80%	47%	98%	95%	97%	11%	100%	100%	99%	17%	50%	96%	51%	74%	8%	99%	88%	98%	95%
Haemoglobin	5%	0%	4%	2%	6%	1%	8%	4%	5%	3%	7%	8%	2%	4%	3%	4%	6%	20%	7%
WBC	5%	0%	4%	2%	6%	1%	8%	4%	5%	3%	7%	8%	2%	4%	3%	5%	6%	20%	7%
RBC	25%	0%	4%	2%	6%	1%	100%	100%	100%	6%	7%	8%	4%	5%	3%	5%	6%	20%	7%
Platelet Count	6%	0%	4%	2%	6%	1%	9%	4%	5%	5%	7%	8%	2%	4%	3%	6%	6%	20%	8%
Haematocrit	63%	73%	4%	5%	100%	1%	100%	100%	100%	3%	7%	8%	2%	3%	3%	5%	6%	20%	100%
Neutrophils	6%	0%	4%	3%	6%	1%	9%	6%	6%	3%	7%	8%	3%	5%	6%	6%	6%	20%	7%
Monocytes	6%	0%	4%	3%	7%	1%	9%	6%	6%	3%	7%	8%	4%	5%	6%	6%	6%	20%	7%
Lymphocytes	6%	0%	4%	3%	6%	1%	9%	6%	6%	4%	7%	8%	4%	5%	6%	6%	6%	20%	7%
Basophils	20%	0%	4%	3%	33%	1%	9%	6%	6%	4%	7%	8%	4%	6%	6%	6%	6%	21%	44%
Eosinophils	16%	0%	4%	3%	28%	1%	9%	6%	6%	4%	7%	8%	4%	6%	6%	6%	6%	20%	34%
APTT	50%	27%	9%	3%	100%	3%	10%	6%	6%	14%	13%	8%	8%	53%	17%	42%	45%	74%	100%
PT	50%	27%	9%	3%	100%	3%	10%	6%	7%	14%	12%	8%	7%	54%	8%	44%	45%	74%	100%
INR	75%	100%	100%	2%	100%	3%	98%	99%	96%	11%	12%	8%	6%	100%	8%	97%	100%	100%	100%
Fibrinogen	50%	27%	40%	16%	23%	10%	100%	100%	100%	99%	34%	52%	22%	55%	17%	70%	56%	76%	38%
Ferritin	63%	47%	98%	75%	57%	18%	100%	100%	100%	19%	58%	68%	44%	72%	31%	32%	80%	100%	56%
D-dimer	48%	60%	100%	72%	63%	17%	11%	11%	11%	21%	58%	60%	49%	73%	6%	31%	93%	94%	63%
Triglicerides	77%	93%	94%	96%	58%	99%	100%	100%	100%	97%	60%	56%	88%	81%	89%	54%	86%	95%	59%
CRP	11%	7%	4%	20%	6%	2%	7%	5%	5%	13%	6%	16%	2%	74%	6%	4%	6%	94%	8%
Procalcitonin	80%	87%	98%	79%	57%	93%	100%	100%	100%	98%	94%	64%	91%	99%	100%	61%	91%	61%	59%
High sensitivity Troponin	64%	80%	100%	79%	55%	7%	100%	100%	100%	92%	47%	52%	44%	73%	33%	43%	88%	98%	55%
NT Pro BNP	97%	80%	100%	78%	97%	100%	100%	100%	100%	97%	89%	100%	100%	100%	97%	98%	98%	97%	96%

Table S4 - Missing values for each parameter – by day

Site	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day10	Day11	Day12	Day13	Day14	Day15	Day16	Day17	Day18	Day19	Day20	Day21
N	**633**	**616**	**588**	**570**	**547**	**522**	**486**	**469**	**435**	**404**	**377**	**344**	**321**	**300**	**275**	**255**	**234**	**219**	**202**	**185**	**174**	**162**
% of Missing Data																						
PaO_2 / FiO_2	5%	2%	2%	3%	3%	2%	2%	3%	4%	3%	5%	3%	5%	5%	5%	6%	6%	6%	9%	6%	8%	8%
Oxygen saturation	19%	19%	18%	18%	18%	19%	19%	19%	18%	19%	20%	22%	21%	22%	21%	23%	22%	22%	22%	23%	24%	23%
pH	2%	1%	2%	2%	3%	2%	2%	3%	3%	2%	3%	2%	3%	3%	3%	4%	4%	5%	5%	4%	6%	7%
PaCO_2	2%	1%	2%	2%	3%	2%	2%	3%	3%	2%	3%	2%	3%	3%	3%	4%	4%	5%	5%	4%	6%	7%
Base excess	3%	1%	2%	3%	4%	3%	2%	4%	4%	3%	4%	3%	4%	5%	4%	5%	6%	6%	7%	5%	7%	9%
HCO^-3	3%	1%	2%	3%	3%	2%	2%	3%	3%	3%	4%	3%	3%	3%	3%	5%	6%	5%	6%	5%	7%	7%
Lactate	7%	5%	6%	7%	7%	6%	7%	8%	9%	7%	8%	8%	9%	9%	8%	9%	9%	9%	9%	8%	11%	10%
Peak pressure	12%	6%	4%	5%	6%	8%	6%	7%	8%	7%	7%	9%	12%	10%	9%	12%	14%	12%	13%	11%	15%	17%
PEEP	10%	6%	8%	9%	11%	12%	9%	11%	12%	12%	11%	11%	11%	13%	11%	11%	14%	13%	13%	14%	16%	18%
Mean airway pressure	46%	39%	37%	37%	38%	39%	36%	37%	39%	37%	36%	35%	36%	35%	36%	38%	40%	39%	41%	41%	41%	41%
Tidal Volume per Kg	32%	25%	24%	25%	27%	27%	24%	26%	26%	26%	27%	28%	30%	29%	28%	29%	29%	28%	28%	26%	28%	30%
Respiratory rate	5%	1%	3%	4%	6%	8%	6%	6%	8%	7%	8%	10%	12%	10%	10%	11%	13%	11%	12%	14%	14%	17%
Minute ventilation	14%	5%	6%	8%	9%	11%	8%	9%	11%	10%	11%	12%	14%	14%	14%	16%	19%	17%	15%	16%	19%	20%
Dynamic Compliance	21%	13%	12%	13%	13%	16%	11%	15%	17%	16%	14%	15%	16%	16%	15%	16%	18%	18%	17%	17%	20%	20%
Oxygenation Index	48%	40%	38%	39%	40%	40%	37%	38%	40%	38%	38%	36%	36%	36%	38%	39%	41%	41%	44%	42%	44%	44%
Ventilatory Ratio	34%	26%	26%	28%	29%	30%	27%	28%	30%	29%	30%	31%	32%	31%	31%	33%	35%	32%	30%	30%	33%	38%
SOFA Score	75%	40%	39%	42%	41%	42%	41%	44%	43%	44%	41%	43%	42%	47%	42%	46%	45%	44%	46%	45%	49%	48%
Non-Respiratory SOFA	71%	38%	36%	37%	38%	39%	38%	42%	41%	42%	38%	40%	40%	43%	38%	44%	43%	40%	42%	43%	44%	42%
Cumulative fluid balance	47%	7%	7%	8%	7%	7%	7%	10%	9%	8%	9%	9%	9%	8%	8%	9%	8%	8%	9%	6%	7%	6%
Glucose	12%	12%	11%	12%	10%	10%	10%	11%	10%	11%	11%	12%	12%	11%	11%	10%	12%	11%	12%	10%	10%	6%
BUN	50%	22%	21%	21%	20%	21%	24%	23%	26%	24%	25%	26%	27%	27%	25%	27%	29%	26%	28%	28%	25%	25%
Creatinine	35%	3%	1%	2%	2%	2%	2%	2%	3%	2%	3%	4%	3%	3%	2%	5%	5%	3%	3%	2%	1%	4%
Sodium	34%	3%	1%	2%	1%	1%	1%	2%	2%	2%	3%	3%	2%	3%	2%	4%	3%	3%	3%	2%	1%	2%
Potassium	35%	3%	1%	2%	2%	1%	1%	2%	3%	2%	3%	3%	3%	2%	3%	4%	3%	4%	3%	2%	1%	2%
Bilirubin	38%	12%	13%	11%	11%	11%	13%	14%	12%	13%	12%	15%	13%	15%	12%	17%	16%	17%	15%	16%	14%	14%
Alkaline Phosphatase	36%	10%	10%	8%	8%	7%	10%	9%	8%	8%	8%	10%	9%	10%	8%	9%	9%	8%	8%	8%	8%	7%
AST	88%	87%	86%	85%	86%	87%	87%	89%	89%	89%	90%	95%	95%	96%	95%	95%	94%	97%	97%	97%	98%	99%
ALT	38%	11%	11%	10%	9%	9%	11%	11%	10%	10%	10%	12%	11%	13%	10%	13%	12%	11%	10%	10%	10%	9%
Creatinine Kinase	70%	67%	67%	65%	67%	66%	67%	67%	66%	68%	67%	72%	71%	73%	71%	67%	72%	71%	76%	71%	73%	71%
LDH	78%	77%	77%	76%	75%	73%	76%	77%	74%	76%	76%	79%	81%	79%	80%	79%	80%	82%	83%	83%	82%	80%
Haemoglobin	34%	3%	1%	2%	1%	2%	1%	1%	2%	2%	2%	4%	3%	3%	2%	4%	6%	4%	3%	3%	3%	3%
WBC	34%	3%	1%	2%	1%	2%	1%	1%	2%	2%	2%	4%	3%	3%	2%	4%	6%	4%	3%	3%	3%	3%
RBC	52%	22%	19%	20%	19%	20%	20%	20%	20%	21%	22%	25%	24%	24%	23%	25%	25%	25%	25%	25%	26%	25%
Platelet Count	34%	3%	2%	2%	2%	3%	1%	1%	2%	2%	2%	4%	4%	2%	3%	4%	6%	4%	3%	4%	3%	2%
Haematocrit	56%	53%	53%	54%	54%	55%	55%	56%	56%	58%	59%	63%	64%	63%	63%	63%	64%	65%	65%	66%	67%	69%
Neutrophils	34%	3%	2%	2%	1%	3%	2%	1%	2%	3%	3%	5%	4%	3%	3%	4%	6%	4%	5%	4%	3%	3%
Monocytes	35%	4%	2%	2%	2%	3%	2%	1%	2%	3%	3%	5%	4%	3%	3%	4%	6%	4%	5%	4%	3%	4%
Lymphocytes	35%	4%	2%	2%	1%	3%	2%	1%	2%	3%	3%	5%	4%	3%	3%	4%	6%	4%	5%	4%	3%	3%
Basophils	38%	24%	23%	25%	23%	23%	21%	21%	18%	22%	19%	20%	19%	16%	16%	15%	15%	13%	14%	11%	12%	14%
Eosinophils	38%	24%	18%	16%	12%	13%	13%	13%	17%	17%	16%	19%	18%	16%	13%	14%	14%	14%	11%	6%	8%	9%
APTT	42%	44%	47%	47%	46%	47%	44%	47%	46%	46%	47%	49%	49%	51%	49%	49%	50%	47%	50%	49%	49%	52%
PT	42%	44%	47%	46%	45%	46%	44%	47%	46%	46%	47%	50%	49%	51%	48%	49%	52%	48%	51%	50%	49%	52%
INR	70%	67%	69%	69%	68%	68%	69%	71%	70%	70%	72%	77%	77%	77%	74%	76%	76%	76%	78%	77%	78%	78%
Fibrinogen	65%	44%	48%	48%	46%	47%	48%	48%	47%	46%	47%	48%	45%	51%	46%	43%	44%	47%	49%	49%	52%	52%
Ferritin	75%	64%	62%	60%	56%	56%	56%	58%	58%	56%	59%	58%	63%	61%	57%	63%	63%	67%	67%	64%	65%	59%
D-dimer	61%	48%	52%	48%	46%	45%	48%	46%	49%	44%	46%	47%	43%	45%	42%	45%	45%	43%	44%	43%	46%	39%
Triglicerides	89%	78%	79%	77%	77%	78%	76%	78%	78%	76%	76%	73%	72%	79%	71%	77%	74%	74%	77%	74%	74%	73%
CRP	39%	13%	11%	9%	10%	8%	9%	8%	8%	9%	7%	9%	8%	8%	7%	7%	9%	8%	8%	8%	5%	7%
Procalcitonin	95%	84%	85%	82%	82%	80%	80%	81%	81%	78%	80%	78%	79%	80%	75%	78%	74%	77%	77%	70%	77%	71%
High sensitivity Troponin	78%	69%	72%	73%	69%	70%	73%	71%	70%	68%	65%	65%	66%	62%	61%	63%	61%	63%	61%	62%	54%	50%
NT Pro BNP	96%	94%	96%	97%	96%	96%	96%	97%	98%	97%	98%	97%	97%	97%	98%	95%	97%	97%	98%	97%	98%	98%

Table S5 - Distribution of co-morbidities with a) severity on admission and b) ICU outcome

Co-morbidity according to severity	ALL			MILD			MODERATE			SEVERE			P value
	Total N	n	%	Group N	n	%	Group N	n	%	Group N	n	%	
BMI>30 kg/m2	524	209	39.9	123	44	35.77	278	107	38.5	123	58	47.2	0.626
Myocardial infarction	573	17	3.0	129	6	4.65	292	7	2.4	152	4	2.6	0.485
Congestive Heart Failure	573	11	1.9	128	2	1.56	293	6	2.0	152	3	2.0	0.922
Peripheral vascular disease	574	9	1.6	129	1	0.78	293	6	2.0	152	2	1.3	0.577
CVA or TIA	574	17	3.0	129	4	3.10	293	9	3.1	152	4	2.6	0.966
Dementia	574	2	0.3	129	1	0.78	293	1	0.3	152	0	0.0	0.564
Hypertension	574	242	42.2	129	51	39.53	293	132	45.1	152	59	38.8	0.283
Pregnancy	366	1	0.3	71	0	0.00	183	1	0.5	112	0	0.0	0.613
COPD	575	41	7.1	129	10	7.75	294	24	8.2	152	7	4.6	0.372
Connective tissue disease	573	5	0.9	129	1	0.78	292	4	1.4	152	0	0.0	0.331
Peptic ulcer disease	573	8	1.4	129	1	0.78	293	5	1.7	151	2	1.3	0.728
Diabetes mellitus	574	176	30.7	129	46	35.66	293	93	31.7	152	37	24.3	0.161
Diabetes mellitus - end organ damage	569	18	3.2	127	5	3.94	291	10	3.4	151	3	2.0	0.637
Hemiplegia	365	2	0.5	70	1	1.43	183	1	0.5	112	0	0.0	0.564
Moderate to severe CKD	366	20	5.5	71	4	5.63	183	13	7.1	112	3	2.7	0.380
Solid tumour	575	24	4.2	129	7	5.43	294	10	3.4	152	7	4.6	0.653
Leukemia	366	8	2.2	71	1	1.41	183	7	3.8	112	0	0.0	0.095
Lymphoma	365	5	1.4	71	1	1.41	182	4	2.2	112	0	0.0	0.331
AIDS	574	5	0.9	129	3	2.33	293	2	0.7	152	0	0.0	0.113
Steroid use	365	14	3.8	71	3	4.23	182	10	5.5	112	1	0.9	0.198
Other Immunosupression use	366	16	4.4	71	4	5.63	183	11	6.0	112	1	0.9	0.166
History of Deep Vein Thrombosis	363	7	1.9	70	4	5.71	181	2	1.1	112	1	0.9	0.102
History of Pulmonary Embolus	364	5	1.4	71	1	1.41	181	3	1.7	112	1	0.9	0.911

Co-morbidity according to outcome	Survivors			Non-Survivors			P value
	Group N	n	%	Group N	n	%	
BMI>30 kg/m2	314	134	42.68	210	75	35.71	0.021
Myocardial infarction	326	4	1.23	247	13	5.26	0.004
Congestive Heart Failure	326	2	0.61	247	9	3.64	0.008
Peripheral vascular disease	326	5	1.53	248	4	1.61	0.898
CVA or TIA	326	10	3.07	248	7	2.82	0.922
Dementia	326	1	0.31	248	1	0.40	0.826
Hypertension	326	129	39.57	248	113	45.56	0.081
Pregnancy	185	0	0.00	181	1	0.55	0.243
COPD	327	19	5.81	248	22	8.87	0.129
Connective tissue disease	326	1	0.31	247	4	1.62	0.087
Peptic ulcer disease	326	3	0.92	247	5	2.02	0.245
Diabetes mellitus	326	95	29.14	248	81	32.66	0.244
Diabetes mellitus - end organ damage	323	8	2.48	246	10	4.07	0.250
Hemiplegia	185	1	0.54	180	1	0.56	0.826
Moderate to severe CKD	185	8	4.32	181	12	6.63	0.104
Solid tumour	326	12	3.68	249	12	4.82	0.439
Leukemia	185	2	1.08	181	6	3.31	0.060
Lymphoma	185	1	0.54	180	4	2.22	0.087
AIDS	326	4	1.23	248	1	0.40	0.310
Steroid use	185	8	4.32	180	6	3.33	0.968
Other Immunosupression use	185	7	3.78	181	9	4.97	0.254
History of Deep Vein Thrombosis	184	2	1.09	179	5	2.79	0.117
History of Pulmonary Embolus	184	2	1.09	180	3	1.67	0.422

Table S6 - Comparison between Covid-ICU and ICNARC

	Covid-19 undergoing IMV	
	COVID-ICU	**ICNARC***
	N=633	**N=7,702**
Patient characteristics		
Age (years), median (IQR)	59.0 [51.0 66.0]	60 (51-67)
Sex, n (%)		
Male	481 (76%)	5,544 (72.0%)
Ethnicity, n (%)		
White	250 (39.5%)	4,653 (60.4%)
Asian	73 (11.5%)	1,256 (16.3%)
Black	115 (18.2%)	804 (10.4%)
Other	103 (16.3%)	693 (9.0%)
Not stated	91 (14.4%)	296 (3.8%)
BMI (kg/m2), median (IQR)	28.1 [24.9 32.8]	28.3 (24.9-33.0)
BMI categories (kg/m^2), n (%)		
>30	209 (39.9%)	39.9%
Acute illness severity[4]		
P/F Ratio (kPa),[5] median (IQR)	18.3 [13.0 25.0]	15.0 (10.8-21.0)
P/F ratio categories (kPa)[5]		
≤13.3kPa (≤100mmHg)	166 (26.2%)	3,033 (40.4%)
13.3-26.7kPa (100-200mmHg)	320 (50.6%)	3,530 (47.0%)
>26.7kPa (>200mmHg)	147 (23.2%)	952 (12.7%)
Organ support[8,9]		
Renal support		
Receipt, n (%)	211 (33.3%)	2,708 (35.2%)
Duration (calendar days), median (IQR)	8.0 [4.0 14.0]	8 (4-15)
Outcome		
Critical care		
Survived, n (%)	365 (57.7%)	4,018 (52.2%)
Died, n (%)	268 (42.3%)	3,684 (47.8%)
Duration of stay (calendar days)		
IMV, median (IQR)	13.0 [7.0 22.0]	13 (7–23)
Survived – median (IQR)	15.0 [8.0 28.0]	-
Died – median (IQR)	11.0 [6.0 16.0]	-
Critical care, median (IQR)	14.0 [8.0 23.0]	15.0 (8.0-27.0)
Survived – median (IQR)	17.0 [9.8 30.0]	22.0 (12.0-36.0)
Died – median (IQR)	11.0 [7.0 18.0]	10.0 (6.0-17.0)

* Richards-Belle, A., Orzechowska, I., Gould, D., Thomas, K., Doidge, J., Mouncey, P., Christian, M., Shankar-Hari, M., Harrison, D., Rowan, K., Banjo, Y., Borowczak, K., Cousins, T., Cummins, P., Dalemo, K., Darnell, R., Demissie, H., Drikite, L., Fleming, A., Frederiksen, D., Furnell, S., Hussein, A., Koelewyn, A., Matthews, T., Peters, S., Samuels, T., Saull, M. (2020). COVID-19 in critical care: epidemiology of the first epidemic wave across England, Wales and Northern Ireland Intensive Care Medicine https://dx.doi.org/10.1007/s00134-

Table S7- Clinical and physiological characteristics, outcomes and interventions according to ICU outcome.

