

# The characteristics, dynamics and the risk of death in COVID-19 positive dialysis patients in London, UK

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## **Abstract:**

Background: Dialysis patients, with frequent co-morbidities, advanced age and frailty, visiting treatment facilities frequently are perhaps more prone to SARS-Cov-2 infection and related death - the risk-factors and dynamics of which are unknown. The aim of this study was to investigate the hospital outcomes in SARS-CoV-2 infected dialysis patients.

Methods: Data on 224 hemodialysis patients between 02/29/2020 and 05/15/2020 with confirmed SARS-CoV-2 were analyzed for outcomes and potential risk factors for death, using competing risk regression model assessed by sub-distribution hazards ratio (SHR).

Results: Crude data analyses suggest an overall case fatality ratio of 22.7(95%CI(17.3-28.3%)) overall but that varies across age groups from 11.4(95%CI(0.9-9.2)) in  $\leq 50$  years old and 32.2(95%CI(17.3-47.5%)) in  $> 80$  years; with 60% of deaths occurring in the first 15 days and 80% within 21 days indicating a rapid deterioration towards death after admission. Almost 90% of surviving patients were discharged within 28 days.

Death was more likely than hospital discharge in more frail (WHO performance status 3-4) [SHR=2.16(1.25-3.74); $p=0.006$ ], ischemic heart disease [SHR=2.28(1.32-3.94), $p=0.003$ ], cerebrovascular disease [SHR=2.11(1.20-3.72), $p=0.010$ ], smoking history [SHR=2.69(1.33-5.45), $p=0.006$ ], and (completely or partially) hospitalized patients [SHR=10.26(3.10-33.94), $p<0.001$ ]; and in patients with high CRP [SHR=1.35(1.10-1.67)] and high neutrophil:lymphocyte ratio [SHR=1.03(1.01-1.04), $p<0.001$ ].

Our data did not support differences in the risk of death associated with gender, ethnicity, dialysis vintage or other comorbidities. However, comparison with the entire dialysis population attending these hospitals, and 12.9% being affected, revealed that non-Caucasians (62% vs. 52% in all patients,  $p=0.001$ ) and diabetic patients (54% vs. 22%,  $p<0.001$ ) were disproportionately affected.

Conclusion: This report discusses the outcomes of a large cohort of dialysis patients with SARS-CoV-2, infection affecting more diabetics and non-Caucasians; with a high case fatality ratio, which increased significantly with age, frailty, smoking, increasing CRP and neutrophil:lymphocyte ratio at presentation.

## **Introduction:**

The SARS-CoV-2 virus is similar to the viruses responsible for SARS and MERS epidemics in 2003 and 2013. (1) It is highly transmissible between humans and can spread easily in dialysis units, where patients are in close contact with each other and their health-care workers at frequent and regular intervals. Dialysis patient populations have high representation from elderly co-morbid and often frail individuals. (2) In addition they may also be more susceptible to infections, due to abnormal monocyte and T lymphocyte responses. (3) The MERS epidemic demonstrated the importance of T cell immunity in fighting SARS-CoV-1 infection and the same may be relevant for SARS-CoV-2 infection. (4)

Measures to protect HD patients have been recommended, including strict protocols for the screening, isolation, de-isolation and management of patients within dialysis facilities. (5-7) There are few reports of outcomes of COVID-19 in dialysis patients. The case fatality of COVID-19 positive hemodialysis (HD) patients in three HD centers in Wuhan varied between 0-16%. (8-10) In one HD facility in Northern Italy, the case fatality was as high as 44% (18 out of 41 infected HD patients) from a cohort of 98 HD patients. (11) Another hospital in Brescia, Italy admitted 21 COVID 19 positive patients; 5(24%) of whom died and 4 were discharged from hospital. (12). The same unit reported 94 patients of whom 61% required hospital admission and 29% died. (13). In a study from US of 59 patients 31% died, very similar to a study from Spain where 30% of 36 patients died. (14,15)

The aim of this observational study was to examine variables which may be associated with risk of death in COVID-19 positive HD patients cared for at 3 large NHS hospitals in South London during the start of the epidemic until 15th May 2020. We also present the daily incidence of COVID-19 and death in this patient cohort as well as the age-dependent case fatality-ratio.