Clinical Characterisitcs					Outcome				
			ALL		Survivors		Non-Survivors		
	label	units	Total N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	P Value
	Male		633	481 (76%)	365	263 (72.1%)	268	218 (81.3%)	0.007
	White		542	250 (46.1%)	310	143 (46.1%)	232	107 (46.1%)	0.849
	Age	years	633	59.0 [51.0 66.0]	365	56.0 [47.0 63.0]	268	63.0 [57.0 70.0]	0.000
	BMI	kg/m2	524	28.1 [24.9 32.8]	314	28.7 [25.1 33.6]	210	27.8 [24.7 31.2]	0.134
	Time since onset of symptoms	days	408	8.0 [6.0 12.0]	242	9.0 [6.0 12.0]	166	7.0 [5.0 12.0]	0.101
	ICU length of stay	days	633	14.0 [8.0 23.0]	365	17.0 [9.8 30.0]	268	11.0 [7.0 18.0]	0.000
	Length of mechanical ventilation	days	633	13.0 [7.0 22.0]	365	15.0 [8.0 28.0]	268	11.0 [6.0 16.0]	0.000
	ICU Mortality	%	633	268 (42.3%)	365	0 (0%)	268	268 (100%)	0.000
Vent	FiO_2 (%)		628	60.0 [45.0 80.0]	360	55.5 [40.0 70.0]	268	65.0 [55.0 80.0]	0.000
	PaO_2 to FiO_2 ratio		626	18.3 [13.0 25.0]	359	19.8 [13.9 27.5]	267	17.0 [12.3 23.0]	0.000
	Tidal Volume (mls/IBW)	ml/Kg(IBW)	472	6.8 [6.0 7.8]	286	6.9 [6.1 7.8]	186	6.8 [6.0 7.7]	0.351
	Respiratory rate	bpm	627	18.8 [16.0 22.0]	360	18.0 [16.0 22.0]	267	20.0 [16.0 22.0]	0.357
	Minute ventilation	L/minute	606	8.5 [6.9 10.4]	348	8.5 [6.9 10.4]	258	8.6 [6.9 10.5]	0.449
	Peak pressure	ml/Kg(RBW)	599	26.0 [23.0 30.0]	344	25.3 [22.0 29.0]	255	27.0 [24.0 30.0]	0.000
	Plateau pressure	ml/Kg(IBW)	80	26.0 [22.5 28.5]	38	24.0 [21.0 28.0]	42	26.5 [24.0 29.0]	0.012
	PEEP	cmH_20	603	10.0 [8.0 12.0]	347	10.0 [8.0 12.0]	256	10.0 [10.0 12.0]	0.000
	Mean airway pressure	cmH_20	387	16.0 [13.2 19.0]	239	15.0 [13.0 18.0]	148	17.0 [14.0 20.0]	0.001
	Pressure support	cmH_20	371	10.0 [5.3 14.0]	217	10.0 [6.0 14.0]	154	10.0 [5.0 12.0]	0.516
	Dynamic Compliance	mls/cmH20	564	31.5 [24.3 40.2]	327	32.5 [25.4 41.2]	237	30.0 [23.3 39.2]	0.033
	Oxygenation Index		387	8.1 [5.1 12.5]	239	7.1 [4.7 10.4]	148	9.7 [6.4 14.4]	0.000
	Ventilatory Ratio		470	1.5 [1.2 2.1]	284	1.5 [1.2 2.0]	186	1.6 [1.3 2.1]	0.033
ABG	Oxygen saturation		518	95.0 [93.0 98.0]	308	96.0 [93.0 98.0]	210	95.0 [92.0 97.0]	0.006
	pH		630	7.4 [7.3 7.4]	363	7.4 [7.3 7.4]	267	7.3 [7.3 7.4]	0.000
	PaO_2	kPa	630	10.7 [9.2 13.1]	363	10.7 [9.1 12.8]	267	10.9 [9.2 13.4]	0.441
	$PaCO_2$	kPa	630	6.0 [5.2 7.2]	363	5.9 [5.2 6.9]	267	6.1 [5.2 7.3]	0.136
	Base excess		630	-0.3 [-2.6 2.2]	363	0.2 [-2.1 2.5]	267	-0.9 [-3.2 1.5]	0.001
	HCO_3^-	mmol/L	629	24.5 [22.5 26.7]	362	24.9 [22.9 27.0]	267	23.9 [21.9 26.0]	0.000
	Lactate	mmol/L	604	1.2 [1.0 1.6]	347	1.1 [0.9 1.5]	257	1.3 [1.1 1.8]	0.000
SOFA	SOFA score		428	9.0 [7.0 11.0]	246	8.0 [6.0 11.0]	182	10.0 [8.0 12.0]	0.000
	SOFA Respiratory		626	3.0 [3.0 4.0]	359	3.0 [2.0 3.0]	267	3.0 [3.0 4.0]	0.000
	SOFA Nervous		508	3.0 [0.0 4.0]	301	0.0 [0.0 4.0]	207	4.0 [0.0 4.0]	0.024
	SOFA Cardiovascular		579	3.0 [3.0 4.0]	328	3.0 [3.0 3.0]	251	3.0 [3.0 4.0]	0.000
	SOFA Liver		588	0.0 [0.0 0.0]	335	0.0 [0.0 0.0]	253	0.0 [0.0 0.0]	0.678
	SOFA Coagulation		619	0.0 [0.0 0.0]	355	0.0 [0.0 0.0]	264	0.0 [0.0 0.0]	0.004
	SOFA Kidneys		629	0.0 [0.0 1.0]	362	0.0 [0.0 1.0]	267	0.0 [0.0 1.0]	0.007
FBC	Haemoglobin	g/dL	619	114.0 [92.0 128.0]	355	115.0 [95.0 128.0]	264	113.0 [85.8 129.0]	0.380
	Haematocrit		312	0.4 [0.3 0.4]	168	0.4 [0.3 0.4]	144	0.4 [0.3 0.4]	0.030
	White blood cell count	x10^9/L	619	9.6 [7.0 13.1]	355	9.4 [6.9 12.6]	264	9.9 [7.3 13.5]	0.209
	Neutrophils	x10^9/L	618	8.1 [5.7 11.3]	355	7.6 [5.3 10.7]	263	8.6 [6.2 12.3]	0.010
	Monocytes	x10^9/L	614	0.4 [0.3 0.7]	355	0.5 [0.3 0.7]	259	0.4 [0.2 0.7]	0.003
	Lymphocytes	x10^9/L	615	0.8 [0.5 1.2]	355	0.9 [0.6 1.3]	260	0.7 [0.5 1.0]	0.000
	Basophils	x10^9/L	498	0.0 [0.0 0.1]	281	0.0 [0.0 0.1]	217	0.0 [0.0 0.0]	0.001
	Eosinophils	x10^9/L	493	0.0 [0.0 0.1]	286	0.0 [0.0 0.1]	207	0.0 [0.0 0.1]	0.000
Coag	Platelet Count	µmol/L	619	246.0 [185.3 320.8]	355	261.0 [199.0 334.8]	264	229.5 [171.0 305.5]	0.001
	APTT	U/L	398	32.1 [28.3 37.4]	209	32.0 [28.7 37.1]	189	32.1 [28.0 37.5]	0.603
	PT	U/L	396	13.9 [12.4 15.2]	209	13.9 [12.5 15.1]	187	13.8 [12.4 15.5]	0.713
	INR	U/L	212	1.1 [1.1 1.2]	113	1.1 [1.1 1.2]	99	1.1 [1.1 1.2]	0.616
	Fibrinogen	U/L	410	6.8 [5.6 8.1]	246	6.8 [5.8 8.0]	164	6.7 [5.4 8.2]	0.321
	D-dimer	IU/L	391	2642.0 [990.5 7701.3]	221	2270.0 [902.3 5680.0]	170	3290.5 [1239.0 15575.0]	0.002
Electrolytes	Blood Urea Nitrogen (BUN)	mmol/L	498	7.4 [4.9 11.8]	277	6.8 [4.7 10.4]	221	8.4 [5.7 13.3]	0.000
	Creatinine	µmol/L	621	88.0 [66.0 140.0]	356	82.0 [63.0 123.0]	265	99.0 [71.8 152.1]	0.000
	Sodium	mmol/L	621	139.0 [136.0 142.0]	357	139.0 [136.0 142.0]	264	138.0 [135.0 141.0]	0.071
	Potassium	mmol/L	620	4.4 [4.0 4.8]	356	4.4 [4.0 4.8]	264	4.4 [4.1 4.8]	0.462
Liver	Bilirubin	µmol/L	588	10.0 [7.0 15.0]	335	10.0 [7.0 14.0]	253	10.0 [7.0 15.0]	0.068
	Alkaline Phosphatase	U/L	600	77.0 [58.5 113.0]	342	76.0 [53.0 116.0]	258	79.5 [62.0 110.0]	0.341
	AST	U/L	99	59.0 [39.3 85.0]	50	53.0 [37.0 63.0]	49	70.0 [43.3 96.8]	0.018
	ALT	U/L	592	37.0 [24.0 59.0]	338	37.0 [23.0 62.0]	254	37.0 [24.0 56.0]	0.820
Inflammation	LDH (Lactate dehydrogenase)	IU/L	194	649.0 [452.0 921.0]	109	614.0 [397.3 818.8]	85	683.0 [506.3 977.3]	0.079
	Ferritin	ng/mL	290	1218.5 [696.0 2320.0]	173	1144.0 [681.5 2056.3]	117	1410.0 [714.8 2814.0]	0.025
	CRP		592	215.7 [135.0 311.0]	350	200.5 [117.4 298.0]	242	242.2 [159.0 325.6]	0.000
	Procalcitonin	ug/L	125	0.7 [0.3 2.2]	86	0.5 [0.3 1.3]	39	1.6 [0.6 5.5]	0.000
Cardiac	Creatinine Kinase	U/L	243	217.0 [83.5 637.3]	132	202.0 [84.0 578.8]	111	222.0 [82.8 639.5]	0.733
	High sensitivity Troponin		253	21.8 [11.0 61.0]	147	16.0 [9.0 41.3]	106	29.4 [13.0 103.0]	0.001
	NT Pro BNP	pg/ml	58	537.5 [165.0 1478.0]	37	349.0 [139.0 823.5]	21	857.0 [565.0 3416.8]	0.005
Fluid	Cumulative Fluid balance	L	589	343.0 [-212.3 1058.3]	342	273.4 [-262.0 938.0]	247	413.0 [-182.4 1360.0]	0.033
Adjunctive interventions									
	Was patient transferred in?		633	159 (25.1%)	365	103 (28.2%)	268	56 (20.9%)	0.036
	Tracheostomy		516	145 (28.1%)	305	122 (40%)	211	23 (10.9%)	0.000
	PEEP>10		622	459 (73.8%)	359	231 (64.3%)	263	228 (86.7%)	0.000
	Neuro-muscular blockade		617	434 (70.3%)	354	215 (60.7%)	263	219 (83.3%)	0.000
	Prone positioning		551	273 (49.5%)	328	129 (39.3%)	223	144 (64.6%)	0.000
	Inhaled nitric oxide		521	73 (14%)	309	29 (9.39%)	212	44 (20.8%)	0.001
	Inhaled prostacyclin		521	55 (10.6%)	309	30 (9.71%)	212	25 (11.8%)	0.624
	Bronchoscopy		521	51 (9.79%)	309	33 (10.7%)	212	18 (8.49%)	0.288
	Renal replacement therapy		555	211 (38%)	322	89 (27.6%)	233	122 (52.4%)	0.000
	Diuretics		598	443 (74.1%)	348	256 (73.6%)	250	187 (74.8%)	0.922
	Corticosteroids		582	304 (52.2%)	342	173 (50.6%)	240	131 (54.6%)	0.712
	Therapeutic heparin		438	55 (12.6%)	255	30 (11.8%)	183	25 (13.7%)	0.624
	Antibiotics		313	219 (70%)	168	109 (64.9%)	145	110 (75.9%)	0.003
	Prone								
	No of proning episodes		273	1.0 [1.0 2.0]	129	1.0 [1.0 2.0]	144	1.0 [1.0 2.0]	0.864
	mech vent prior first prone	days	273	3.0 [1.8 6.0]	129	3.0 [1.0 6.0]	144	4.0 [2.0 7.0]	0.065
	durationn of first prone	days	273	2.0 [1.0 4.0]	129	2.0 [1.0 4.0]	144	2.0 [1.0 3.5]	0.552
	responsders to proning		270	119 (44.1%)	128	82 (64.1%)	142	37 (26.1%)	0.006
	missed windows prior to prone		273	3.0 [1.0 6.0]	129	2.0 [0.8 5.0]	144	3.0 [1.0 7.0]	0.020
	missed windows - unproned		360	3.0 [1.0 10.0]	236	2.0 [0.0 6.0]	124	7.0 [3.0 15.5]	0.000
	Tracheostomy								
	mech vent prior to tracheostomy	days	145	13.0 [9.0 18.0]	122	14.0 [10.0 18.0]	23	13.0 [4.0 18.8]	0.127
	durationn of tracheostomy	days	145	14.0 [6.0 21.3]	122	15.0 [7.0 22.0]	23	6.0 [2.3 12.8]	0.001
End of life parameters									
	life sustaining therapy withdrawn		130	85 (65.4%)	0	0 (NaN%)	130	85 (65.4%)	0.000
	cardiac arrest during admission		244	21 (8.61%)	122	8 (6.56%)	122	13 (10.7%)	0.065

Table S8- ICU admission profiles per quartile of patients admitted across the first surge.