## Methods

### Participant identification

Dialysis patients were tested for SARS-CoV-2, by nasal and throat swab for real-time RT-PCR (RdRp gene) testing if they were symptomatic with persistent cough and or fever, in accordance with guidance from Public Health England (PHE). (16)

### Data collection

Data were collected for SARS-CoV-2 infected dialysis patients admitted to hospitals or isolation hemodialysis facilities across three South London NHS renal centres between 29 February 2020 and 15 May 2020, including demographics, comorbidities, World Health Organization (WHO) performance status, clinical symptoms, laboratory parameters at presentation, hospital management and outcomes. Data were sourced from electronic clinical databases including laboratory systems, clinical notes and written communications. Aggregate comparative data were obtained from the UK Renal Registry. Baseline laboratory results were from the day of presentation or within 24 hours. The performance status was based on clinical data on the patients' usual mobility, exercise tolerance, frailty and required assistance. WHO performance status is a simple tool for assessment of functional status and frailty used mostly in the oncology for prognostication and to identify patients suitable for treatment (17,18). It estimates the patient's daily activity and ability to perform activities of daily living using a progressive score from 0-5, where 0 indicates a completely active patient, 3 for a patient capable of only limited self-care and a value of 5 indicating death. Given the sample size of our data, a binary variable based on WHO performance was created upon disease severity, i.e. 0-2 indicating less severe and 3-4 indicating a severe frailty.

We have also pulled aggregated statistics regarding the background populations, i.e. that of hemodialysis (HD) and peritoneal dialysis (PD) across the three hospitals. The data have been used to

assess our sample of COVID-19 positive patients' characteristics distributions against those in the corresponding populations. The study was approved by NHS Research Ethics Committee 20/SW/0077 and Health Research Authority IRAS 283130.

## Statistical methods

All the available variables have been graphically explored and summarized according to their nature, i.e. means, standard deviations, medians, interquartile limits and ranges for continuous variables and proportions for those that were categorical or binary. Log transformation has been performed for highly skewed variables where appropriate. Daily time series of admissions and deaths (counts) have graphically displayed in Figure 1.

A binary statistical outcome was defined indicating death or discharged alive before 15<sup>th</sup> May 2020; those still under care on that date were set as censored. The analysis modelled the time since admission to discharge from care (hospital or isolation dialysis facility) or death during care (hospital or outpatient) using the Fine & Grey method for competing risk. Death is the primary statistical event of interest and hospital discharge is assumed to be a competing event. A sub-distribution hazard ratio (SHR) model has been fit to the data accounting for the censored patients and quantifying the effects of each available variable on the risk of death through SHR (19-23). Predicted cumulative incidence functions (CIF) are similar to the cumulative distribution functions in classical survival analysis and indicate the daily cumulative rate of death or discharge since admission in association with each potential explanatory variable. We have also built a multivariable model based on Akaike information criterion (AIC- the smaller the value the better the model) used on similar number of observations in the data. Sensitivity analyses to missing data have been conducted - results not shown or discussed except for smoking variables as all others did not alter the qualitative or quantitative conclusions based on complete data. The approach is different from that of cause-specific hazard –

details on differences has been thoroughly discussed elsewhere (20). A value of SHR greater than 1 indicates a harmful effect of the corresponding explanatory variable; less than 1 indicates a protective effect. Also, a steep increase in the CIFs with time since admission corresponding to death indicates a rapid deterioration in patients who died. A p-value less than 0.05 is interpreted as a statistically significant association. Comparisons with the UK Renal Registry COVID 19 population data for dialysis patients have been made using elementary statistical tests according to the nature of the variables. Meta-analyses estimating pooled case-fatality ratios in HD population from recent published studies around the world are also presented (Table 4). All analyses have been carried out in Stata 16 (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.).

## Results

### Demographics and clinical characteristics of SARS-Cov-2 infected hemodialysis patients

Data on 224 hemodialysis patients from three large South London NHS renal centers, admitted to hospital or isolation facility between 29 February and 15 May 2020 with confirmed SARS-CoV-2, have been collated and analysed to explore potential risk factors for death. Descriptive statistics for this population, survival status until 15 May and associations with SHR of death vs. Survival are presented in Table 1. Within this cohort of patients 51 (22.8%) died, 154 (68.8%) were discharged alive and 19 (8.5%) were still under care in hospital or an isolation facility when we stopped the data collection (censored). The first hospital admission was on 29 February and the daily time series of admissions showed a steady increase until the peak between 30 March and 2 April, followed by a decline in admissions (Figure 1). The first death occurred on 22 March 2020.

The mean patient age was  $66 \pm 14$  (SD) years with 133 (59%) men, 85 (38%) Caucasian, 182 (81%) hypertensives, 120 (54%) diabetics, 64 (29%) ischemic heart disease, 49 (22%) cerebrovascular disease, 40 (18%) heart failure with reduced ejection fraction (HFrEF), 56 (25%) chronic lung disease and 33 (15%) with history of cancer (Table 1). Comparative results with the overall HD population are presented in Table 2.

Smoking status was reported in 165 (73.7%) patients and 71 (32%) were ex or current smokers. Median (Q1-Q3) dialysis vintage was 2.82 years (1.11-5.46 years). Overall, 124 (55.4%) patients dialyzed with a fistula or arteriovenous graft and 98 (43.8%) patients with a line. WHO performance status at the time of presentation was 0, 1 or 2 in 134 (60%) and 3 or 4 in 83 (37%) patients. Median (Q1-Q3) serum albumin at the last routine monthly blood review prior to presentation was 34 g/L (30-38) and 56 (34%) patients were taking an ACE inhibitor/Angiotensin receptor blocker (ACEi/ARB) at the time of COVID-19 diagnosis.



Symptoms at presentation were fever in 186 (83%), shortness of breath in 92 (41%), dry cough in 82 (37%), productive cough in 37 (17%), diarrhea in 30 (13%), vomiting in 30 (13%), headache in 20 (9%), aches and pains in 37 (17%) patients and only 10 (4.5%) patients were asymptomatic.

At presentation the median (Q1-Q3) blood C-reactive protein (CRP) was 74 mg/L (32-129), white cell count  $5.4 \times 10^9/L$  (3.9-7.4), neutrophil count  $3.8 \times 10^9/L$  (2.6-5.9), lymphocyte count  $0.80 \times 10^9/L$  (0.58-1.1), neutrophil to lymphocyte ratio median (Q1-Q3) 4.7 (3.1-7.8), hemoglobin 105 g/L (97-114).

### Management of SARS-CoV-2 infected hemodialysis patients

Overall, 81 (36%) of hemodialysis patients were managed exclusively as outpatients dialysing initially in isolation facilities belonging to the hospitals and then discharged to satellite units when clinically improved; 115 (51.8%) were cared for exclusively as inpatients and 28(12%) were managed as outpatients before hospitalization. .

Of these 143 (64%) patients who were admitted to hospital, a 'ceiling of care' was determined, meaning the highest level of medical intervention deemed appropriate should the patient's clinical condition deteriorate. This decision was made by the medical team taking into account the patient's wishes and whether the patient was likely to benefit from more invasive care. A ward-based ceiling of care decision was made for 73 (51%) patients, escalation for non-invasive ventilation in 24 (17%) and for mechanical ventilation in 46 (32%).

Ninety-two (64%) of the hospitalized patients required maximum respiratory support from respiratory support devices that could be delivered on the 'ceiling of care' ward setting, including nasal cannulae and non-rebreathing masks. There were 12 hospitalized patients that required non-invasive ventilation (NIV). Only 11 (8%) patients of hospitalized patients were ultimately admitted to the intensive care unit (ICU), with 9 patients requiring mechanical ventilation.

At the end of follow-up, 19 (8.5%) of patients were still inpatients because of their COVID-19 related illnesses.

## Associations with the SHR of death vs. discharge in SARS-CoV-2 infected hemodialysis patients

At the end of follow-up, 51 (22.8%) hemodialysis patients had unfortunately died (time series in Figure 1), 154 (68.8%) were discharged from either inpatient care or outpatient isolation hemodialysis and 19 (8.5%) were still under clinical care.

Figure 2 showing the cumulative incidence of death suggests that patients deteriorated relatively quickly, at a steadily increasing pace during the first 23 days of admission. The daily incidence of discharge after admission increased sharply between 5-20 days since admission. This latter trend slowed down afterwards - driven by 38 patients who required long (21-55 days) hospitalization. The effects of age and other variables on the dynamics of death and hospital discharge can be seen in Table 1.

Patients that required admission to hospital were 6.83 (95%CI 2.07-22.48) times more likely to die than patients managed exclusively or partially as outpatients. Based on these data, there is not enough evidence to suggest that gender, ethnicity, BMI or dialysis vintage were associated with death in these patients (all corresponding p-values for SHR >0.05).

A 5-year increase in the age at admission is associated with an increase in the SHR of death vs. discharge of 1.16 (1.03-1.30),  $p=0.013$ . There was an average 22.8% case-fatality ratio, which exhibited heterogeneity across the age groups in this cohort, with 11.4% of deaths among patients under 50 years of age, 33.3% in those 75-80 years of age and 32.4% in those over 80 years of age.