Clinical Characterisitcs					Admission Quartile								
			ALL		Q1		Q2		Q3		Q4		
	label	units	Total N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	p(KruskalWallis/Chi^2)
	Male		633	481 (76%)	177	138 (78%)	156	122 (78.2%)	148	117 (79.1%)	152	104 (68.4%)	0.097
	White		542	250 (46.1%)	152	73 (48%)	134	64 (47.8%)	123	50 (40.7%)	133	63 (47.4%)	0.450
	Age	years	633	59.0 [51.0 66.0]	177	59.0 [50.0 69.0]	156	60.0 [54.0 66.0]	148	58.5 [49.5 64.0]	152	60.0 [51.0 65.0]	0.153
	BMI	kg/m2	524	28.1 [24.9 32.8]	146	28.7 [24.9 33.5]	124	28.9 [24.5 32.1]	127	27.5 [25.0 31.7]	127	28.4 [25.3 32.9]	0.653
	Time since onset of symptoms	days	408	8.0 [6.0 12.0]	129	8.0 [6.0 11.0]	108	8.0 [7.0 12.0]	90	9.0 [6.0 13.0]	81	7.0 [5.0 13.0]	0.653
	ICU length of stay	days	633	14.0 [8.0 23.0]	177	14.0 [8.0 22.0]	156	13.0 [8.0 23.5]	148	15.0 [8.5 24.5]	152	12.5 [7.5 22.0]	0.632
	Length of mechanical ventilation	days	633	13.0 [7.0 22.0]	177	14.0 [8.0 20.3]	156	12.0 [7.0 23.0]	148	14.0 [8.0 22.5]	152	11.0 [6.0 18.5]	0.191
	ICU Mortality	%	633	268 (42.3%)	177	71 (40.1%)	156	79 (50.6%)	148	64 (43.2%)	152	54 (35.5%)	0.053
Vent	FiO_2 (%)		628	60.0 [45.0 80.0]	175	60.0 [40.0 71.5]	156	60.0 [50.0 72.5]	146	60.0 [50.0 80.0]	151	60.0 [45.0 80.0]	0.285
	PaO_2 to FiO_2 ratio		626	18.3 [13.0 25.0]	175	20.3 [14.3 27.5]	156	18.9 [13.3 24.0]	146	17.1 [12.6 24.7]	149	17.2 [11.8 25.1]	0.047
	Tidal Volume (mls/IBW)	ml/Kg(IBW)	472	6.8 [6.0 7.8]	138	6.8 [5.8 7.6]	110	6.8 [6.2 7.6]	114	6.9 [6.0 7.8]	110	7.2 [5.9 8.5]	0.304
	Respiratory rate	bpm	627	18.8 [16.0 22.0]	176	18.0 [14.0 22.0]	156	18.1 [16.0 22.0]	146	20.0 [16.0 24.0]	149	19.0 [16.0 23.3]	0.013
	Minute ventilation	L/minute	606	8.5 [6.9 10.4]	172	8.3 [6.4 10.0]	154	8.5 [7.0 10.4]	139	8.9 [7.4 10.8]	141	8.5 [6.8 10.2]	0.083
	Peak pressure	ml/Kg(RBW)	599	26.0 [23.0 30.0]	174	25.0 [22.0 28.0]	152	26.5 [24.0 30.0]	138	26.3 [23.0 30.0]	135	27.0 [22.3 30.8]	0.003
	Plateau pressure	ml/Kg(IBW)	80	26.0 [22.5 28.5]	22	24.5 [23.0 28.0]	19	26.0 [25.0 28.0]	19	25.0 [23.3 30.0]	20	25.0 [20.5 28.5]	0.649
	PEEP	cmH_20	603	10.0 [8.0 12.0]	169	10.0 [8.5 12.0]	148	10.0 [10.0 13.0]	142	10.0 [8.0 12.0]	144	10.0 [8.0 12.0]	0.000
	Mean airway pressure	cmH_20	387	16.0 [13.2 19.0]	126	16.0 [14.0 18.0]	96	16.0 [14.0 19.0]	90	16.0 [13.0 19.0]	75	16.0 [12.3 19.0]	0.681
	Pressure support	cmH_20	371	10.0 [5.3 14.0]	111	10.0 [5.0 12.0]	97	10.0 [5.0 15.0]	83	10.0 [8.0 14.0]	80	10.0 [6.0 12.5]	0.401
	Dynamic Compliance	mls/cmH20	564	31.5 [24.3 40.2]	167	32.7 [26.0 41.2]	141	32.1 [24.3 40.0]	130	30.4 [22.9 38.4]	126	30.1 [24.0 40.0]	0.116
	Oxygenation Index		387	8.1 [5.1 12.5]	126	7.3 [5.1 11.4]	96	8.1 [5.7 13.0]	90	8.2 [4.7 13.3]	75	8.9 [5.4 13.5]	0.414
	Ventilatory Ratio		470	1.5 [1.2 2.1]	137	1.4 [1.1 1.9]	110	1.5 [1.3 2.1]	114	1.7 [1.2 2.1]	109	1.6 [1.3 2.1]	0.062
ABG	Oxygen saturation		518	95.0 [93.0 98.0]	154	96.0 [93.0 98.0]	136	95.0 [93.0 97.0]	117	95.0 [93.0 97.0]	111	95.0 [92.0 98.0]	0.533
	pH		630	7.4 [7.3 7.4]	177	7.4 [7.3 7.4]	156	7.3 [7.3 7.4]	147	7.4 [7.3 7.4]	150	7.4 [7.3 7.4]	0.301
	PaO_2	kPa	630	10.7 [9.2 13.1]	177	10.7 [9.0 13.4]	156	10.9 [9.8 13.5]	147	10.7 [9.1 12.7]	150	10.6 [8.9 12.7]	0.350
	$PaCO_2$	kPa	630	6.0 [5.2 7.2]	177	5.9 [5.2 6.8]	156	6.1 [5.1 7.2]	147	6.2 [5.4 7.5]	150	5.8 [5.1 7.1]	0.106
	Base excess		630	-0.3 [-2.6 2.2]	177	-0.5 [-2.5 1.7]	156	-0.1 [-2.8 1.8]	147	0.1 [-2.3 2.5]	150	-0.4 [-3.0 2.7]	0.515
	HCO_3^-	mmol/L	629	24.5 [22.5 26.7]	177	24.1 [22.2 26.2]	156	24.2 [22.5 26.0]	146	24.9 [22.8 27.5]	150	24.4 [22.1 27.1]	0.107
	Lactate	mmol/L	604	1.2 [1.0 1.6]	172	1.2 [1.0 1.5]	150	1.2 [1.0 1.7]	135	1.3 [1.0 1.6]	147	1.2 [1.0 1.6]	0.108
SOFA	SOFA score		428	9.0 [7.0 11.0]	112	8.0 [6.0 11.0]	110	8.5 [7.0 11.0]	97	9.0 [7.0 11.0]	109	9.0 [7.8 11.0]	0.068
	SOFA Respiratory		626	3.0 [3.0 4.0]	175	3.0 [2.0 3.0]	156	3.0 [3.0 3.0]	146	3.0 [3.0 4.0]	149	3.0 [3.0 4.0]	0.036
	SOFA Nervous		508	3.0 [0.0 4.0]	132	0.0 [0.0 4.0]	122	0.0 [0.0 4.0]	124	4.0 [0.0 4.0]	130	4.0 [0.0 4.0]	0.011
	SOFA Cardiovascular		579	3.0 [3.0 4.0]	169	3.0 [3.0 4.0]	149	3.0 [3.0 4.0]	127	3.0 [3.0 4.0]	134	3.0 [3.0 4.0]	0.946
	SOFA Liver		588	0.0 [0.0 0.0]	162	0.0 [0.0 0.0]	147	0.0 [0.0 0.0]	136	0.0 [0.0 0.0]	143	0.0 [0.0 0.0]	0.006
	SOFA Coagulation		619	0.0 [0.0 0.0]	168	0.0 [0.0 0.0]	156	0.0 [0.0 0.0]	145	0.0 [0.0 0.0]	150	0.0 [0.0 0.0]	0.614
	SOFA Kidneys		629	0.0 [0.0 1.0]	176	0.0 [0.0 1.0]	154	0.0 [0.0 1.0]	148	0.0 [0.0 1.0]	151	0.0 [0.0 1.0]	0.030
FBC	Haemoglobin	g/dL	619	114.0 [92.0 128.0]	168	117.0 [90.0 129.5]	156	117.5 [98.5 131.5]	145	112.0 [95.8 126.0]	150	112.0 [89.0 126.0]	0.243
	Haematocrit		312	0.4 [0.3 0.4]	78	0.4 [0.3 0.4]	84	0.4 [0.3 0.4]	70	0.4 [0.3 0.4]	80	0.3 [0.3 0.4]	0.003
	White blood cell count	x10^9/L	619	9.6 [7.0 13.1]	168	8.5 [6.4 11.5]	156	10.1 [7.5 12.8]	145	9.5 [7.1 13.2]	150	10.5 [7.7 14.5]	0.001
	Neutrophils	x10^9/L	618	8.1 [5.7 11.3]	168	7.0 [4.9 10.1]	156	8.6 [6.2 11.1]	145	7.9 [5.8 11.2]	149	8.7 [6.3 13.1]	0.002
	Monocytes	x10^9/L	614	0.4 [0.3 0.7]	166	0.4 [0.3 0.7]	155	0.4 [0.3 0.7]	145	0.5 [0.3 0.7]	148	0.5 [0.3 0.8]	0.203
	Lymphocytes	x10^9/L	615	0.8 [0.5 1.2]	166	0.8 [0.5 1.1]	155	0.8 [0.5 1.1]	145	0.8 [0.5 1.3]	149	0.8 [0.6 1.3]	0.095
	Basophils	x10^9/L	498	0.0 [0.0 0.1]	123	0.0 [0.0 0.1]	125	0.0 [0.0 0.1]	118	0.0 [0.0 0.1]	132	0.0 [0.0 0.1]	0.505
	Eosinophils	x10^9/L	493	0.0 [0.0 0.1]	119	0.0 [0.0 0.1]	121	0.0 [0.0 0.1]	119	0.0 [0.0 0.1]	134	0.0 [0.0 0.1]	0.042
Coag	Platelet Count	µmol/L	619	246.0 [185.3 320.8]	168	231.5 [183.0 292.0]	156	252.5 [199.0 321.0]	145	256.0 [184.5 339.5]	150	254.5 [181.0 339.0]	0.110
	APTT	U/L	398	32.1 [28.3 37.4]	94	32.2 [28.0 36.0]	97	32.0 [28.0 36.1]	92	33.7 [28.5 39.2]	115	32.1 [29.0 38.1]	0.319
	PT	U/L	396	13.9 [12.4 15.2]	92	13.5 [11.9 14.4]	97	13.9 [11.9 15.0]	92	14.1 [12.9 15.8]	115	14.1 [12.9 15.6]	0.023
	INR	U/L	212	1.1 [1.1 1.2]	58	1.1 [1.1 1.2]	53	1.1 [1.0 1.2]	41	1.1 [1.1 1.2]	60	1.1 [1.1 1.2]	0.662
	Fibrinogen	U/L	410	6.8 [5.6 8.1]	130	6.7 [5.6 8.0]	110	7.0 [5.8 8.4]	89	6.9 [5.5 8.1]	81	6.3 [4.8 7.6]	0.054
	D-dimer	IU/L	391	2642.0 [990.5 7701.3]	67	2310.0 [882.5 5795.0]	108	2418.0 [1115.0 5513.5]	97	2782.0 [888.8 12457.5]	119	3115.0 [1071.0 7509.5]	0.587
Electrolyte	Blood Urea Nitrogen (BUN)	mmol/L	498	7.4 [4.9 11.8]	135	7.8 [4.9 11.9]	128	7.8 [5.4 11.9]	114	7.2 [5.3 12.1]	121	6.4 [4.5 10.5]	0.150
	Creatinine	µmol/L	621	88.0 [66.0 140.0]	172	100.0 [73.5 153.0]	153	90.0 [67.0 144.0]	146	81.0 [64.0 140.0]	150	78.0 [56.0 118.0]	0.000
	Sodium	mmol/L	621	139.0 [136.0 142.0]	172	139.0 [136.0 141.0]	154	138.0 [135.0 141.0]	146	139.0 [136.0 142.0]	149	138.0 [136.0 142.0]	0.167
	Potassium	mmol/L	620	4.4 [4.0 4.8]	172	4.3 [4.0 4.8]	154	4.5 [4.1 4.9]	145	4.4 [4.0 4.8]	149	4.4 [4.0 4.8]	0.447
Liver	Bilirubin	µmol/L	588	10.0 [7.0 15.0]	162	10.0 [7.0 13.0]	147	11.0 [8.0 15.0]	136	10.0 [7.0 13.5]	143	10.0 [7.0 15.8]	0.256
	Alkaline Phosphatase	U/L	600	77.0 [58.5 113.0]	165	69.0 [50.0 105.0]	149	79.0 [61.0 109.0]	138	77.5 [56.0 122.0]	148	85.5 [64.0 127.5]	0.001
	AST	U/L	99	59.0 [39.3 85.0]	26	70.0 [41.0 109.0]	29	61.0 [40.0 79.0]	17	60.0 [42.3 70.5]	27	49.0 [34.8 84.3]	0.336
	ALT	U/L	592	37.0 [24.0 59.0]	164	36.0 [23.0 62.5]	146	41.0 [28.0 60.0]	136	37.0 [25.0 61.5]	146	33.5 [21.0 56.0]	0.219
Inflammati	LDH (Lactate dehydrogenase)	IU/L	194	649.0 [452.0 921.0]	40	557.5 [432.0 891.0]	55	649.0 [478.5 796.5]	38	765.5 [523.0 1174.0]	61	682.0 [379.3 935.5]	0.210
	Ferritin	ng/mL	290	1218.5 [696.0 2320.0]	56	1010.0 [628.5 1735.0]	91	1372.0 [828.5 2688.5]	65	1127.0 [639.3 2334.5]	78	1260.0 [691.0 2397.0]	0.134
	CRP		592	215.7 [135.0 311.0]	160	222.5 [145.0 305.5]	143	231.0 [151.6 308.9]	140	225.8 [148.0 323.1]	149	187.0 [83.5 302.3]	0.007
	Procalcitonin	ug/L	125	0.7 [0.3 2.2]	30	0.9 [0.3 2.5]	39	1.1 [0.3 4.9]	26	0.4 [0.3 0.9]	30	0.6 [0.3 1.4]	0.195
Cardiac	Creatinine Kinase	U/L	243	217.0 [83.5 637.3]	60	209.5 [90.5 676.5]	59	337.0 [135.5 657.5]	55	183.0 [80.0 730.3]	69	194.0 [63.5 408.5]	0.116
	High sensitivity Troponin		253	21.8 [11.0 61.0]	66	19.1 [11.0 37.0]	72	27.9 [11.0 75.0]	51	16.0 [9.8 57.8]	64	25.1 [11.0 102.2]	0.514
	NT Pro BNP	pg/ml	58	537.5 [165.0 1478.0]	21	629.0 [149.0 889.5]	14	319.0 [127.0 1683.0]	4	1824.5 [101.5 4682.0]	19	529.0 [361.5 1679.0]	0.868
Fluid	Cumulative Fluid balance	L	589	343.0 [-212.3 1058.3]	172	118.9 [-291.5 927.5]	146	286.5 [-192.0 887.0]	131	384.0 [-189.5 1208.3]	140	655.9 [-45.4 1336.5]	0.010
Adjunctive interventions													
	Was patient transferred in?		633	159 (25.1%)	177	45 (25.4%)	156	37 (23.7%)	148	45 (30.4%)	152	32 (21.1%)	0.295
	Tracheostomy		516	145 (28.1%)	153	37 (24.2%)	136	39 (28.7%)	116	28 (24.1%)	111	41 (36.9%)	0.315
	PEEP>10		622	459 (73.8%)	174	135 (77.6%)	153	127 (83%)	147	110 (74.8%)	148	87 (58.8%)	0.000
	Neuro-muscular blockade		617	434 (70.3%)	173	114 (65.9%)	155	115 (74.2%)	147	117 (79.6%)	142	88 (62%)	0.000
	Prone positioning		551	273 (49.5%)	158	63 (39.9%)	137	65 (47.4%)	128	78 (60.9%)	128	67 (52.3%)	0.020
	Inhaled nitric oxide		521	73 (14%)	155	18 (11.6%)	136	15 (11%)	118	24 (20.3%)	112	16 (14.3%)	0.239
	Inhaled prostacyclin		521	55 (10.6%)	155	9 (5.81%)	136	12 (8.82%)	118	19 (16.1%)	112	15 (13.4%)	0.087
	Bronchoscopy		521	51 (9.79%)	155	16 (10.3%)	136	13 (9.56%)	118	9 (7.63%)	112	13 (11.6%)	0.783
	Renal replacement therapy		555	211 (38%)	162	64 (39.5%)	143	57 (39.9%)	130	47 (36.2%)	120	43 (35.8%)	0.353
	Diuretics		598	443 (74.1%)	173	139 (80.3%)	149	111 (74.5%)	139	99 (71.2%)	137	94 (68.6%)	0.008
	Corticosteroids		582	304 (52.2%)	163	66 (40.5%)	148	75 (50.7%)	137	83 (60.6%)	134	80 (59.7%)	0.004
	Therapeutic heparin		438	55 (12.6%)	129	14 (10.9%)	119	17 (14.3%)	100	14 (14%)	90	10 (11.1%)	0.560
	Antibiotics		313	219 (70%)	79	52 (65.8%)	84	61 (72.6%)	70	50 (71.4%)	80	56 (70%)	0.271
	Prone												
	No of proning episodes		273	1.0 [1.0 2.0]	63	1.0 [1.0 2.0]	65	1.0 [1.0 2.0]	78	1.0 [1.0 2.0]	67	1.0 [1.0 2.0]	0.093
	mech vent prior first prone	days	273	3.0 [1.8 6.0]	63	5.0 [2.3 8.0]	65	4.0 [2.0 6.3]	78	2.0 [1.0 5.0]	67	2.0 [1.0 5.0]	0.000
	durationn of first prone	days	273	2.0 [1.0 4.0]	63	2.0 [1.3 5.0]	65	2.0 [1.0 3.0]	78	2.0 [1.0 5.0]	67	2.0 [1.0 3.8]	0.381
	responsders to proning		270	119 (44.1%)	62	30 (48.4%)	63	29 (46%)	78	35 (44.9%)	67	25 (37.3%)	0.357
	missed windows prior to prone		273	3.0 [1.0 6.0]	63	3.0 [1.0 7.0]	65	4.0 [1.0 7.0]	78	2.0 [0.0 6.0]	67	2.0 [1.0 5.0]	0.124
	missed windows - unproned		360	3.0 [1.0 10.0]	114	3.0 [1.0 10.0]	91	5.0 [1.0 11.0]	70	4.0 [1.0 9.0]	85	1.0 [0.0 7.0]	0.060
	Tracheostomy												
	mech vent prior to tracheostomy	days	145	13.0 [9.0 18.0]	37	15.0 [11.0 18.3]	39	14.0 [10.3 17.0]	28	17.0 [12.0 21.0]	41	10.0 [5.8 15.3]	0.005
	durationn of tracheostomy	days	145	14.0 [6.0 21.3]	37	15.0 [8.0 22.0]	39	16.0 [7.3 28.0]	28	15.0 [6.0 23.0]	41	11.0 [4.8 15.8]	0.041
	Proportion of Withdrawal		130	85 (65.4%)	34	19 (55.9%)	42	31 (73.8%)	31	22 (71%)	23	13 (56.5%)	0.018
	Proportion of Cardiac arrest		244	21 (8.61%)	67	7 (10.4%)	64	6 (9.38%)	52	5 (9.62%)	61	3 (4.92%)	0.749

Table S9- Uni- and multi-variate model analysis of factors associated with ICU mortality.

		Univariate				Multivariate			
FieldLabel	**median [IQR]**	**Odds ratio**	**95% CI**		**P Value**	**Odds ratio**	**95% CI**		**P Value**
Age		2.017	1.694	2.401	0.000	1.951	1.584	2.402	0.000
Male		1.560	1.032	2.357	0.035	2.052	1.168	3.607	0.012
BMI	28.13 [24.90 32.76]	0.850	0.724	0.997	0.046	0.844	0.687	1.038	0.108
Height	173.00 [165.00 178.00]	0.929	0.788	1.095	0.381				
symptoms days	8.00 [6.00 12.00]	0.880	0.745	1.040	0.133				
Hypertension		1.318	0.932	1.863	0.119				
Diabetes mellitus		1.191	0.815	1.741	0.366				
Oxygen saturation	95.00 [93.00 98.00]	0.816	0.695	0.959	0.013	1.078	0.872	1.332	0.487
pH	7.36 [7.30 7.42]	0.796	0.683	0.928	0.004	0.849	0.670	1.074	0.172
PaCO_2	5.96 [5.16 7.15]	1.056	0.907	1.230	0.484				
HCO^-3	24.50 [22.48 26.70]	0.764	0.654	0.892	0.001	0.807	0.641	1.018	0.070
Lactate	1.20 [1.00 1.60]	1.522	1.294	1.791	0.000	1.523	1.210	1.917	0.000
Peak pressure	26.00 [23.00 30.00]	1.240	1.061	1.449	0.007	0.963	0.731	1.268	0.788
PEEP	10.00 [8.00 12.00]	1.407	1.175	1.685	0.000	1.150	0.896	1.475	0.272
Minute ventilation	8.53 [6.88 10.44]	0.967	0.831	1.125	0.663				
Dynamic Comp	31.47 [24.26 40.19]	0.860	0.735	1.005	0.058	0.706	0.543	0.919	0.010
Oxygenation Index	8.10 [5.09 12.45]	1.371	1.160	1.621	0.000	1.204	0.903	1.605	0.205
Ventilatory Ratio	1.54 [1.22 2.07]	1.152	0.983	1.349	0.081	1.151	0.911	1.453	0.238
Cum fluid balance	343.00 [-212.25 1058.32]	1.163	0.997	1.356	0.055	0.874	0.715	1.068	0.188
Glucose	8.39 [6.79 10.95]	1.246	1.065	1.457	0.006	1.067	0.876	1.300	0.521
BUN	7.40 [4.90 11.80]	1.412	1.202	1.657	0.000	1.058	0.805	1.392	0.685
Sodium	139.00 [136.00 142.00]	0.880	0.754	1.026	0.103				
Potassium	4.40 [4.00 4.80]	1.040	0.891	1.213	0.620				
ALP	77.00 [58.50 113.00]	1.056	0.908	1.227	0.480				
ALT	37.00 [24.00 59.00]	0.966	0.830	1.124	0.652				
Haemoglobin	114.00 [92.00 128.00]	0.928	0.800	1.078	0.329				
Neutrophils	8.10 [5.71 11.30]	1.206	1.034	1.407	0.017	1.078	0.858	1.354	0.520
Monocytes	0.41 [0.30 0.70]	0.794	0.682	0.925	0.003	0.838	0.671	1.046	0.119
Lymphocytes	0.80 [0.50 1.20]	0.700	0.593	0.827	0.000	0.967	0.771	1.213	0.773
Basophils	0.00 [0.00 0.10]	0.465	0.304	0.712	0.000	0.684	0.391	1.195	0.182
Eosinophils	0.00 [0.00 0.10]	0.400	0.276	0.579	0.000	0.442	0.267	0.733	0.002
APTT	32.10 [28.30 37.40]	0.968	0.817	1.148	0.710				
PT	13.85 [12.40 15.20]	1.105	0.937	1.303	0.236				
Fibrinogen	6.80 [5.60 8.10]	0.953	0.808	1.125	0.571				
D-dimer	2642.00 [990.50 7701.25]	1.356	1.149	1.602	0.000	1.164	0.941	1.439	0.161
CRP	215.65 [135.00 311.00]	1.286	1.100	1.505	0.002	1.039	0.842	1.281	0.722
SOFA Respiratory		1.419	1.160	1.736	0.001	1.235	0.858	1.776	0.256
SOFA Nervous		1.100	1.008	1.201	0.032	1.110	0.877	1.405	0.386
SOFA Cardio		1.227	1.050	1.433	0.010	1.115	0.861	1.445	0.409
SOFA Liver		1.079	0.787	1.479	0.638				
SOFA Coagulation		1.590	1.138	2.221	0.007	1.951	1.167	3.262	0.011
SOFA Kidneys		1.192	1.017	1.399	0.031	1.172	0.836	1.643	0.356
SOFA score		1.195	1.113	1.284	0.000	0.921	0.740	1.147	0.463
	* Died (N=235) vs Discharged (N=314)								

Table S10 - Time series mixed model ANOVA according to ICU outcome.

		p-values			
label	**N**	**Dead vs Alive**	**parameter over time**	**interaction**	**FDR interaction**
PaO_2 / FiO_2	472	0.000	0.000	**0.000**	**0.000**
Dynamic Compliance	341	0.001	0.000	**0.000**	**0.000**
Respiratory rate	458	0.062	0.001	0.561	0.632
FiO_2 (%)	503	0.000	0.000	**0.000**	**0.000**
Tidal Volume per Kg	347	0.993	0.343	0.537	0.632
Tidal Volume	433	0.285	0.388	0.699	0.724
Minute ventilation	404	0.039	0.000	0.285	0.405
Peak pressure	426	0.000	0.000	**0.000**	**0.000**
PEEP	390	0.000	0.001	0.104	0.204
Dynamic delta pressure (peakP-peep)	124	0.001	0.058	**0.009**	**0.022**
Mean airway pressure	256	0.000	0.000	**0.000**	**0.000**
I:E ratio	93	0.050	0.552	0.261	0.391
Pressure support	169	0.021	0.045	0.063	0.134
Oxygen saturation	417	0.000	0.125	**0.002**	**0.007**
pH	487	0.000	0.000	**0.000**	**0.000**
PaO_2	484	0.482	0.274	0.167	0.280
PaCO_2	487	0.000	0.105	**0.000**	**0.000**
Base excess	478	0.000	0.000	0.405	0.513
HCO^-3	479	0.000	0.000	0.380	0.504
Lactate	451	0.000	0.187	**0.011**	**0.026**
Oxygenation Index	237	0.000	0.000	**0.000**	**0.000**
Ventilatory Ratio	314	0.009	0.000	0.116	0.212
Mean arterial pressure (lowest)	386	0.000	0.000	**0.000**	**0.000**
Liver-Bilirubin	167	0.017	0.103	0.248	0.382
Daily fluid balance	480	0.000	0.000	0.348	0.472
Cumulative fluid balance	480	0.000	0.006	**0.000**	**0.000**
SOFA Score	192	0.000	0.000	**0.000**	**0.000**
Non-Respiratory SOFA	224	0.000	0.000	**0.000**	**0.000**
Glucose	465	0.021	0.020	0.114	0.212
BUN	382	0.000	0.004	**0.001**	**0.002**
Creatinine	520	0.000	0.120	**0.000**	**0.000**
Sodium	523	0.706	0.000	0.393	0.509
Potassium	518	0.000	0.781	**0.008**	**0.020**
Bilirubin	401	0.003	0.000	**0.000**	**0.000**
Alkaline Phosphatase	441	0.893	0.000	0.339	0.471
AST	55	0.988	0.517	0.559	0.632
ALT	418	0.092	0.000	0.231	0.366
Creatinine Kinase	127	0.643	0.275	0.467	0.579
LDH	66	0.845	0.001	0.283	0.405
Haemoglobin	515	0.001	0.080	0.081	0.165
WBC	513	0.017	0.003	**0.014**	**0.031**
RBC	415	0.256	0.486	0.535	0.632
Platelet Count	511	0.000	0.000	**0.001**	**0.002**
Haematocrit	252	0.754	0.000	**0.001**	**0.003**
Neutrophils	511	0.000	0.019	**0.002**	**0.006**
Monocytes	509	0.000	0.000	0.138	0.238
Lymphocytes	509	0.000	0.000	**0.008**	**0.020**
Basophils	361	0.020	0.007	0.570	0.632
Eosinophils	386	0.000	0.000	0.614	0.660
APTT	255	0.008	0.223	**0.002**	**0.005**
PT	260	0.671	0.632	0.654	0.691
INR	163	0.895	0.954	0.836	0.836
Fibrinogen	137	0.518	0.007	0.577	0.632
Ferritin	75	0.123	0.184	0.119	0.212
D-dimer	147	0.000	0.949	0.772	0.785
CRP	457	0.000	0.000	**0.007**	**0.019**
High sensitivity Troponin	62	0.204	0.069	0.198	0.323

Table S11 - Progression of hypoxaemia in COVID-19 as compared to pre-COVID ARDS publications.

COVID-ICU

P/F on Admission	P/F on Day 7 >26.7	13.3-26.6	<13.3	Total
>26.7	51	71	18	140
13.3-26.6	55	137	75	267
<13.3	8	58	42	108
	114	266	135	515

P/F on Admission	P/F on Day 7 >26.7	13.3-26.6	<13.3	
>26.7	36.4%	50.7%	12.9%	**31.8%**
13.3-26.6	20.6%	51.3%	28.1%	
<13.3	7.4%	53.7%	38.9%	
	23.5%			**44.7%**

LUNG SAFE

P/F on Admission	P/F on Day 7 26.7-40	13.3-26.6	<13.3	Total
26.7-40		184	32	714
13.3-26.6			140	1106
<13.3				557
				2377

P/F on Admission	P/F on Day 7 26.7-40	13.3-26.6	<13.3	Overall
26.7-40		25.8%	4.5%	**15.0%**
13.3-26.6			12.7%	
<13.3				

Berlin Definition

P/F on Admission	P/F on Day 7 26.7-40	13.3-26.6	<13.3	Total
26.7-40		234	33	819
13.3-26.6			230	1820
<13.3				1031
				3670

P/F on Admission	P/F on Day 7 26.7-40	13.3-26.6	<13.3	Overall
26.7-40		28.6%	4.0%	**13.5%**
13.3-26.6			12.6%	
<13.3				

Table S12 - Clinical and physiological characteristics, outcomes and interventions according to resolution of hypoxaemia over first week of invasive mechanical ventilation.

Clinical Characterisitcs					Trajectory between admission and day7				
			ALL		Resolving		Non resolving		
	label	units	Total N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	P Value
	Male		633	481 (76%)	267	196 (73.4%)	366	285 (77.9%)	0.194
	White		542	250 (46.1%)	216	98 (45.4%)	326	152 (46.6%)	0.220
	Age	years	633	59.0 [51.0 66.0]	267	57.0 [47.0 64.0]	366	60.0 [54.0 67.0]	0.000
	BMI	kg/m2	524	28.1 [24.9 32.8]	222	28.0 [24.8 32.9]	302	28.2 [25.1 32.3]	0.666
	Time since onset of symptoms	days	408	8.0 [6.0 12.0]	164	9.0 [6.5 13.5]	244	7.0 [6.0 11.0]	0.004
	ICU length of stay	days	633	14.0 [8.0 23.0]	267	13.0 [7.3 20.0]	366	15.0 [8.0 25.0]	0.025
	Length of mechanical ventilation	days	633	13.0 [7.0 22.0]	267	12.0 [6.0 18.8]	366	14.0 [8.0 24.0]	0.003
	ICU Mortality	%	633	268 (42.3%)	267	47 (17.6%)	366	221 (60.4%)	0.000
Vent	FiO_2 (%)		628	60.0 [45.0 80.0]	263	60.0 [40.0 80.0]	365	60.0 [50.0 72.8]	0.269
	PaO_2 to FiO_2 ratio		626	18.3 [13.0 25.0]	262	17.9 [11.7 27.5]	364	18.4 [14.6 24.1]	0.323
	Tidal Volume (mls/IBW)	ml/Kg(IBW)	472	6.8 [6.0 7.8]	202	6.9 [6.1 7.8]	270	6.8 [6.0 7.7]	0.373
	Respiratory rate	bpm	627	18.8 [16.0 22.0]	263	18.0 [16.0 22.0]	364	19.2 [16.0 22.4]	0.249
	Minute ventilation	L/minute	606	8.5 [6.9 10.4]	255	8.5 [7.0 10.2]	351	8.5 [6.9 10.5]	0.500
	Peak pressure	ml/Kg(RBW)	599	26.0 [23.0 30.0]	253	25.0 [22.0 29.0]	346	26.7 [24.0 30.0]	0.005
	Plateau pressure	ml/Kg(IBW)	80	26.0 [22.5 28.5]	28	24.5 [21.5 29.0]	52	26.0 [23.0 28.0]	0.438
	PEEP	cmH_20	603	10.0 [8.0 12.0]	257	10.0 [8.0 12.0]	346	10.0 [8.5 12.0]	0.008
	Mean airway pressure	cmH_20	387	16.0 [13.2 19.0]	174	15.8 [13.0 18.0]	213	16.0 [14.0 20.0]	0.037
	Pressure support	cmH_20	371	10.0 [5.3 14.0]	160	10.0 [5.0 12.5]	211	10.0 [6.3 14.0]	0.651
	Dynamic Compliance	mls/cmH20	564	31.5 [24.3 40.2]	242	32.5 [25.2 40.9]	322	30.3 [24.0 40.1]	0.253
	Oxygenation Index		387	8.1 [5.1 12.5]	174	7.7 [4.6 13.0]	213	8.2 [5.3 11.6]	0.600
	Ventilatory Ratio		470	1.5 [1.2 2.1]	200	1.4 [1.2 2.0]	270	1.6 [1.3 2.1]	0.250
ABG	Oxygen saturation		518	95.0 [93.0 98.0]	224	96.0 [93.0 98.0]	294	95.0 [92.0 97.0]	0.060
	pH		630	7.4 [7.3 7.4]	265	7.4 [7.3 7.4]	365	7.4 [7.3 7.4]	0.058
	PaO_2	kPa	630	10.7 [9.2 13.1]	265	10.4 [8.8 12.4]	365	10.9 [9.4 13.4]	0.019
	$PaCO_2$	kPa	630	6.0 [5.2 7.2]	265	6.0 [5.2 7.2]	365	6.0 [5.2 7.1]	0.959
	Base excess		630	-0.3 [-2.6 2.2]	265	0.3 [-1.9 2.5]	365	-0.7 [-3.0 1.8]	0.001
	HCO_3	mmol/L	629	24.5 [22.5 26.7]	265	24.9 [23.0 27.2]	364	24.0 [22.0 26.4]	0.001
	Lactate	mmol/L	604	1.2 [1.0 1.6]	260	1.2 [1.0 1.6]	344	1.3 [1.0 1.6]	0.045
SOFA	SOFA score		428	9.0 [7.0 11.0]	184	9.0 [7.0 11.0]	244	9.0 [7.0 11.0]	0.780
	SOFA Respiratory		626	3.0 [3.0 4.0]	262	3.0 [2.0 4.0]	364	3.0 [3.0 3.0]	0.042
	SOFA Nervous		508	3.0 [0.0 4.0]	218	2.0 [0.0 4.0]	290	4.0 [0.0 4.0]	0.663
	SOFA Cardiovascular		579	3.0 [3.0 4.0]	242	3.0 [1.0 4.0]	337	3.0 [3.0 4.0]	0.004
	SOFA Liver		588	0.0 [0.0 0.0]	252	0.0 [0.0 0.0]	336	0.0 [0.0 0.0]	0.971
	SOFA Coagulation		619	0.0 [0.0 0.0]	257	0.0 [0.0 0.0]	362	0.0 [0.0 0.0]	0.281
	SOFA Kidneys		629	0.0 [0.0 1.0]	264	0.0 [0.0 1.0]	365	0.0 [0.0 1.0]	0.453
FBC	Haemoglobin	g/dL	619	114.0 [92.0 128.0]	257	113.0 [90.0 126.0]	362	115.0 [94.0 130.0]	0.164
	Haematocrit		312	0.4 [0.3 0.4]	126	0.4 [0.3 0.4]	186	0.4 [0.3 0.4]	0.049
	White blood cell count	x10^9/L	619	9.6 [7.0 13.1]	257	9.6 [6.9 12.7]	362	9.6 [7.1 13.5]	0.818
	Neutrophils	x10^9/L	618	8.1 [5.7 11.3]	257	7.9 [5.4 11.1]	361	8.3 [5.8 11.5]	0.514
	Monocytes	x10^9/L	614	0.4 [0.3 0.7]	256	0.5 [0.3 0.7]	358	0.4 [0.3 0.7]	0.084
	Lymphocytes	x10^9/L	615	0.8 [0.5 1.2]	257	0.8 [0.6 1.3]	358	0.8 [0.5 1.1]	0.048
	Basophils	x10^9/L	498	0.0 [0.0 0.1]	201	0.0 [0.0 0.1]	297	0.0 [0.0 0.1]	0.251
	Eosinophils	x10^9/L	493	0.0 [0.0 0.1]	205	0.0 [0.0 0.1]	288	0.0 [0.0 0.1]	0.003
Coag	Platelet Count	µmol/L	619	246.0 [185.3 320.8]	257	245.0 [191.0 325.0]	362	246.0 [182.0 318.0]	0.372
	APTT	U/L	398	32.1 [28.3 37.4]	162	32.3 [28.3 38.0]	236	32.1 [28.3 36.5]	0.633
	PT	U/L	396	13.9 [12.4 15.2]	162	13.6 [12.1 15.1]	234	14.0 [12.7 15.4]	0.297
	INR	U/L	212	1.1 [1.1 1.2]	98	1.1 [1.1 1.2]	114	1.1 [1.0 1.2]	0.381
	Fibrinogen	U/L	410	6.8 [5.6 8.1]	179	6.6 [5.7 7.7]	231	6.9 [5.6 8.3]	0.280
	D-dimer	IU/L	391	2642.0 [990.5 7701.3]	177	2920.0 [977.5 8104.8]	214	2418.0 [1060.0 7530.0]	0.946
Electrolytes	Blood Urea Nitrogen (BUN)	mmol/L	498	7.4 [4.9 11.8]	200	6.8 [4.5 10.8]	298	7.8 [5.4 12.1]	0.009
	Creatinine	µmol/L	621	88.0 [66.0 140.0]	258	84.0 [64.0 129.0]	363	90.0 [67.0 148.0]	0.050
	Sodium	mmol/L	621	139.0 [136.0 142.0]	259	139.0 [137.0 142.0]	362	138.0 [135.0 141.0]	0.003
	Potassium	mmol/L	620	4.4 [4.0 4.8]	258	4.4 [4.0 4.8]	362	4.4 [4.1 4.8]	0.480
Liver	Bilirubin	µmol/L	588	10.0 [7.0 15.0]	252	10.0 [7.0 14.0]	336	10.0 [7.0 15.0]	0.143
	Alkaline Phosphatase	U/L	600	77.0 [58.5 113.0]	255	79.0 [58.3 120.8]	345	75.0 [58.8 107.3]	0.279
	AST	U/L	99	59.0 [39.3 85.0]	43	56.0 [34.8 69.5]	56	62.0 [41.5 90.5]	0.128
	ALT	U/L	592	37.0 [24.0 59.0]	252	36.0 [23.0 59.5]	340	37.0 [24.0 59.0]	0.649
Inflammation	LDH (Lactate dehydrogenase)	IU/L	194	649.0 [452.0 921.0]	82	678.0 [443.0 1032.0]	112	615.5 [459.5 873.0]	0.224
	Ferritin	ng/mL	290	1218.5 [696.0 2320.0]	129	1023.0 [665.8 2080.3]	161	1374.0 [780.5 2492.3]	0.031
	CRP		592	215.7 [135.0 311.0]	255	208.0 [119.3 308.9]	337	218.0 [145.0 312.3]	0.189
	Procalcitonin	ug/L	125	0.7 [0.3 2.2]	61	0.6 [0.3 2.2]	64	0.8 [0.3 2.1]	0.456
Cardiac	Creatinine Kinase	U/L	243	217.0 [83.5 637.3]	108	194.5 [79.0 563.0]	135	226.0 [95.8 664.8]	0.219
	High sensitivity Troponin		253	21.8 [11.0 61.0]	116	17.5 [9.0 48.3]	137	25.7 [12.0 62.0]	0.079
	NT Pro BNP	pg/ml	58	537.5 [165.0 1478.0]	28	454.0 [196.5 1498.5]	30	611.0 [161.0 1478.0]	0.834
Fluid	Cumulative Fluid balance	L	589	343.0 [-212.3 1058.3]	256	287.0 [-244.5 991.8]	333	361.0 [-201.1 1160.3]	0.412
Adjunctive interventions									
	Was patient transferred in?		633	159 (25.1%)	267	79 (29.6%)	366	80 (21.9%)	0.027
	Tracheostomy		516	145 (28.1%)	220	59 (26.8%)	296	86 (29.1%)	0.679
	PEEP>10		622	459 (73.8%)	262	159 (60.7%)	360	300 (83.3%)	0.000
	Neuro-muscular blockade		617	434 (70.3%)	256	152 (59.4%)	361	282 (78.1%)	0.000
	Prone positioning		551	273 (49.5%)	234	90 (38.5%)	317	183 (57.7%)	0.000
	Inhaled nitric oxide		521	73 (14%)	224	21 (9.38%)	297	52 (17.5%)	0.014
	Inhaled prostacyclin		521	55 (10.6%)	224	18 (8.04%)	297	37 (12.5%)	0.137
	Bronchoscopy		521	51 (9.79%)	224	20 (8.93%)	297	31 (10.4%)	0.655
	Renal replacement therapy		555	211 (38%)	238	75 (31.5%)	317	136 (42.9%)	0.017
	Diuretics		598	443 (74.1%)	247	171 (69.2%)	351	272 (77.5%)	0.005
	Corticosteroids		582	304 (52.2%)	247	115 (46.6%)	335	189 (56.4%)	0.033
	Therapeutic heparin		438	55 (12.6%)	176	18 (10.2%)	262	37 (14.1%)	0.137
	Antibiotics		313	219 (70%)	127	74 (58.3%)	186	145 (78%)	0.002
	Prone								
	No of proning episodes		273	1.0 [1.0 2.0]	90	1.0 [1.0 2.0]	183	1.0 [1.0 2.0]	0.941
	mech vent prior first prone	days	273	3.0 [1.8 6.0]	90	2.0 [1.0 5.0]	183	4.0 [2.0 7.0]	0.007
	durationn of first prone	days	273	2.0 [1.0 4.0]	90	2.0 [1.0 4.0]	183	2.0 [1.0 4.0]	0.943
	responsders to proning		270	119 (44.1%)	88	53 (60.2%)	182	66 (36.3%)	0.563
	missed windows prior to prone		273	3.0 [1.0 6.0]	90	2.0 [1.0 5.0]	183	3.0 [1.0 7.0]	0.026
	missed windows - unproned		360	3.0 [1.0 10.0]	177	1.0 [0.0 4.0]	183	6.0 [3.0 13.0]	0.000
	Tracheostomy								
	mech vent prior to tracheostomy	days	145	13.0 [9.0 18.0]	59	13.0 [7.0 16.0]	86	15.0 [10.0 19.0]	0.015
	durationn of tracheostomy	days	145	14.0 [6.0 21.3]	59	11.0 [4.3 22.0]	86	15.0 [8.0 21.0]	0.078
End of life parameters									
	life sustaining therapy withdrawn		130	85 (65.4%)	19	12 (63.2%)	111	73 (65.8%)	0.000
	cardiac arrest during admission		244	21 (8.61%)	85	4 (4.71%)	159	17 (10.7%)	0.029

Table S13 - Time series mixed model ANOVA according to resolution of hypoxaemia over first week of mechanical ventilation.