Smoking history was associated with a increased sub-hazard of death by almost 3 times (2.69 (1.33-5.45)) compared to no smoking history. Given the great deal of missing information for this variable (26%) a sensitivity analysis in which all these patients were assumed to be non-smokers still preserves

the harmful effect of smoking, i.e. SHR=1.78 (1.03-3.08),  $p=0.041$ . There is also some evidence ( $p=0.003$ ) and ( $p=0.01$ ) for a higher chance of death in ischemic heart disease and cerebrovascular disease patients compared with those without these comorbidities, respectively. In addition, those with a WHO frailty score of 3-4 were 2.16 (95%CI (1.25-3.74)) times more likely to die compared with those with a WHO score of 0-2. The data presented in this population were consistent with no effect of ACEi/ARB on the hazard of death ( $p=0.518$ ).

The only evidence for an association of death with symptoms on admission was with shortness of breath (SHR=2.32 (1.29-4.17,  $p=0.005$ )) (Table 1). Among patients who died compared to patients who were discharged alive, blood CRP concentration was higher (median (Q1-Q3) 113 (47-212) vs. 65 (28-104), log lymphocyte count was lower and neutrophil:lymphocyte ratio was higher (median (Q1-Q3) 7.2 (4.2-13.4) vs. 4.3 (2.9-6.7) (Figure 3). Furthermore, each unit increase in neutrophil:lymphocyte ratio was associated with a 3% (1.7%-5%) increase in SHR for death vs. hospital discharge and similarly each 10 mg/L rise in CRP was associated with a 3% (1%-5%) increased SHR of death. Our multivariable model included the predictors which remain strong ( $p<0.05$ ) and for which the AIC value was the smallest. The WHO score includes elements of age so the two confound each other as expected. However, the model including the age, neutrophil:lymphocyte ratio and hospital management was better than including WHO score neutrophil:lymphocyte ratio and hospital management (AIC= 471.933 vs. AIC= 473.400, respectively). The adjusted effects of these variables are only slightly modified compared to their univariate counterparts (Table1).

## Demographics and clinical characteristics and outcomes of SARS-CoV-2 infected peritoneal dialysis patients

Among the 10 SARS-CoV-2 infected PD patients aged 69.5 (59-75) year [median (Q1-Q3)], with 8 males; 5 Caucasians; 3 smokers and 6 diabetics; 1 was managed as an outpatient. Of the 9 inpatients, 3 required NIV, 2 required ICU admission and 1 required mechanical ventilation. Six of the admitted patients (60% of the total) died and 4 were discharged alive.

## Comparison of SARS-CoV-2 patients with reference populations

Unless otherwise specified, the reference populations are collectively those patients who have their usual dialysis provided by the South London renal centers (Table 2).

Up until 15 May 2020, 224 (approximately 13%) of all HD patients (1727) and 10 (approximately 4.4%) of all PD patients (228) from the 3 renal centers tested positive for COVID-19. Of those that were COVID-19 positive, 51 (22.8%) HD patients and 5 (50%) PD patients have died, such that approximately 2.96% of all HD patients and approximately 2.6% of all PD patients managed at the three centers died from COVID-19 disease during the period of data collection.

The demographic data for COVID-19 positive patients presented here was broadly consistent with that of the HD ( $p=0.383$ ) and PD ( $p=0.137$ ) populations respectively across the 3 hospitals. The distribution of gender in our COVID-19 positive cohort was also similar to that observed in the local dialysis populations ( $p=0.066$  for HD and  $p=0.198$ , respectively). There was, however, a suggestion that SARS-CoV-2 infections seemed to have affected more non-Caucasian HD patients than Caucasian patients (Table 2,  $p=0.001$ ) despite no differences between case-fatality ratios supported by these data. The numbers in the PD population are too small for meaningful analyses using individual records. The proportion of diabetics among COVID-19 positive patients is also higher than might be expected from the reference dialysis populations (54% vs. 46% in HD,  $p<0.001$  and 60% vs. 19% in PD,  $p=0.004$ ). Our data suggest some evidence that the case-fatality ratio is higher ( $p=0.015$ ) in PD (6/10) patients than in HD (51/224).

Also, based on the size of the dialysis population of the renal centers, approximately 13% (224/1737) were affected with the SARS-CoV-2 infection and 2.96% (51/1737) died by the date when we stopped data collection.

The case fatality ratio described for our dialysis patients that tested COVID-19 positive appears to be commensurate with national renal data shown in Table 3 by the time of our censoring. (24)

The numbers in the PD COVID-19 positive patients are too small for meaningful analyses using individual records as in hemodialysis COVID 19 positive patients.

In a meta-analysis based on another six similar studies the case fatality ratio was 24% (17-31%) and including the present study was 23% (18-29%). There was some high level of heterogeneity in the data mainly caused by China -Wuhan estimate but we felt that the study should be left in the analysis (Figure 4).