		p-values			
label	**N**	**Resolvers vs Non-Resolvers**	**parameter over time**	**interaction**	**FDR interaction**
PaO_2 / FiO_2	472	0.000	0.000	**0.000**	**0.000**
Dynamic Compliance	341	0.408	0.039	0.226	0.379
Respiratory rate	458	0.556	0.000	0.678	0.721
FiO_2 (%)	503	0.000	0.000	**0.000**	**0.000**
Tidal Volume per Kg	347	0.782	0.411	0.624	0.711
Tidal Volume	433	0.193	0.612	0.654	0.721
Minute ventilation	404	0.292	0.000	0.516	0.626
Peak pressure	426	0.002	0.000	**0.001**	**0.003**
PEEP	390	0.001	0.000	**0.001**	**0.003**
Dynamic delta pressure (peakP-peep)	124	0.559	0.813	0.197	0.341
Mean airway pressure	256	0.004	0.000	**0.000**	**0.000**
I:E ratio	93	0.280	0.487	0.458	0.567
Pressure support	169	0.110	0.032	0.076	0.166
Oxygen saturation	417	0.000	0.175	**0.001**	**0.004**
pH	487	0.001	0.000	**0.001**	**0.005**
PaO_2	484	0.008	0.033	**0.000**	**0.001**
PaCO_2	487	0.035	0.003	**0.000**	**0.000**
Base excess	478	0.048	0.000	0.063	0.149
HCO^-3	479	0.106	0.000	**0.005**	**0.014**
Lactate	451	0.001	0.310	**0.026**	0.069
Oxygenation Index	237	0.000	0.000	**0.000**	**0.000**
Ventilatory Ratio	314	0.301	0.026	0.103	0.195
Mean arterial pressure (lowest)	386	0.003	0.000	**0.001**	**0.005**
Liver-Bilirubin	167	0.262	0.040	0.158	0.285
Daily fluid balance	480	0.001	0.000	0.081	0.172
Cumulative fluid balance	480	0.015	0.074	**0.001**	**0.005**
SOFA Score	192	0.157	0.000	**0.000**	**0.000**
Non-Respiratory SOFA	224	0.349	0.000	**0.001**	**0.004**
Glucose	465	0.963	0.012	0.056	0.138
BUN	382	0.002	0.010	**0.004**	**0.012**
Creatinine	520	0.042	0.096	**0.000**	**0.001**
Sodium	523	0.796	0.008	0.258	0.421
Potassium	518	0.010	0.167	0.160	0.285
Bilirubin	401	0.284	0.000	**0.002**	**0.007**
Alkaline Phosphatase	441	0.171	0.000	0.706	0.721
AST	55	0.914	0.743	0.279	0.430
ALT	418	0.226	0.000	0.098	0.195
Creatinine Kinase	127	0.921	0.174	0.580	0.674
LDH	66	0.182	0.046	0.397	0.539
Haemoglobin	515	0.787	0.285	0.076	0.166
WBC	513	0.516	0.043	0.269	0.426
RBC	415	0.857	0.840	0.709	0.721
Platelet Count	511	0.048	0.000	0.099	0.195
Haematocrit	252	0.866	0.000	**0.026**	0.069
Neutrophils	511	0.994	0.442	0.309	0.452
Monocytes	509	0.005	0.000	0.303	0.452
Lymphocytes	509	0.124	0.000	**0.026**	0.069
Basophils	361	0.138	0.162	0.683	0.721
Eosinophils	386	0.001	0.000	0.564	0.670
APTT	255	0.236	0.660	0.326	0.465
PT	260	0.912	0.456	0.431	0.558
INR	163	0.815	0.175	0.440	0.558
Fibrinogen	137	0.063	0.062	0.690	0.721
Ferritin	75	0.201	0.472	0.404	0.539
D-dimer	147	0.967	0.388	0.406	0.539
CRP	457	0.001	0.000	**0.000**	**0.000**
High sensitivity Troponin	62	0.704	0.596	0.790	0.790

Table S14 - Uni- and multi-variate model analysis of factors associated with progression of hypoxaemia over the first week of invasive mechanical ventilation

		Univariate				Multivariate			
FieldLabel	**median [IQR]**	**Odds ratio**	**95% CI**		**P Value**	**Odds ratio**	**95% CI**		**P Value**
Age		1.366	1.186	1.572	0.000	1.236	1.060	1.441	0.007
Male		1.314	0.882	1.959	0.179				
BMI	28.13 [24.90 32.76]	0.903	0.770	1.059	0.210				
Height	173.00 [165.00 178.00]	0.942	0.799	1.110	0.473				
symptoms days	8.00 [6.00 12.00]	0.857	0.724	1.013	0.071	0.940	0.784	1.127	0.503
Hypertension		1.233	0.869	1.749	0.240				
Diabetes mellitus		1.549	1.047	2.293	0.029	1.381	0.886	2.153	0.155
Oxygen saturation	95.00 [93.00 98.00]	0.864	0.735	1.016	0.077	0.998	0.834	1.194	0.981
pH	7.36 [7.30 7.42]	0.919	0.789	1.070	0.274				
PaCO_2	5.96 [5.16 7.15]	0.964	0.827	1.123	0.635				
HCO^-3	24.50 [22.48 26.70]	0.784	0.671	0.915	0.002	0.870	0.733	1.032	0.111
Lactate	1.20 [1.00 1.60]	1.197	1.024	1.398	0.024	1.030	0.862	1.231	0.748
Peak pressure	26.00 [23.00 30.00]	1.158	0.992	1.351	0.062	1.158	0.967	1.385	0.110
PEEP	10.00 [8.00 12.00]	1.268	1.067	1.508	0.007	1.109	0.902	1.363	0.328
Minute ventilation	8.53 [6.88 10.44]	0.968	0.831	1.127	0.674				
Dynamic Comp	31.47 [24.26 40.19]	0.898	0.768	1.050	0.178				
Oxygenation Index	8.10 [5.09 12.45]	1.020	0.866	1.201	0.812				
Ventilatory Ratio	1.54 [1.22 2.07]	1.088	0.929	1.274	0.295				
Cum fluid balance	343.00 [-212.25 1058.32]	1.104	0.947	1.287	0.207				
Glucose	8.39 [6.79 10.95]	1.163	0.995	1.359	0.058	1.026	0.854	1.232	0.786
BUN	7.40 [4.90 11.80]	1.237	1.057	1.449	0.008	1.183	0.983	1.422	0.075
Sodium	139.00 [136.00 142.00]	0.793	0.678	0.926	0.004	0.818	0.686	0.974	0.024
Potassium	4.40 [4.00 4.80]	1.064	0.912	1.241	0.430				
ALP	77.00 [58.50 113.00]	0.941	0.809	1.094	0.429				
ALT	37.00 [24.00 59.00]	1.050	0.902	1.223	0.526				
Haemoglobin	114.00 [92.00 128.00]	1.116	0.960	1.296	0.152				
Neutrophils	8.10 [5.71 11.30]	1.090	0.935	1.270	0.271				
Monocytes	0.41 [0.30 0.70]	0.844	0.725	0.982	0.028	0.921	0.767	1.106	0.376
Lymphocytes	0.80 [0.50 1.20]	0.848	0.721	0.998	0.047	0.976	0.806	1.181	0.800
Basophils	0.00 [0.00 0.10]	0.811	0.544	1.208	0.302				
Eosinophils	0.00 [0.00 0.10]	0.503	0.353	0.717	0.000	0.648	0.430	0.976	0.038
APTT	32.10 [28.30 37.40]	0.926	0.781	1.098	0.376				
PT	13.85 [12.40 15.20]	1.065	0.903	1.256	0.456				
Fibrinogen	6.80 [5.60 8.10]	1.052	0.891	1.242	0.552				
D-dimer	2642.00 [990.50 7701.25]	0.964	0.818	1.134	0.655				
CRP	215.65 [135.00 311.00]	1.109	0.950	1.294	0.192				
SOFA Respiratory		0.929	0.769	1.123	0.447				
SOFA Nervous		1.028	0.942	1.121	0.541				
SOFA Cardio		1.241	1.068	1.442	0.005	1.197	1.011	1.418	0.037
SOFA Liver		0.983	0.715	1.350	0.915				
SOFA Coagulation		1.207	0.865	1.683	0.267				
SOFA Kidneys		1.059	0.901	1.245	0.484				
SOFA score		1.036	0.968	1.109	0.301				
	* NonResolvers (N=318) vs Resolvers (N=231)								

Table S15 - The application, median start date and duration of the first episode of interventions

	Start day of first intervention	Duration of first intervention	Number of periods
interventions	median [IQR]	median [IQR]	median [IQR]
Neuro-muscular blockade	1.0 [0.0 3.0]	4.0 [1.0 7.0]	1.0 [1.0 2.0]
Prone positioning	2.0 [0.8 5.0]	2.0 [1.0 4.0]	1.0 [1.0 2.0]
Inhaled nitric oxide	6.0 [3.0 9.0]	4.0 [2.0 7.3]	1.0 [1.0 1.0]
Inhaled prostacyclin	7.0 [3.0 15.0]	3.0 [1.0 6.8]	1.0 [1.0 1.0]
Tracheostomy	14.0 [9.0 18.0]	13.0 [6.0 20.0]	1.0 [1.0 1.0]
APRV	3.0 [0.5 6.0]	3.0 [2.0 5.0]	1.0 [1.0 1.0]
Bronchoscopy	9.0 [3.0 15.8]	1.0 [1.0 1.0]	1.0 [1.0 1.0]
Renal replacement therapy	3.0 [1.0 6.0]	5.0 [3.0 11.0]	1.0 [1.0 2.0]
Diuretics	1.0 [1.0 3.0]	3.0 [1.0 5.0]	2.0 [1.0 3.0]
Corticosteroids	5.0 [1.0 10.0]	4.0 [2.0 9.0]	1.0 [1.0 2.0]
Therapeutic heparin	9.0 [6.0 14.0]	5.0 [2.0 8.8]	1.0 [1.0 1.0]
Anti-Bacterial	0.0 [0.0 0.0]	6.0 [4.0 9.0]	1.0 [1.0 2.0]

Table S16 - Clinical and physiological characteristics, outcomes and interventions according to prone responsiveness.

Clinical Characterisitcs					Prone responsivness				
			ALL		Responders		Non-Responders		
	label	units	Total N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	Group N	median [IQR] / N (%)	P Value
	Male		270	203 (75.2%)	119	93 (78.2%)	151	110 (72.8%)	0.316
	White		219	115 (52.5%)	90	43 (47.8%)	129	72 (55.8%)	0.057
	Age	years	270	60.0 [54.0 66.0]	119	58.0 [50.0 64.0]	151	60.0 [56.3 66.0]	0.001
	BMI	kg/m2	239	29.0 [25.3 33.2]	107	29.4 [26.2 33.2]	132	28.0 [24.8 33.2]	0.220
	Time since onset of symptoms	days	181	7.0 [6.0 11.0]	75	8.0 [6.0 12.8]	106	7.0 [6.0 11.0]	0.282
	ICU length of stay	days	270	18.0 [11.0 29.0]	119	19.0 [12.3 30.8]	151	16.0 [10.0 26.0]	0.043
	Length of mechanical ventilation	days	270	16.0 [10.0 26.0]	119	18.0 [11.0 28.5]	151	15.0 [10.0 23.8]	0.055
	ICU Mortality	%	270	142 (52.6%)	119	37 (31.1%)	151	105 (69.5%)	0.000
Vent	FiO_2 (%)		269	65.0 [50.0 80.0]	119	60.0 [50.0 80.0]	150	70.0 [60.0 80.0]	0.022
	PaO_2 to FiO_2 ratio		269	16.4 [12.1 21.9]	119	17.9 [13.5 23.3]	150	15.0 [11.4 19.6]	0.000
	Tidal Volume (mls/IBW)	ml/Kg(IBW)	220	6.8 [6.1 7.8]	99	6.8 [6.2 7.9]	121	6.8 [6.0 7.7]	0.581
	Respiratory rate	bpm	268	20.0 [16.0 24.0]	118	20.0 [18.0 24.0]	150	18.0 [16.0 22.0]	0.021
	Minute ventilation	L/minute	256	8.7 [6.9 10.4]	115	9.1 [7.7 10.6]	141	8.5 [6.7 10.1]	0.024
	Peak pressure	ml/Kg(RBW)	256	27.0 [24.0 30.0]	117	27.0 [24.0 29.0]	139	28.0 [25.0 30.8]	0.032
	Plateau pressure	ml/Kg(IBW)	48	28.0 [24.0 29.0]	20	26.5 [22.0 29.5]	28	28.0 [25.5 28.5]	0.612
	PEEP	cmH_20	259	10.0 [10.0 12.0]	116	10.0 [10.0 12.0]	143	10.8 [10.0 14.0]	0.124
	Mean airway pressure	cmH_20	143	17.0 [14.3 19.0]	73	17.0 [15.0 18.0]	70	16.5 [14.0 21.0]	0.805
	Pressure support	cmH_20	150	10.0 [8.0 14.0]	60	10.0 [7.0 15.0]	90	10.0 [8.0 14.0]	0.504
	Dynamic Compliance	mls/cmH20	237	30.0 [24.0 38.1]	109	31.0 [23.5 39.9]	128	29.4 [24.4 36.6]	0.509
	Oxygenation Index		143	9.3 [6.4 13.6]	73	8.7 [5.9 11.1]	70	11.0 [6.9 16.2]	0.003
	Ventilatory Ratio		219	1.7 [1.4 2.2]	98	1.8 [1.4 2.2]	121	1.7 [1.2 2.3]	0.617
ABG	Oxygen saturation		242	94.5 [92.0 97.0]	113	95.0 [92.0 97.0]	129	94.0 [92.0 96.0]	0.167
	pH		270	7.3 [7.3 7.4]	119	7.3 [7.3 7.4]	151	7.4 [7.3 7.4]	0.916
	PaO_2	kPa	270	10.6 [9.0 12.4]	119	10.5 [9.2 12.6]	151	10.6 [8.8 12.3]	0.539
	$PaCO_2$	kPa	270	6.2 [5.3 7.4]	119	6.2 [5.3 7.3]	151	6.4 [5.4 7.4]	0.358
	Base excess		270	0.2 [-2.6 2.7]	119	0.2 [-2.4 2.3]	151	0.2 [-2.6 3.2]	0.794
	HCO_3^-	mmol/L	269	24.4 [22.4 27.0]	118	24.6 [22.4 26.7]	151	24.2 [22.4 27.1]	0.739
	Lactate	mmol/L	256	1.2 [1.0 1.6]	110	1.1 [0.9 1.5]	146	1.3 [1.1 1.7]	0.000
SOFA	SOFA score		174	9.0 [7.0 11.0]	75	8.0 [7.0 10.0]	99	9.0 [7.3 11.0]	0.239
	SOFA Respiratory		269	3.0 [3.0 4.0]	119	3.0 [3.0 3.0]	150	3.0 [3.0 4.0]	0.000
	SOFA Nervous		205	4.0 [0.0 4.0]	88	4.0 [0.0 4.0]	117	4.0 [0.0 4.0]	0.208
	SOFA Cardiovascular		248	3.0 [1.0 4.0]	110	3.0 [1.0 3.0]	138	3.0 [3.0 4.0]	0.000
	SOFA Liver		252	0.0 [0.0 0.0]	110	0.0 [0.0 0.0]	142	0.0 [0.0 0.0]	0.968
	SOFA Coagulation		267	0.0 [0.0 0.0]	116	0.0 [0.0 0.0]	151	0.0 [0.0 0.0]	0.877
	SOFA Kidneys		269	0.0 [0.0 1.0]	118	0.0 [0.0 1.0]	151	0.0 [0.0 1.0]	0.257
FBC	Haemoglobin	g/dL	267	116.0 [91.3 128.0]	116	115.5 [95.0 127.8]	151	117.0 [88.3 129.0]	0.783
	Haematocrit		178	0.4 [0.3 0.4]	86	0.4 [0.3 0.4]	92	0.4 [0.3 0.4]	0.564
	White blood cell count	x10^9/L	267	9.7 [7.3 12.8]	116	9.6 [7.1 12.6]	151	9.8 [7.5 12.9]	0.643
	Neutrophils	x10^9/L	267	8.3 [6.1 11.3]	116	8.1 [5.6 11.1]	151	8.3 [6.5 11.7]	0.347
	Monocytes	x10^9/L	264	0.4 [0.3 0.6]	115	0.4 [0.3 0.6]	149	0.4 [0.3 0.6]	0.808
	Lymphocytes	x10^9/L	265	0.7 [0.5 1.1]	115	0.8 [0.5 1.2]	150	0.7 [0.5 1.1]	0.632
	Basophils	x10^9/L	223	0.0 [0.0 0.1]	100	0.0 [0.0 0.1]	123	0.0 [0.0 0.0]	0.517
	Eosinophils	x10^9/L	220	0.0 [0.0 0.1]	101	0.0 [0.0 0.1]	119	0.0 [0.0 0.1]	0.412
Coag	Platelet Count	µmol/L	267	247.0 [190.3 331.0]	116	247.5 [196.0 329.5]	151	247.0 [190.0 333.5]	0.812
	APTT	U/L	193	31.7 [28.0 35.3]	86	31.8 [28.0 35.6]	107	31.4 [27.8 34.9]	0.451
	PT	U/L	192	13.6 [12.1 14.9]	86	13.3 [12.1 14.7]	106	13.8 [12.1 15.4]	0.196
	INR	U/L	127	1.1 [1.1 1.2]	66	1.1 [1.1 1.2]	61	1.1 [1.1 1.2]	0.521
	Fibrinogen	U/L	188	6.9 [5.7 8.2]	93	6.9 [5.6 8.0]	95	7.1 [5.9 8.3]	0.144
	D-dimer	IU/L	171	2540.0 [947.0 6208.5]	73	1694.0 [880.0 3895.0]	98	3213.5 [1385.0 8329.0]	0.009
Electrolytes	Blood Urea Nitrogen (BUN)	mmol/L	189	7.0 [5.0 11.0]	67	6.6 [5.0 9.9]	122	7.6 [5.1 11.9]	0.345
	Creatinine	µmol/L	267	84.0 [63.0 125.8]	117	85.0 [65.8 133.3]	150	82.0 [63.0 118.0]	0.309
	Sodium	mmol/L	268	138.0 [136.0 141.0]	118	138.0 [135.0 140.0]	150	139.0 [136.0 143.0]	0.128
	Potassium	mmol/L	268	4.4 [4.1 4.7]	118	4.5 [4.2 4.8]	150	4.4 [4.0 4.7]	0.204
Liver	Bilirubin	µmol/L	252	10.0 [7.0 15.0]	110	10.0 [7.0 15.0]	142	10.0 [8.0 15.0]	0.245
	Alkaline Phosphatase	U/L	257	76.0 [56.8 109.0]	113	76.0 [53.0 110.0]	144	75.5 [60.5 108.0]	0.548
	AST	U/L	52	61.0 [41.0 80.5]	22	59.0 [42.0 91.0]	30	61.5 [40.0 79.0]	0.985
	ALT	U/L	253	37.0 [26.0 56.3]	111	37.0 [26.3 57.8]	142	36.5 [25.0 56.0]	0.978
Inflammation	LDH (Lactate dehydrogenase)	IU/L	110	712.5 [520.0 1004.0]	55	783.0 [532.0 1141.8]	55	677.0 [514.0 968.3]	0.404
	Ferritin	ng/mL	149	1297.0 [711.8 2520.0]	68	1038.0 [629.5 2215.0]	81	1410.0 [773.3 2776.8]	0.115
	CRP		252	235.0 [158.6 322.6]	117	229.8 [155.5 323.3]	135	239.3 [160.0 321.7]	0.597
	Procalcitonin	ug/L	47	0.9 [0.4 2.4]	19	0.6 [0.3 2.3]	28	1.2 [0.6 2.9]	0.190
Cardiac	Creatinine Kinase	U/L	122	248.5 [122.0 638.0]	61	373.0 [187.1 847.3]	61	155.0 [92.8 515.8]	0.004
	High sensitivity Troponin		132	21.9 [11.8 57.5]	65	15.0 [8.8 50.8]	67	25.0 [14.4 61.8]	0.022
	NT Pro BNP	pg/ml	26	621.0 [173.0 1983.0]	10	313.5 [165.0 680.0]	16	810.5 [502.0 2587.0]	0.058
Fluid	Cumulative Fluid balance	L	251	384.0 [-196.6 1160.0]	109	143.0 [-272.3 753.8]	142	622.0 [-114.0 1363.0]	0.004
Adjunctive interventions									
	Was patient transferred in?		270	87 (32.2%)	119	48 (40.3%)	151	39 (25.8%)	0.011
	Tracheostomy		243	77 (31.7%)	113	41 (36.3%)	130	36 (27.7%)	0.055
	PEEP>10		268	239 (89.2%)	119	102 (85.7%)	149	137 (91.9%)	0.199
	Neuro-muscular blockade		269	246 (91.4%)	118	107 (90.7%)	151	139 (92.1%)	0.540
	Prone positioning		270	270 (100%)	119	119 (100%)	151	151 (100%)	
	Inhaled nitric oxide		243	66 (27.2%)	113	20 (17.7%)	130	46 (35.4%)	0.010
	Inhaled prostacyclin		243	35 (14.4%)	113	9 (7.96%)	130	26 (20%)	0.019
	Bronchoscopy		243	34 (14%)	113	18 (15.9%)	130	16 (12.3%)	0.265
	Renal replacement therapy		250	112 (44.8%)	115	48 (41.7%)	135	64 (47.4%)	0.735
	Diuretics		268	210 (78.4%)	118	90 (76.3%)	150	120 (80%)	0.451
	Corticosteroids		264	154 (58.3%)	118	65 (55.1%)	146	89 (61%)	0.477
	Therapeutic heparin		187	33 (17.6%)	75	14 (18.7%)	112	19 (17%)	0.839
	Antibiotics		179	119 (66.5%)	87	46 (52.9%)	92	73 (79.3%)	0.111
	Prone								
	No of proning episodes		270	1.0 [1.0 2.0]	119	1.0 [1.0 2.0]	151	1.0 [1.0 2.0]	0.073
	mech vent prior first prone	days	270	3.0 [1.0 6.0]	119	3.0 [2.0 5.8]	151	3.0 [1.0 7.0]	0.357
	durationn of first prone	days	270	2.0 [1.0 4.0]	119	2.0 [1.0 4.0]	151	2.0 [1.0 4.0]	0.413
	responsders to proning		270	119 (44.1%)	119	119 (100%)	151	0 (0%)	0.000
	missed windows prior to prone		270	3.0 [1.0 6.0]	119	2.0 [1.0 5.0]	151	3.0 [1.0 7.0]	0.022
			0	NaN [NaN NaN]	0	NaN [NaN NaN]	0	NaN [NaN NaN]	
	Tracheostomy								
	mech vent prior to tracheostomy	days	77	16.0 [11.0 20.0]	41	16.0 [12.0 19.3]	36	14.5 [8.5 20.0]	0.352
	durationn of tracheostomy	days	77	14.0 [6.0 21.3]	41	15.0 [7.8 22.0]	36	11.5 [4.0 20.0]	0.129
End of life parameters									
	life sustaining therapy withdrawn		90	61 (67.8%)	31	22 (71%)	59	39 (66.1%)	0.152
	cardiac arrest during admission		139	13 (9.35%)	58	7 (12.1%)	81	6 (7.41%)	0.467