## Discussion

In this study of SARS-CoV-2 infected dialysis patients the case fatality ratio was high, 22.8%. The patients who died, compared to those recovered, were older, more likely to be smokers and hospitalized, more likely to have ischemic and cerebrovascular disease and have worse WHO performance status. COVID-19 disease was observed more frequently in diabetic and non-white patients.

The infection rate of 13% in our hemodialysis population likely represents an underestimate, as only patients with symptoms were screened, therefore missing asymptomatic and falsely negative PCR COVID-19 patients. This has been illustrated in a recent study of 356 HD patients, where 22% were PCR positive for COVID-19 with symptom-based screening, however the seroprevalence rate was 36%, therefore with 40% of patients with positive antibodies having been either asymptomatic or negative on PCR testing (25).

The impact of age is clearly visible from Figure 1 which shows that more than 30% of patients above the age of 75 years died as opposed to less than 15% of the patients who were under 60 years of age. The case fatality ratio presented in this report, is broadly consistent with that observed in other reports of dialysis patients with COVID 19 as seen in the meta-analysis of six studies from Europe, Asia and North-America (Table 4); and similar to other hospitalised patients with COVID-19 in the UK and elsewhere, but lower than patients admitted to ICU. (26).

In our dialysis population, smokers were more likely to die, which may be due to the fact that the SARS-COV-2 virus is an airborne disease which predominantly affects the lungs. Smokers and individuals with COPD have recently been reported to have increased expression of ACE-2 receptors, which is the site for SARS-Co-V-2 entry into cells, in small airway epithelial cells. This may explain why current and ex-smokers have poorer COVID-19 related respiratory outcomes. (27). The evidence for this finding is preserved even after sensitivity analysis (Table 1).

The presence of healthy adaptive immunity, which requires the presence of healthy T&B lymphocyte populations, is important in mounting an appropriate response to viral infection, which may be defective in dialysis patients. (28) In our study, patients who died had a higher neutrophil count, lower lymphocyte (log) count and a higher neutrophil:lymphocyte ratio at presentation. This is consistent with earlier reports in the general population where poor prognosis was associated with low lymphocyte and higher neutrophil:lymphocyte ratio in the blood. (29,30) . The effects of age, neutrophil:lymphocyte ratio in the blood and hospital management remain strong even after adjusting one for another (Table 1).

Compared to the aggregate data from the haemodialysis population in the three hospitals, the patients who were infected with SARS-CoV-2 had a higher proportion of diabetics than non-diabetics and a higher proportion of non-Caucasians compared to Caucasians. This is also broadly consistent with what is seen in the general population, particularly in the UK. (31,32)

The investigation into the impact of frailty score of COVID-19 in hemodialysis patient is a major strength of the study. In this patient cohort, 51% of inpatients had an established ceiling of care decision for ward-based care and within this group approximately 1 in 2 patient's died, totalling 74% of the total case fatality. As shown in Table 4, the ward-based care decision seemed appropriate as the patients within this category were older, more frail and co-morbid than those for treatment escalation and for those that ultimately were admitted to ICU. Only one out of the nine mechanically ventilated patients was discharged alive, whereas six patients died and the other two remained ventilator dependent, indicating poor outcome.

This study has several limitations. First, data were collected retrospectively through electronic health records and medical notes used for routine clinical care and some data for those managed as outpatients were missing. We did not systematically collect detailed data on dialysis and non-dialysis

treatments given to patient. In the UK, the Chief Medical Officers strongly discouraged the use of off-licence treatments outside of a clinical trial. Treatment was therefore largely supportive unless patients participated in a clinical trial. There were 20 HD and 3 PD patients in this cohort who did participate in the RECOVERY trial (randomly assigned to supportive care (12) or to one of four treatments: lopinavir-ritonavir (2), low dose dexamethasone (3), hydroxychloroquine (3), or azithromycin (3)), and it is possible that these interventions may have affected their clinical course and outcomes.

## **Conclusions**

This report describes the outcomes of dialysis patients with COVID-19, more likely to be diabetic and non-Caucasian; from a large cohort of dialysis patients from 3 NHS hospitals in south London. Case fatality ratio among those infected with SARS-CoV-2 was high, 22.8%, in line with the pooled estimate from the meta-analysis. The patients who died, compared to those who survived, were older, more likely to be smokers, cardiovascular disease and have worse WHO performance status. The case fatality ratio in this patient population, known to have high burden of co-morbidities, is broadly comparable to other reports in SARS-Cov-2 dialysis patients, the UK dialysis population and rates of hospital deaths in the UK population.