Table S17 - Time series mixed model ANOVA according to prone responsiveness.

		p-values			
label	**N**	**Prone Responders vs non-Responders**	**parameter over time**	**interaction**	**FDR interaction**
PaO_2 / FiO_2	234	0.000	0.000	**0.000**	**0.000**
Dynamic Compliance	171	0.813	0.819	0.817	0.872
Respiratory rate	219	0.993	0.645	0.143	0.590
FiO_2 (%)	239	0.000	0.000	**0.000**	**0.001**
Tidal Volume per Kg	186	0.477	0.779	0.867	0.883
Tidal Volume	216	0.186	0.659	0.799	0.872
Minute ventilation	197	0.803	0.449	0.368	0.619
Peak pressure	212	0.002	0.649	0.333	0.619
PEEP	197	0.699	0.929	0.826	0.872
Dynamic delta pressure (peakP-peep)	78	0.014	0.487	0.929	0.929
Mean airway pressure	117	0.670	0.019	**0.003**	**0.021**
I:E ratio	42	0.881	0.923	0.711	0.811
Pressure support	84	0.775	0.766	0.703	0.811
Oxygen saturation	218	0.000	0.119	**0.002**	**0.015**
pH	239	0.047	0.021	0.316	0.619
PaO_2	239	0.000	0.011	**0.001**	**0.010**
PaCO_2	239	0.004	0.003	0.442	0.619
Base excess	234	0.689	0.000	0.367	0.619
HCO^-3	236	0.529	0.000	0.857	0.883
Lactate	216	0.000	0.505	0.385	0.619
Oxygenation Index	113	0.000	0.001	**0.001**	**0.010**
Ventilatory Ratio	167	0.053	0.404	0.427	0.619
Mean arterial pressure (lowest)	198	0.320	0.409	0.513	0.676
Liver-Bilirubin	70	0.668	0.727	0.696	0.811
Daily fluid balance	227	0.038	0.295	0.257	0.619
Cumulative fluid balance	227	0.035	0.129	0.108	0.558
SOFA Score	97	0.045	0.445	0.298	0.619
Non-Respiratory SOFA	108	0.100	0.541	0.346	0.619
Glucose	208	0.930	0.771	0.677	0.811
BUN	158	0.703	0.000	0.785	0.872
Creatinine	249	0.855	0.757	0.065	0.372
Sodium	251	0.192	0.036	0.194	0.619
Potassium	246	0.915	0.492	0.413	0.619
Bilirubin	192	0.884	0.277	0.227	0.619
Alkaline Phosphatase	205	0.808	0.000	0.342	0.619
AST	35	0.098	0.054	0.225	0.619
ALT	197	0.054	0.000	**0.000**	**0.005**
Creatinine Kinase	88	0.132	0.417	0.419	0.619
LDH	52	0.162	0.374	0.359	0.619
Haemoglobin	246	0.433	0.202	0.351	0.619
WBC	246	0.441	0.001	0.138	0.590
RBC	220	0.074	0.651	0.582	0.737
Platelet Count	244	0.040	0.000	**0.000**	**0.005**
Haematocrit	162	0.608	0.000	0.437	0.619
Neutrophils	246	0.143	0.057	0.340	0.619
Monocytes	244	0.956	0.000	0.522	0.676
Lymphocytes	245	0.881	0.000	**0.043**	0.275
Basophils	191	0.683	0.037	0.468	0.635
Eosinophils	193	0.874	0.002	0.153	0.590
APTT	137	0.424	0.800	0.420	0.619
PT	140	0.718	0.306	0.445	0.619
INR	110	0.381	0.667	0.266	0.619
Fibrinogen	80	0.033	0.021	0.654	0.811
Ferritin	55	0.224	0.565	0.344	0.619
D-dimer	70	0.009	0.562	0.374	0.619
CRP	217	0.203	0.042	0.227	0.619
High sensitivity Troponin	47	0.963	0.395	0.155	0.590

Table S18 - Uni- and multi-variate model analysis of pre-pronation factors associated prone responsiveness.

		Univariate				Multivariate			
FieldLabel	**median [IQR]**	**Odds ratio**	**95% CI**		**P Value**	**Odds ratio**	**95% CI**		**P Value**
Age		1.555	1.197	2.019	0.001	1.557	1.165	2.081	0.003
Male		0.875	0.474	1.617	0.671				
BMI	29.00 [25.28 33.18]	0.865	0.681	1.099	0.234				
Height	172.35 [165.00 178.00]	1.045	0.821	1.330	0.718				
symptoms days	7.00 [6.00 11.00]	1.039	0.810	1.332	0.764				
Hypertension		1.061	0.616	1.827	0.832				
Diabetes mellitus		1.393	0.749	2.591	0.296				
Oxygen saturation	93.00 [91.00 96.00]	0.758	0.589	0.975	0.031	0.982	0.714	1.351	0.911
pH	7.37 [7.31 7.42]	0.865	0.683	1.094	0.225				
PaCO_2	6.70 [5.80 7.67]	1.257	0.989	1.598	0.062	1.198	0.890	1.611	0.234
HCO^-3	26.60 [24.00 30.65]	0.988	0.784	1.247	0.922				
Lactate	1.30 [1.10 1.80]	1.610	1.260	2.057	0.000	1.331	0.992	1.785	0.057
Peak pressure	28.06 [25.00 31.00]	1.568	1.232	1.995	0.000	1.423	1.063	1.906	0.018
PEEP	11.00 [10.00 13.00]	1.359	1.062	1.738	0.015	1.256	0.927	1.702	0.142
Minute ventilation	9.88 [8.19 11.96]	1.083	0.854	1.374	0.510				
Dynamic Comp	30.14 [24.00 38.59]	0.981	0.770	1.251	0.880				
Ventilatory Ratio	2.11 [1.61 2.57]	1.159	0.903	1.488	0.246				
Cum fluid balance	1743.00 [216.14 4269.60]	1.445	1.133	1.843	0.003	1.232	0.919	1.650	0.162
Glucose	9.10 [7.50 11.10]	0.982	0.775	1.244	0.882				
BUN	10.00 [6.93 15.60]	1.095	0.857	1.399	0.466				
Sodium	141.00 [139.00 146.00]	1.217	0.964	1.537	0.099	1.189	0.890	1.589	0.241
Potassium	4.53 [4.30 4.90]	1.107	0.877	1.397	0.392				
ALP	85.00 [65.00 136.00]	0.991	0.782	1.255	0.940				
ALT	40.00 [27.00 58.00]	0.834	0.659	1.056	0.132				
Haemoglobin	103.00 [75.50 116.88]	0.931	0.738	1.174	0.543				
Haematocrit	0.33 [0.30 0.38]	0.970	0.753	1.250	0.816				
Neutrophils	8.80 [6.92 11.78]	1.149	0.910	1.453	0.244				
Monocytes	0.40 [0.30 0.70]	0.920	0.718	1.179	0.510				
Lymphocytes	0.80 [0.55 1.10]	0.898	0.715	1.128	0.356				
Basophils	0.02 [0.00 0.10]	1.232	0.921	1.650	0.160				
Eosinophils	0.10 [0.00 0.20]	0.986	0.715	1.360	0.931				
APTT	32.83 [29.00 37.85]	0.874	0.681	1.123	0.293				
PT	14.00 [12.10 15.30]	1.138	0.883	1.466	0.318				
Fibrinogen	7.30 [6.10 8.91]	0.967	0.758	1.235	0.790				
D-dimer	4017.50 [1630.00 10580.00]	1.141	0.886	1.470	0.308				
CRP	277.50 [183.45 339.00]	1.080	0.850	1.371	0.530				
SOFA Respiratory	3.00 [3.00 3.00]	1.894	1.352	2.654	0.000	1.708	1.168	2.499	0.006
SOFA Nervous		0.932	0.810	1.072	0.326				
SOFA Cardio		1.442	1.168	1.781	0.001	1.346	1.039	1.742	0.024
SOFA Liver		0.933	0.615	1.414	0.744				
SOFA Coagulation		1.616	0.866	3.017	0.132				
SOFA Kidneys		0.948	0.749	1.199	0.654				
Prone initiation day		1.044	0.981	1.110	0.175				
	* non-resp (N=127) vs repsonsive (N=101)								

Table S19 - Uni- and multi-variate model analysis of post- pronation factors associated prone responsiveness.

		Univariate				Multivariate			
FieldLabel	**median [IQR]**	**Odds ratio**	**95% CI**		**P Value**	**Odds ratio**	**95% CI**		**P Value**
Age		1.485	1.164	1.893	0.001	1.431	1.082	1.892	0.012
Male		1.344	0.734	2.460	0.338				
BMI	29.00 [25.28 33.18]	0.849	0.672	1.073	0.171				
Height	172.35 [165.00 178.00]	1.057	0.835	1.339	0.643				
symptoms days	7.00 [6.00 11.00]	1.057	0.829	1.347	0.654				
Hypertension		1.085	0.644	1.828	0.758				
Diabetes mellitus		1.395	0.777	2.505	0.265				
Oxygen saturation	93.00 [91.00 95.00]	0.683	0.540	0.864	0.001	0.799	0.603	1.059	0.119
pH	7.35 [7.29 7.41]	0.851	0.680	1.065	0.160				
PaCO_2	6.85 [6.01 8.10]	1.225	0.976	1.536	0.080	1.210	0.930	1.575	0.156
HCO^-3	26.80 [23.90 30.20]	1.011	0.808	1.264	0.926				
Lactate	1.30 [1.00 1.70]	1.640	1.290	2.086	0.000	1.316	0.998	1.737	0.052
Peak pressure	28.00 [25.88 31.00]	1.468	1.163	1.854	0.001	1.432	1.101	1.862	0.007
PEEP	11.00 [10.00 13.00]	1.214	0.961	1.535	0.104				
Minute ventilation	9.89 [7.91 11.38]	0.956	0.764	1.196	0.693				
Dynamic Comp	30.18 [21.83 40.96]	0.924	0.733	1.166	0.506				
Ventilatory Ratio	2.05 [1.64 2.50]	1.184	0.934	1.501	0.162				
Cum fluid balance	2319.00 [389.06 5227.73]	1.217	0.965	1.536	0.098	0.922	0.693	1.227	0.579
Glucose	8.95 [7.39 11.33]	1.181	0.933	1.494	0.167				
BUN	10.65 [6.90 16.35]	1.152	0.911	1.458	0.238				
Sodium	142.00 [138.00 146.00]	1.151	0.916	1.446	0.227				
Potassium	4.60 [4.30 5.00]	0.963	0.766	1.212	0.748				
ALP	94.00 [67.00 142.25]	1.051	0.837	1.320	0.666				
ALT	41.00 [30.00 61.00]	0.928	0.738	1.168	0.525				
Haemoglobin	100.00 [79.00 117.25]	0.941	0.750	1.179	0.596				
Haematocrit	0.34 [0.29 0.37]	0.922	0.727	1.171	0.507				
Neutrophils	8.60 [6.86 11.90]	1.128	0.903	1.410	0.289				
Monocytes	0.43 [0.30 0.70]	0.818	0.652	1.027	0.083	0.758	0.581	0.990	0.042
Lymphocytes	0.72 [0.50 1.10]	0.865	0.687	1.090	0.219				
Basophils	0.01 [0.00 0.10]	0.965	0.712	1.307	0.817				
Eosinophils	0.10 [0.00 0.20]	0.947	0.697	1.285	0.725				
APTT	32.40 [28.65 37.82]	1.042	0.821	1.323	0.733				
PT	13.70 [11.90 14.95]	1.117	0.881	1.416	0.360				
CRP	289.00 [183.50 348.75]	0.946	0.751	1.192	0.638				
SOFA Respiratory	3.00 [3.00 4.00]	2.233	1.513	3.297	0.000	1.946	1.231	3.078	0.004
SOFA Nervous		0.910	0.791	1.046	0.186				
SOFA Cardio		1.420	1.163	1.735	0.001	1.134	0.893	1.441	0.301
SOFA Liver		0.996	0.654	1.518	0.986				
SOFA Coagulation		1.190	0.726	1.951	0.490				
SOFA Kidneys		0.932	0.747	1.162	0.531				
Prone initiation day		1.044	0.982	1.111	0.167				

* non-resp (N=138) vs repsonsive (N=109)

Table S20 - Time series mixed model ANOVA according to ARDS on admission

		p-values			
label	**N**	**ARDS Group**	**parameter over time**	**interaction**	**FDR interaction**
PaO_2 / FiO_2	472	0.000	0.000	**0.000**	**0.000**
Dynamic Compliance	341	0.000	0.011	0.304	0.656
Respiratory rate	458	0.118	0.000	0.820	0.922
FiO_2 (%)	503	0.000	0.000	**0.000**	**0.000**
Tidal Volume per Kg	347	0.506	0.267	0.854	0.922
Tidal Volume	433	0.606	0.119	0.811	0.922
Minute ventilation	404	0.041	0.000	0.750	0.913
Peak pressure	426	0.000	0.000	**0.000**	**0.003**
PEEP	390	0.000	0.103	0.566	0.798
Dynamic delta pressure (peakP-peep)	124	0.022	0.001	0.227	0.656
Mean airway pressure	256	0.000	0.173	0.117	0.450
I:E ratio	93	0.015	0.656	0.461	0.798
Pressure support	169	0.415	0.878	0.917	0.934
Oxygen saturation	417	0.001	0.000	**0.001**	**0.007**
pH	487	0.000	0.014	0.574	0.798
PaO_2	484	0.000	0.000	**0.000**	**0.000**
PaCO_2	487	0.000	0.000	**0.043**	0.196
Base excess	478	0.022	0.000	0.577	0.798
HCO^-3	479	0.001	0.000	0.525	0.798
Lactate	451	0.046	0.000	**0.009**	0.065
Oxygenation Index	237	0.000	0.000	**0.000**	**0.000**
Ventilatory Ratio	314	0.003	0.000	0.381	0.736
Mean arterial pressure (lowest)	386	0.610	0.045	0.847	0.922
Liver-Bilirubin	167	0.574	0.133	0.294	0.656
Daily fluid balance	480	0.042	0.194	0.281	0.656
Cumulative fluid balance	480	0.013	0.424	0.145	0.497
SOFA Score	192	0.019	0.712	0.740	0.913
Non-Respiratory SOFA	224	0.019	0.066	0.163	0.517
Glucose	465	0.290	0.312	0.761	0.913
BUN	382	0.075	0.000	0.532	0.798
Creatinine	520	0.314	0.841	**0.011**	0.065
Sodium	523	0.431	0.000	0.820	0.922
Potassium	518	0.139	0.853	**0.010**	0.065
Bilirubin	401	0.124	0.192	0.706	0.913
Alkaline Phosphatase	441	0.116	0.000	0.147	0.497
AST	55	0.018	0.729	0.626	0.845
ALT	418	0.912	0.000	**0.014**	0.076
Creatinine Kinase	127	0.433	0.796	0.719	0.913
Haemoglobin	515	0.978	0.147	0.083	0.343
WBC	513	0.751	0.002	0.487	0.798
RBC	415	0.049	0.743	0.967	0.967
Platelet Count	511	0.191	0.000	0.264	0.656
Haematocrit	252	0.190	0.001	**0.039**	0.192
Neutrophils	511	0.054	0.020	0.288	0.656
Monocytes	509	0.002	0.000	0.563	0.798
Lymphocytes	509	0.256	0.001	0.558	0.798
Basophils	361	0.883	0.002	0.369	0.736
Eosinophils	386	0.899	0.000	0.539	0.798
APTT	255	0.146	0.309	0.248	0.656
PT	260	0.322	0.697	0.469	0.798
INR	163	0.002	0.741	0.907	0.934
Fibrinogen	137	0.711	0.090	0.916	0.934
D-dimer	147	0.027	0.504	0.282	0.656
CRP	457	0.000	0.039	0.326	0.676

Supplementary Figure Legends

Figure S1. (**A**) Age, ethnicities, and pre-admission co-morbidities of COVID-19 patients undergoing invasive mechanical ventilation [Cardiovascular Disease (CVD); Hypertension (HT), Chronic Kidney Disease (CKD), Venous thromboembolism (VTE), Chronic Obstructive Pulmonary Disease (COPD), Immunosuppression (IS). (**B**) Outcome to ICU admission. Grey vertical lines labelled 25%, 50%, 75% indicate the time points (8, 14 and 23 days, respectively) by which the stated proportion of patients that were either discharged or deceased. (**C**) Admission dates to intensive care unit (ICU) across first pandemic surge; Grey vertical lines represent quartiles based on number of patients admitted.

Figure S2. Time-series analyses of ICU outcome. (**A**) Each panel presents the time-series of a physiological measure of patients who were discharged (green) versus died (red) over the first 3 weeks of IMV (*P<0.05 interaction with mixed model ANOVA over the first week of IMV, see table S14). The Solid lines are the group medians, and the shaded areas are the semi-interquartile range. The number of subjects decay over time as patients die and discharge and the initial and final numbers available for each measure are presented on the graph. (**B**) Correlation matrix between all variables considered for the logistic regression (the final set of parameters was based on less then 40% missingness, see table S2). (**C**) The odds ratio and their 95% confidence interval for Univariate and Multivariate logistic regression models where a higher odds ratio is the increased likelihood of dying for each step increase in the admission variable and physiological measures. Continuous variables were discretely sized by a split into quartiles (see supplementary methods for details and table S14 for the full stats). All variables (of the list in table S2) with less than 40% missingness were included in the model. Subjects with more than 20% missing data were removed from the analysis.

Figure S3. (**A**) Legend listing all clinical features available in SHAP plots. The clinical features were arranged from most important to least important. The colour shade of each clinical measurement represents the clinical grouping. The clinical grouping/colour pair are grey for CVS physiology, purple for Renal / Liver, green for Pulmonary physiology, blue for Haematology / Coagulation, and red for Inflammation / Infection. (**B**) Concept figure depicting four different clinical parameters groupings based on their varying importance characteristic in predicting mortality outcome. The colour and shape of each polygon represent groupings of each clinical parameter importance in predicting mortality which is 1. increasing (yellow), 2. decreasing (blue), 3. constant high (green), and 4. constant low importance (red). (**C**)(**D**) Two-days rolling average of mean absolute SHAP values of various importance characteristic changes day-by-day. Each panel represents groupings of each clinical parameter

importance as described in (**B**). (**C**) mean absolute SHAP plots of our logistic regression model. (**D**) mean absolute SHAP plots of our three-layer multilayer perceptron model.

Figure S4. (**A**) Time-series analyses of first week resolution. Each panel presents the time-series of a physiological measure of resolvers (light blue) versus non-resolvers (yellow) over the first 3 weeks of IMV (*P<0.05 interaction with mixed model ANOVA over the first week of IMV, see table S7). The Solid lines are the group medians, and the shaded areas are the semi-interquartile range. The number of subjects decay over time as patients die and discharge and the initial and final numbers available for each measure are presented on the graph. (**B**) ICU survival curves for patients who were showing improvement in hypoxaemia category over the first week on IMV (resolvers, light blue) versus deterioration in hypoxaemia category (non-resolvers, yellow). (**C**) Correlation matrix between all variables considered for the logistic regression (the final set of parameters was based on less then 40% missingness, see table S2). (**D**) The odds ratio and their 95% confidence interval for Multivariate logistic regression models where a higher odds ratio is the increased likelihood for progression of hypoxaemia for each step increase in the admission variable and physiological measures. Continuous variables were discretely sized by a split into quartiles (see supplementary methods for details and table S8 for the full stats). All variables (of the list in table S2) with less than 40% missingness were included in the model. Subjects with more than 20% missing data were removed from the analysis.

Figure S5. (**A**) Outcome of adjunctive interventions application (bold colours) versus no application (lighter colours): from the bottom we stack discharged and intervened (solid green), deceased and intervened (solid red), discharged and not-intervention (light green), deceased and non-intervention (light red). Percentages are out of the total number of patients (N=633). Most patients will have had multiple interventions, so the bar chart does double count. (**B**) Percentages of patients being in a low or high hypoxaemia severity (PaO_2/FiO_2 ratio > or < 20kPa) at the last time point before the intervention (i.e. either morning of the day of the intervention or the evening before). (**C**) Visualisation of the variability of when and how long interventions were applied for and their associated patient outcome (green - discharge, red - deceased) showing data in a separate boxed panel for each intervention. Each boxed panel contains a scatter plot of the number of days of invasive mechanical ventilation (IMV) at which first intervention was applied (x-Axis) vs duration of the first period of that intervention in days (y-Axis). Parallel to the respective axis we show the marginal histogram of the data points in the scatter plot (e.g. the histogram for start of first intervention on the x-Axis). In the bottom left of the boxed panel we show the histogram of the number of repeated intervention periods a patient underwent (see main text for details). NMBA was commenced on admission (1[0-3] days) and lasted 4(1-7) days. Prone

position was applied on day 2(1-5) and lasted 2(1-4) days. Inhaled nitric oxide and prostacyclin were commenced on day 6(3-9) and 7(3-15) and were continued for 4(2-7) days and 3(1-7) days, respectively. Tracheostomy was performed in 29% at a median 14(9-18) days in patients mainly likely to survive (40% versus 10.9%; P<0.001). Diuresis was utilised in 74% and applied on day 1(1-3) and lasted 3(1-5) days. Renal replacement therapy was utilised in 38% of patients with a median commencement on day 3(1-6) after IMV, and a median duration of 5(3-11) days. Anti-microbial prescribing was common in 70% of patients and were administer on or before day of admission, often lasting 6(4-9) days, however, these data was only available in less than 50% of the population as it was missing in some of the sites. From the sites where it was reported the missingness was less then 5%. See Table S5 for an overview of the interventions and their respective use statistics. Most patients will have had multiple interventions, see our online interface (www.covidUK.icu) to explore the interactions between interventions.

Figure S6. Variations in the reported application of interventions between sites. On the y axis are the percentages of patients who received each intervention in each site. On the bars are the number of the patients who received each intervention in each site over the total number of patients from that site.

Figure S7. Overview of weight effect on tidal volume and PEEP management. (**A**) The distributions of reported (light blue) and calculated ideal (light red) body weights highlighting systematic differences. (**B**) The distributions tidal volumes in ml/Kg for reported and ideal body weights. (**C**) The management of PEEP as a function of FiO_2 plotted in a scatter plot for non-morbidly obese patients (BMI<40, left) and morbidly obese (BMI>=40, right). Each plot shows the pre-COVID recommended PEEP ladder of ARDSNet (solid black line) against actual data points showing clearly visible departure from recommended pre-COVID PEEP ladder. Data points are colour coded by Days after initiation of IMV (see colour bar in the next sub-figure). (**D**) Visualisation of the changes in PEEP against the change in PaO_2/FiO_2 ratio. The changes are measured across two adjacent time points with the PEEP change being introduced at some point between the two time points. Data points are colour coded by days after initiation of IMV (see colour bar).

Figure S8. Responsiveness to prone position with responders defined as maintenance of a mean PaO_2/FiO_2 >20kPa over 7 days after the first prone episode. (**A**) Each panel presents the time-series of a physiological measure of prone responders (blue) versus non-responders (red) from a day before the first prone manoeuvre to 7 days after (*P<0.05 interaction with mixed model ANOVA over this period, see table S10). The Solid lines are the group medians and the shaded areas are the semi-interquartile range. The number of subjects decay over time as patients die and discharge and the initial and final

numbers available for each measure are presented on the graph. (**B**) Changes in PaO_2/FiO_2 ratio over 36 hours around the first prone manoeuvre (from the last measurement before until the first measurement the day after) as a function of the duration of IMV prior to the manoeuvre. The dots are colour coded by ARDS severity prior to the manoeuvre. The red line presents an exponential fit, and the reported r is the Spearman rank correlation. (**C and E**) Correlation matrix between all pre-pronation (**C**) and post-pronation (**E**) variables considered for the logistic regression (the final set of parameters was based on less then 40% missingness, see table S2). (**D and F**) The odds ratio and their 95% confidence interval for Univariate and Multivariate logistic regression models where a higher odds ratio is the increased likelihood of not responding to prone position for each step increase in the admission variable and in the (**D**) pre-pronation (the last record within 24 hours prior intervention) or (**F**) post-pronation (the first record in the day after intervention) physiological measures. Continuous variables were discretely sized by a split into quartiles (see supplementary methods for details and table S11 and s12 for the full stats for pre- and post-prone respectively). All variables (of the list in table S2) with less than 40% missingness were included in the model. Subjects with more than 20% missing data were removed from the analysis.

Figure S9. Oxygenation Index (OI) dependency on P/F ratio. Scatter plot of admission measurements of Oxygenation Index vs PaO_2/FiO_2 (in red) shows a strong exponential link. Twice daily measurements of Oxygenation Index vs PaO_2/FiO_2 of all patients during the entire ICU stay (black) shows the same strong exponential link.

Figure S10. Comparison between PPCA-reconstructed and original clinical data. Scatter plots of all the weeklong clinical measurement with normal or log-normal distributions vs PPCA-reconstructed of the same features show a strong 1-to-1 linear relationship. These imply high reconstruction accuracy.

Figure S1 – Demographics, admission dates during surge, and outcomes of cohort

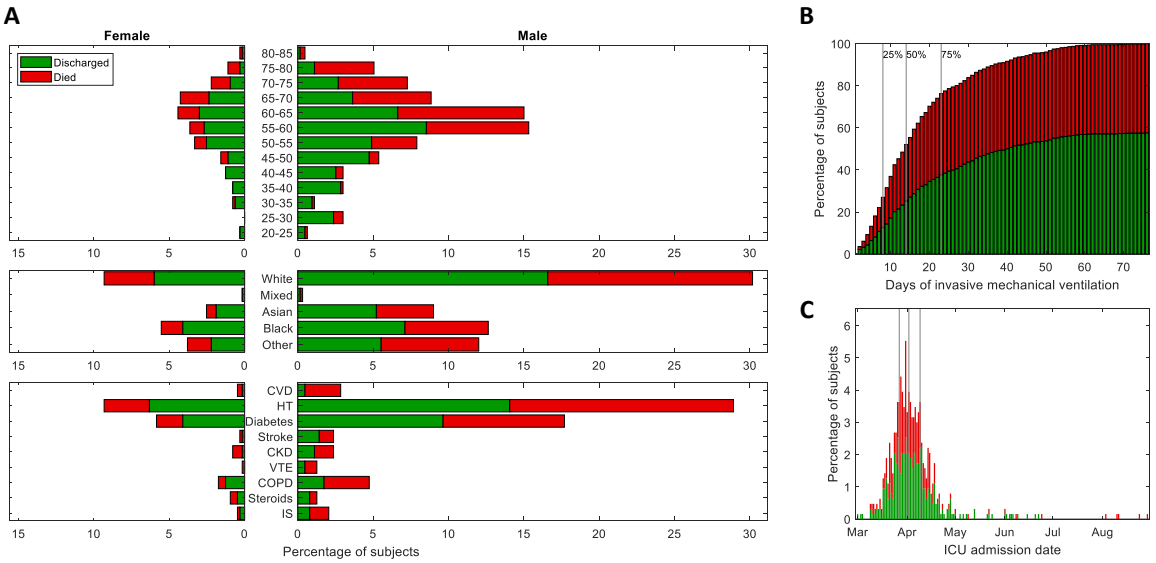


Figure S2 – Comparisons between ICU survivors and non-survivors.

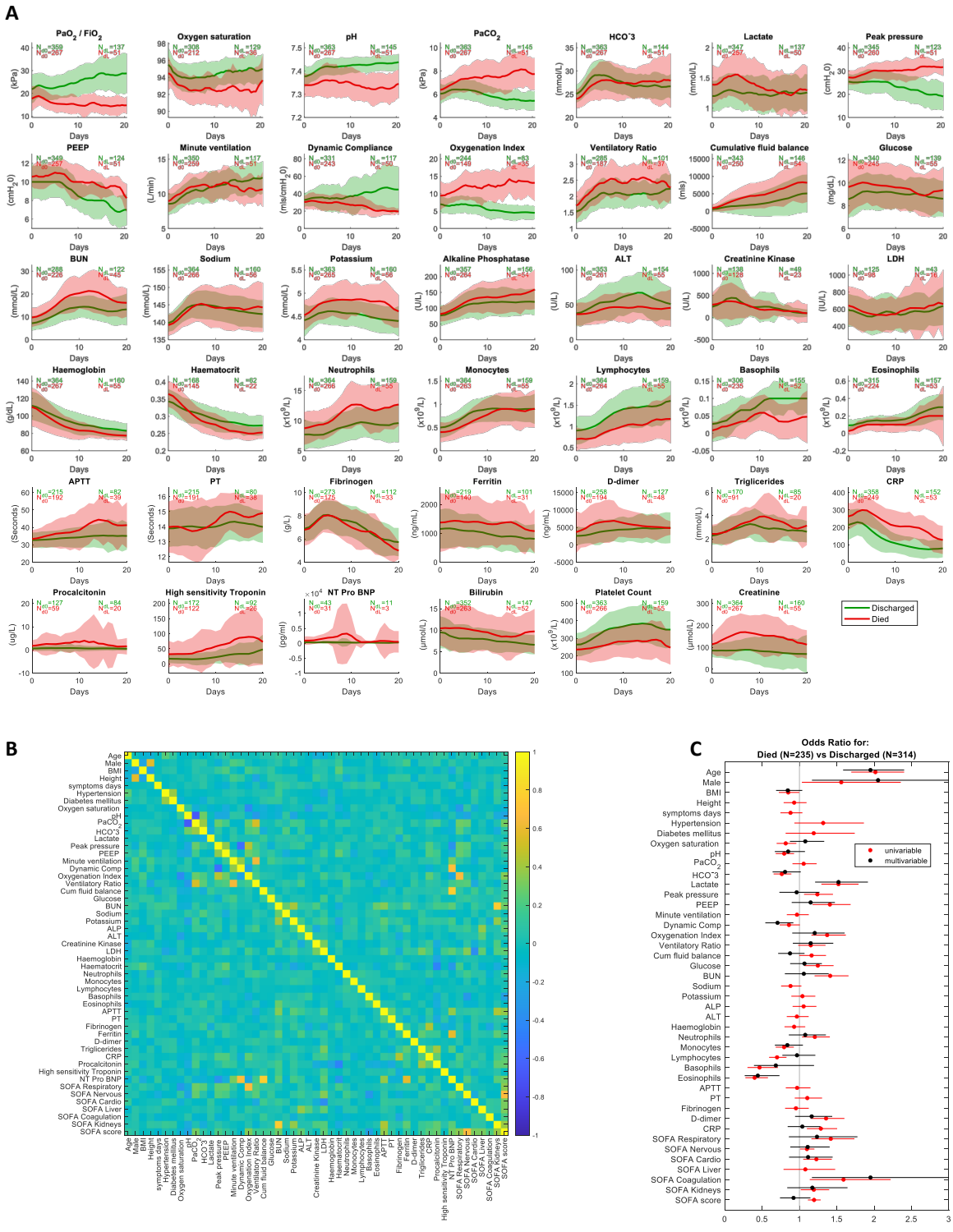


Figure S3 – Machine Learning and Explainability Artificial Intelligence analysis of predictors of ICU mortality

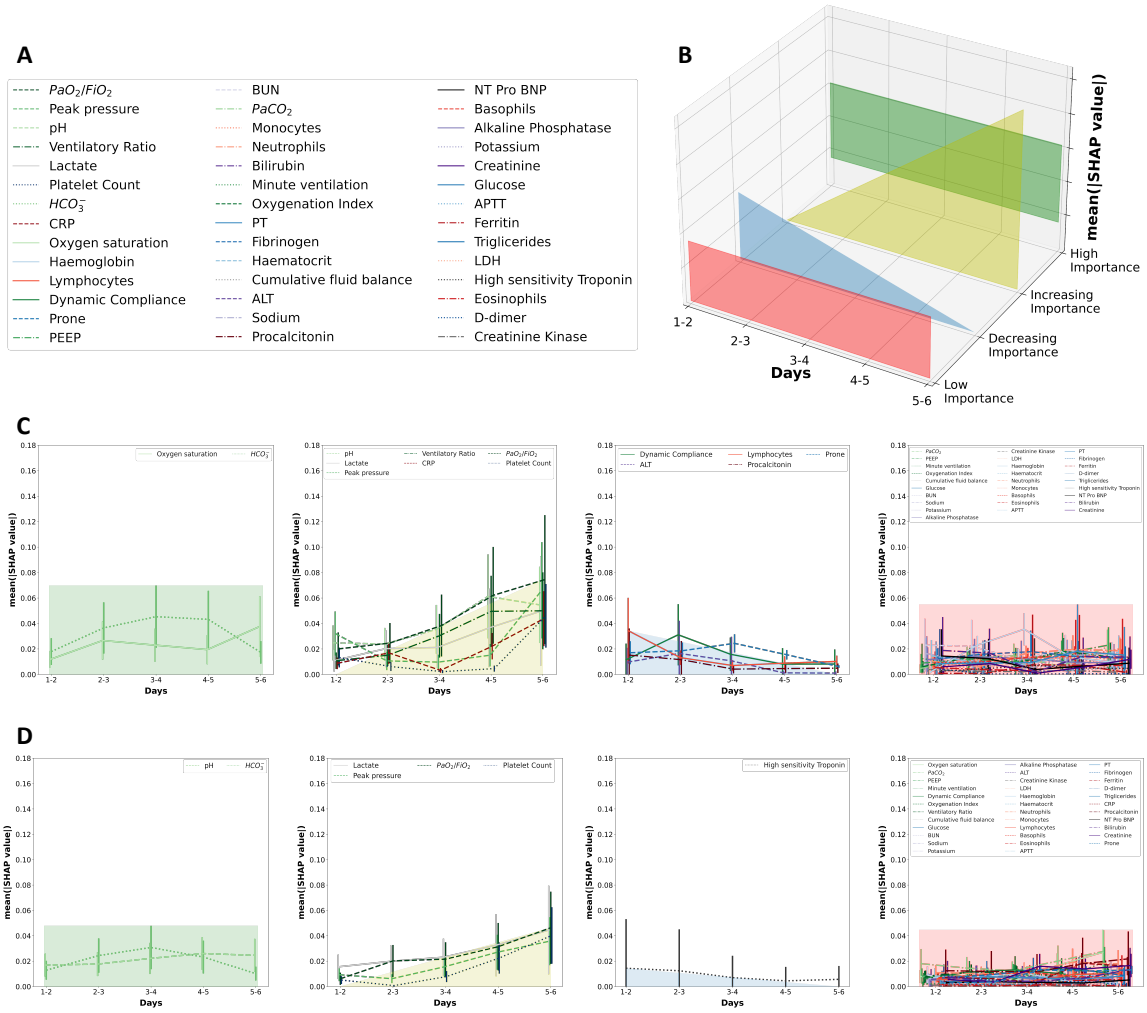


Figure S4 – Comparisons between hypoxaemia resolvers and non-resolvers.