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# Tables

Table 1

|                                 | VARIABLES NAME                  | SUMMARY TYPE/CATEGORY | ALL PATIENTS     | DISCHARGE ALIVE  | DIED           | STILL IN CARE    | SUB-DISTRIBUTION HAZARD RATIO |                  |                   | ADJUSTED SUB-DISTRIBUTION HAZARD RATIO (210 obs. - 94%) |         |
|---------------------------------|---------------------------------|-----------------------|------------------|------------------|----------------|------------------|-------------------------------|------------------|-------------------|---|---------|
|                                 |                                 |                       |                  |                  |                |                  | DIED vs. SURV                 | p-value          | NO                | DIED vs. SURV   | p-value |
| Demographics                    | GENDER                          | Male                  | 133 (59.38%)     | 89 (57.79%)      | 35 (68.63%)    | 9 (47.36%)       | 1                             |                  |                   |   |         |
|                                 |                                 | Female                | 91 (40.63%)      | 65 (42.21%)      | 16 (31.37%)    | 10 (52.63%)      | 0.66 (0.36-1.20)              | 0.172            | 220               |   |         |
|                                 | ETHNICITY (binary)              | White                 | 85 (37.95%)      | 54 (35.06%)      | 21 (41.18%)    | 10 (52.63%)      | 0.85 (0.49-1.48)              | 0.571            | 220               |   |         |
|                                 |                                 | Other                 | 139 (62.05%)     | 100 (64.94%)     | 30 (58.82%)    | 9 (47.36%)       |                               |                  |                   |   |         |
|                                 | ETHNICITY (detailed)            | White                 | 85 (37.95%)      | 54 (35.07%)      | 21 (41.18%)    | 10 (52.63%)      |                               |                  |                   |   |         |
|                                 |                                 | South Asian           | 41 (18.30%)      | 27 (17.53%)      | 11 (21.57%)    | 3 (15.79%)       |                               |                  |                   |   |         |
|                                 |                                 | East Asian            | 8 (3.57%)        | 5 (3.25%)        | 3 (5.88%)      | 0 (0%)           |                               |                  |                   |   |         |
|                                 |                                 | Black                 | 77 (34.38%)      | 59 (38.31%)      | 13 (25.49%)    | 5 (26.32%)       |                               |                  |                   |   |         |
|                                 |                                 | Other                 | 13 (5.80%)       | 9 (5.84%)        | 3 (5.88%)      | 1 (5.26%)        |                               |                  |                   |   |         |
|                                 | SMOKING status                  | Never                 | 94 (41.96%)      | 71 (46.10%)      | 12 (23.53%)    | 11 (57.89%)      | 1                             | 2.69 (1.33-5.45) | 0.006             | 161   |         |
| Ever                            |                                 | 71 (31.70%)           | 43 (27.92%)      | 22 (43.14%)      | 6 (31.58%)     |                  |                               |                  |                   |   |         |
| Missing=NO                      | Never                           | 59 (26.34%)           | 40 (25.97%)      | 17 (33.33%)      | 2 (10.53%)     | 1                | 1.78 (1.03-3.08)              | 0.041            | 220               |   |         |
|                                 | Ever                            | 153 (68.30%)          | 111 (72.08%)     | 29 (56.86%)      | 13 (68.42%)    |                  |                               |                  |                   |   |         |
| Missing=YES                     | Never                           | 71 (31.70%)           | 43 (27.92%)      | 22 (43.14%)      | 6 (31.58%)     | 1                | 2.57 (1.34-4.93)              | 0.005            | 220               |   |         |
|                                 | Ever                            | 94 (41.96%)           | 71 (46.10%)      | 12 (23.53%)      | 11 (57.89%)    |                  |                               |                  |                   |   |         |
| AGE at admission (5 yrs effect) | Mean (SD)                       | 65.83 (14.39)         | 63.90 (14.43)    | 70.47 (13.79)    | 69 (12.77)     | 1.16 (1.03-1.30) | 0.013                         | 220              | 1.15 (1.002-1.31) | 0.047   |         |
|                                 | Median (Q1-Q3)                  | 67.5 (57-77)          | 65 (57-76)       | 73 (62-80)       | 73 (59-81)     |                  |                               |                  |                   |   |         |
|                                 | Range                           | 25-90                 | 26-90            | 25-90            | 38-82          |                  |                               |                  |                   |   |         |
| BMI (kg/m <sup>2</sup> )        | Mean (SD)                       | 28.2 (7.6)            | 28.5 (8)         | 26.9 (6.3)       | 28.9 (7.9)     | 0.97 (0.93-1.01) | 0.186                         | 193              |                   |   |         |
|                                 | Median (Q1-Q3)                  | 26.3 (23.1-31.2)      | 26.2 (23.2-31.4) | 26.1 (21.7-30.0) | 26.6 (16.5-42) |                  |                               |                  |                   |   |         |
|                                 | Range                           | 16.5-57.8             | 18.7-57.8        | 17.4-49.2        | 16.5-42.1      |                  |                               |                  |                   |   |         |
|                                 | Missing                         | 27 (12.05%)           | 17 (11.04%)      | 8 (15.67%)       | 2 (10.53%)     |                  |                               |                  |                   |   |         |
| Comorbidities                   | WHO performance status detailed | 0                     | 16 (7.14%)       | 15 (9.74%)       | 1 (1.96%)      | 0 (0%)           |                               |                  |                   |   |         |
|                                 |                                 | 1                     | 51 (22.77%)      | 42 (27.27%)      | 6 (11.76%)     | 3 (15.79%)       |                               |                  |                   |   |         |
|                                 |                                 | 2                     | 67 (29.91%)      | 43 (27.92%)      | 16 (31.37%)    | 8 (42.11%)       |                               |                  |                   |   |         |
|                                 |                                 | 3                     | 54 (24.11%)      | 34 (22.08%)      | 15 (29.41%)    | 5 (26.32%)       |                               |                  |                   |   |         |
|                                 |                                 | 4                     | 29 (12.95%)      | 13 (8.44%)       | 13 (25.49%)    | 3 (15.79%)       |                               |                  |                   |   |         |
|                                 | WHO performance binary          | 0-2                   | 7 (3.13%)        | 7 (4.55%)        | 0 (0%)         | 0 (0%)           | 2.16 (1.25-3.74)              | 0.006            | 213               |   |         |
|                                 |                                 | 3-4                   | 134 (59.82%)     | 100 (64.94%)     | 23 (45.10%)    | 11 (57.90%)      |                               |                  |                   |   |         |
|                                 |                                 | Missing               | 83 (37.05%)      | 47 (30.52%)      | 28 (54.90%)    | 8 (42.11%)       |                               |                  |                   |   |         |
|                                 | History of cancer               | No                    | 7 (3.13%)        | 7 (4.55%)        | 0 (0%)         | 0 (0%)           | 1.25 (0.613-2.57)             | 0.537            | 218               |   |         |
|                                 |                                 | Yes                   | 189 (84.38%)     | 132 (85.71%)     | 42 (82.35%)    | 15 (78.95%)      |                               |                  |                   |   |         |
| Missing                         |                                 | 33(14.73%)            | 20 (12.99%)      | 9 (17.65%)       | 4 (21.05%)     |                  |                               |                  |                   |   |         |
| Hypertension                    | No                              | 2(0.89%)              | 2 (1.30%)        | 0 (0%)           | 0 (0%)         | 1.27 (0.61-2.66) | 0.528                         | 219              |                   |   |         |
|                                 | Yes                             | 41(18.30%)            | 24 (15.58%)      | 8 (15.69%)       | 9 (47.37%)     |                  |                               |                  |                   |   |         |
|                                 | Missing                         | 182(81.25%)           | 129 (83.80%)     | 43 (84.31%)      | 10 (52.63%)    |                  |                               |                  |                   |   |         |
| DIABETES                        | No                              | 1(0.45%)              | 1 (0.65%)        | 0 (0%)           | 0 (0%)         | 1.31 (0.76-2.28) | 0.335                         | 219              |                   |   |         |
|                                 | Yes                             | 103(45.98%)           | 71 (46.10%)      | 21 (41.18%)      | 11 (57.90%)    |                  |                               |                  |                   |   |         |
|                                 | Missing                         | 120 (53.57%)          | 82 (53.25%)      | 30 (58.82%)      | 8 (42.11%)     |                  |                               |                  |                   |   |         |
| HFrEF                           | No                              | 40(17.86%)            | 27 (17.53%)      | 11 (21.57%)      | 2 (10.53%)     | 1.38 (0.69-2.73) | 0.363                         | 217              |                   |   |         |
|                                 | Yes                             | 181 (80.80%)          | 124 (80.52%)     | 40 (78.43%)      | 17 (89.47%)    |                  |                               |                  |                   |   |         |
|                                 | Missing                         | 3 (1.34%)             | 3 (1.95%)        | 0 (0%)           | 0 (0%)         |                  |                               |                  |                   |   |         |
| CHRONIC LUNG DISEASE DETAILED   | NO                              | 168 (75%)             | 115 (74.68%)     | 39 (76.47%)      | 14 (73.68%)    | NA               |                               |                  |                   |   |         |
|                                 | Asthma                          | 16 (7.14%)            | 13 (8.44%)       | 0 (0%)           | 3 (15.79%)     |                  |                               |                  |                   |   |         |
|                                 | Bronchiectasis                  | 1 (0.45%)             | 1 (0.65%)        | 0 (0%)           | 0 (0%)         |                  |                               |                  |                   |   |         |
|                                 | COPD                            | 15 (6.70%)            | 6 (3.90%)        | 8 (15.69%)       | 1 (5.26%)      |                  |                               |                  |                   |   |         |
|                                 | Fibrosis                        | 4 (1.79%)             | 3 (1.95%)        | 1 (1.96%)        | 0 (0%)         |                  |                               |                  |                   |   |         |
|                                 | Other                           | 17 (7.59%)            | 13 (8.44%)       | 3 (5.88%)        | 1 (5.26%)      |                  |                               |                  |                   |   |         |
| CHRONIC LUNG                    | No                              | 168 (75%)             | 115 (74.68%)     | 39 (76.47%)      | 14 (73.68%)    |                  |                               |                  |                   |   |         |