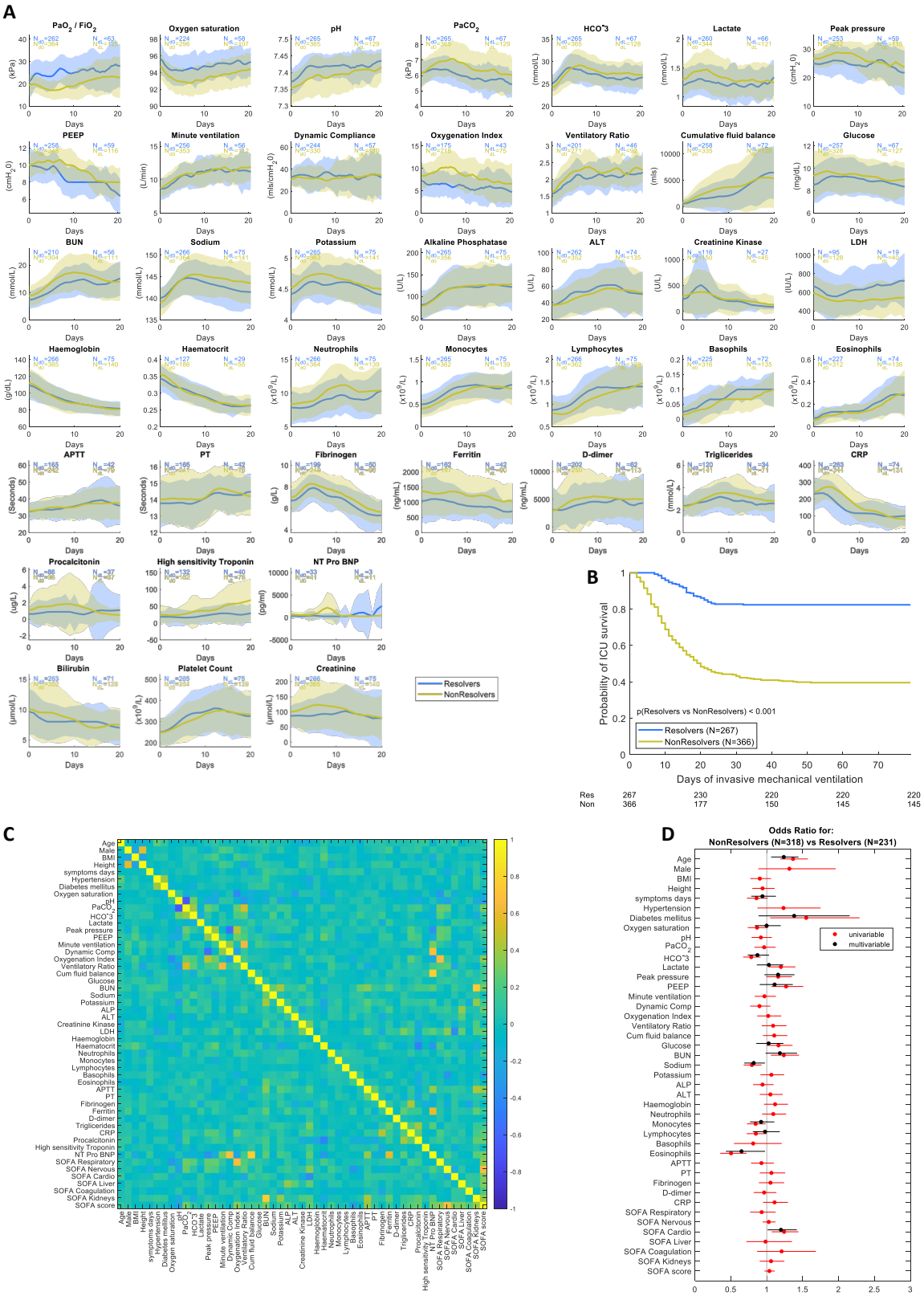


Figure S5 – Application of ICU and ARDS specific interventions

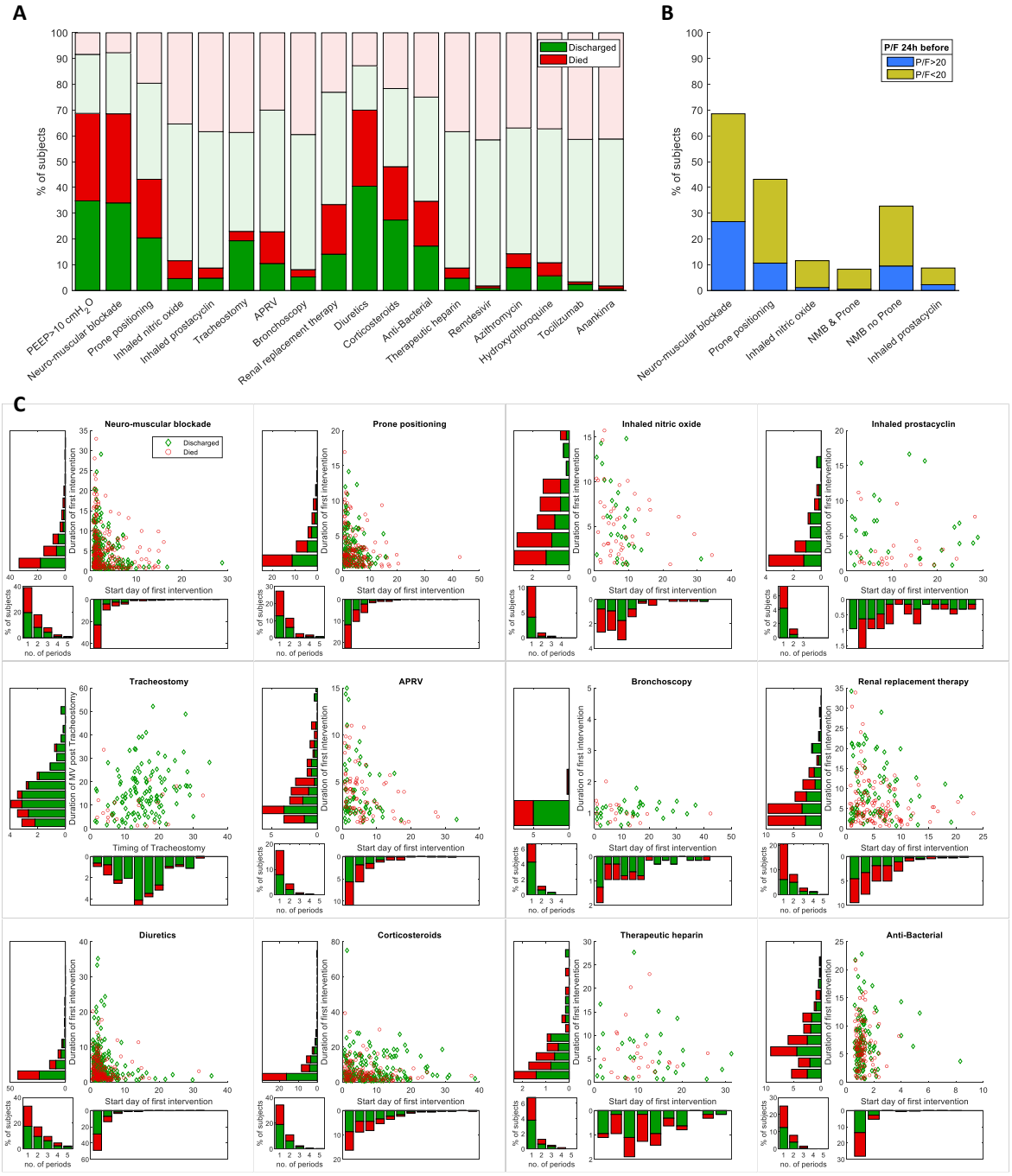


Figure S6 – Site Variations in ICU and ARDS specific interventions

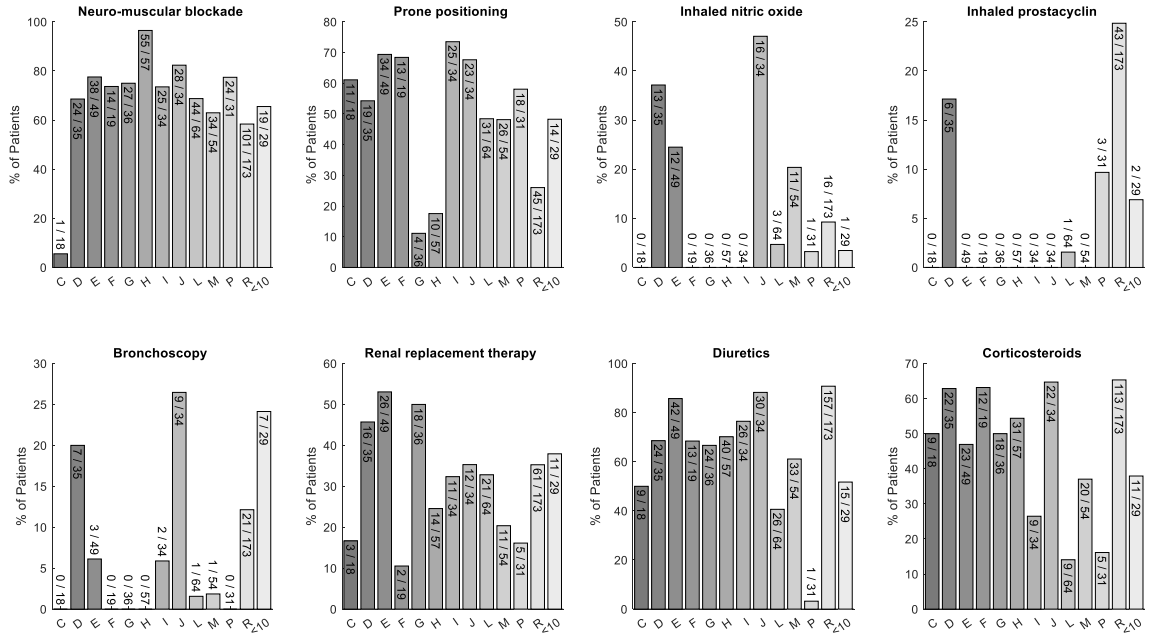


Figure S7 – Lung protective tidal volume and open lung strategies

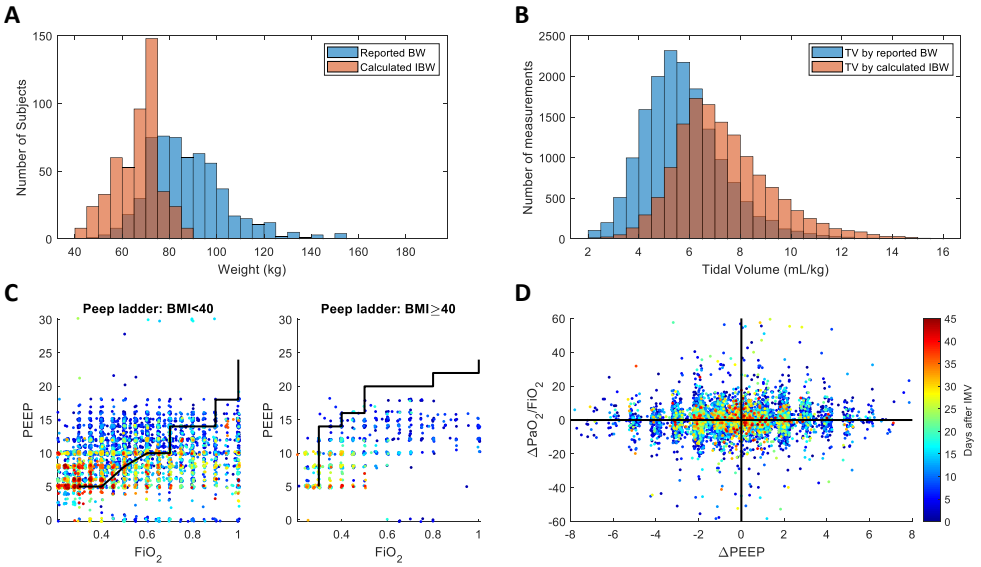


Figure S8 – Comparisons between hypoxaemia resolvers and non-resolvers.

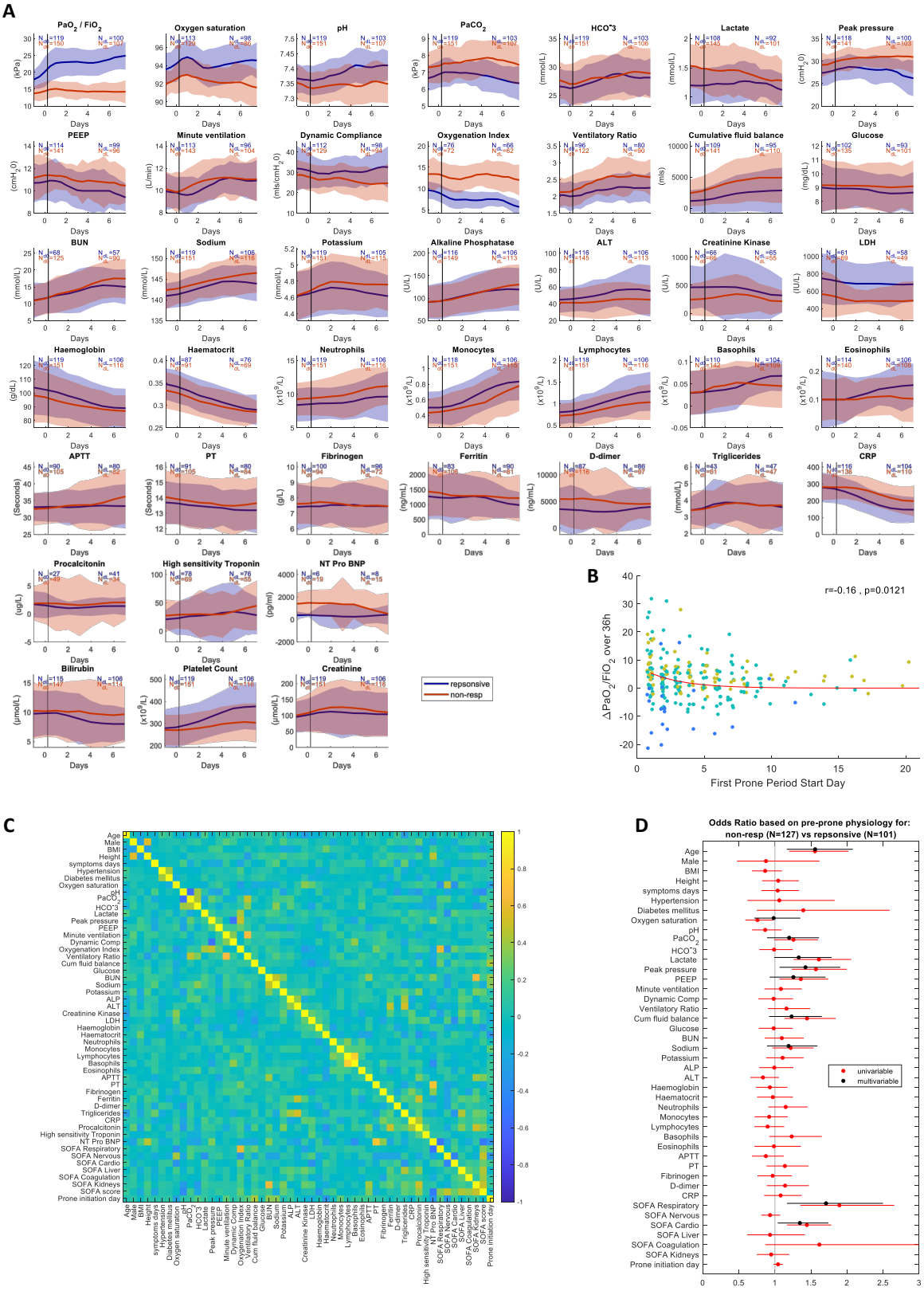
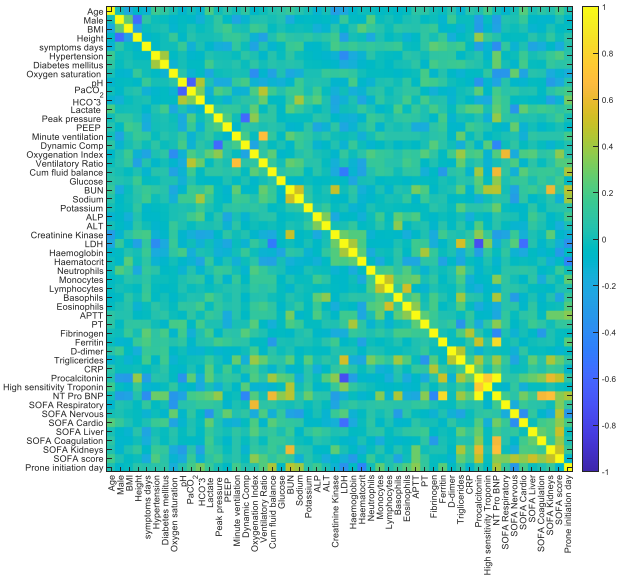


Figure S8 continued – Comparisons between hypoxaemia resolvers and non-resolvers

E



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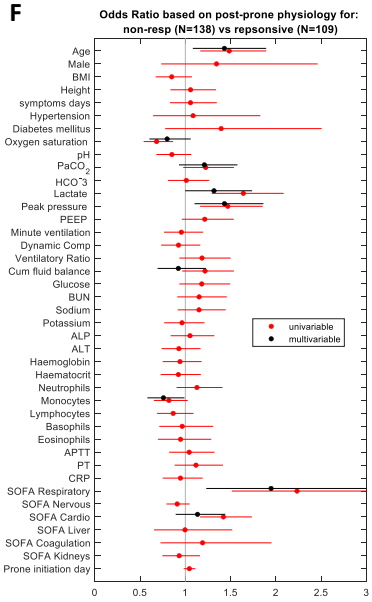

Figure S9 – Oxygenation Index dependency on PaO2/FiO2 ratio

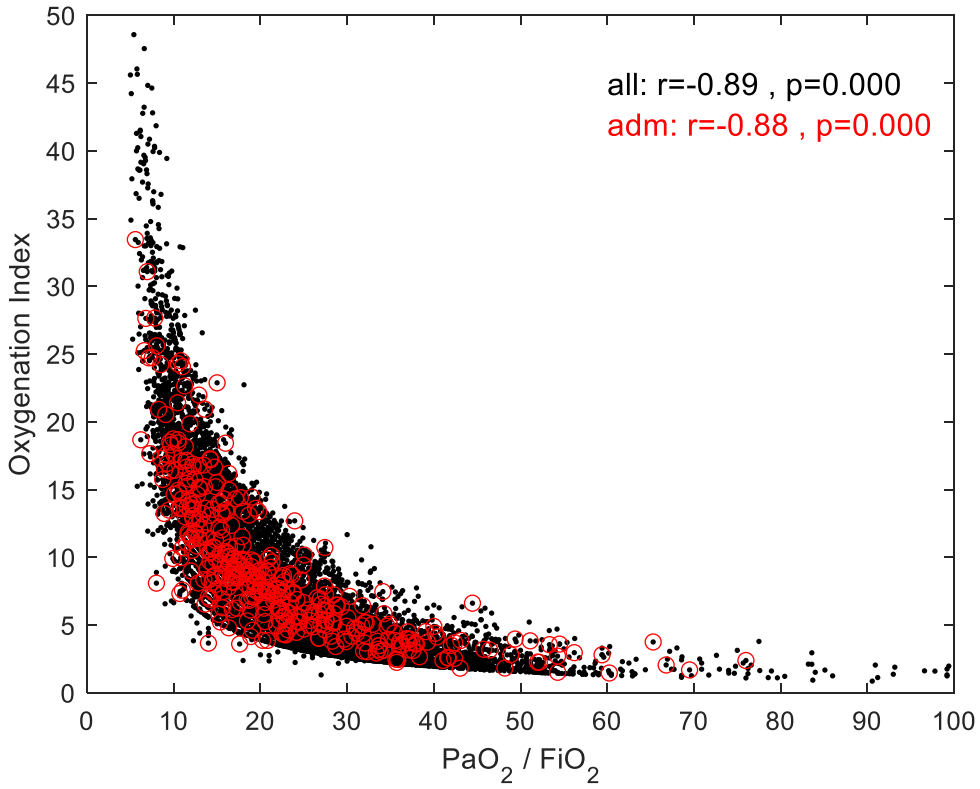

Figure S10 – Comparison between PPCA-reconstructed and original clinical data.