|                                     |                                |                  |                  |                  |                 |                           |                           |                  |     |                          |              |  |
|-------------------------------------|--------------------------------|------------------|------------------|------------------|-----------------|---------------------------|---------------------------|------------------|-----|--------------------------|--------------|--|
| Hospital management                 | <b>DISEASE</b>                 | Yes              | 56 (25%)         | 39 (25.33%)      | 12 (23.53%)     | 5 (26.32%)                | 0.9 2 (0.48-1.77)         | 0.810            | 220 |                          |              |  |
|                                     | <b>Ischaemic heart disease</b> | No               | 157 (70.09%)     | 116 (75.33%)     | 28 (54.90%)     | 13 (68.42%)               |                           |                  |     |                          |              |  |
|                                     |                                | Yes              | 64 (28.57%)      | 35 (22.72%)      | 23 (45.10%)     | 6 (31.58%)                | <b>2.28 (1.32-3.94)</b>   | <b>0.003</b>     | 217 |                          |              |  |
|                                     |                                | Missing          | 3 (1.34%)        | 3 (1.95%)        | 0 (0%)          | 0 (0%)                    |                           |                  |     |                          |              |  |
|                                     | <b>CEREBROVASCULAR DISEASE</b> | No               | 173 (77.23%)     | 124 (80.52%)     | 33 (64.71%)     | 16 (84.21%)               |                           |                  |     |                          |              |  |
|                                     |                                | Yes              | 49 (21.88%)      | 28 (18.18%)      | 18 (35.29%)     | 3 (15.79%)                | <b>2.11 (1.20-3.72)</b>   | <b>0.010</b>     | 218 |                          |              |  |
|                                     |                                | Missing          | 2 (0.89%)        | 2 (1.30%)        | 0 (0%)          | 0 (0%)                    |                           |                  |     |                          |              |  |
|                                     | <b>Length of stay</b>          | Mean (SD)        | 19.01 (12.4)     | 17.4 (9.8)       | 15.6 (10.3)     | NA                        |                           |                  |     |                          |              |  |
|                                     |                                | Median (Q1-Q3)   | 16 (11-23.5)     | 16 (11-22)       | 14 (7-19)       |                           |                           |                  |     |                          |              |  |
|                                     |                                | Range            | 1-60             | 1-55             | 2-43            |                           |                           |                  |     |                          |              |  |
|                                     |                                | Missing          | 4 (1.8%)         | 4 (2.60%)        | 0 (0%)          |                           |                           |                  |     |                          |              |  |
|                                     | <b>MANAGE</b>                  | OUTPATIENT       | 81 (36.16%)      | 78 (50.65%)      | 3 (5.88%)       | 0 (0%)                    | <b>1</b>                  |                  | 220 |                          |              |  |
|                                     |                                | OUT to IN        | 28 (12.50%)      | 18 (11.69%)      | 6 (11.77%)      | 4 (21.05%)                | <b>6.40 (1.55-26.36)</b>  | <b>0.010</b>     |     | <b>5.50 (1.33-22.79)</b> | <b>0.040</b> |  |
|                                     |                                | INPATIENT        | 115 (51.34%)     | 58 (37.66%)      | 42 (82.35%)     | 15 (78.95%)               | <b>11.24 (3.38-37.37)</b> | <b>&lt;0.001</b> |     | <b>8.56 (2.54-28.83)</b> | <b>0.001</b> |  |
|                                     | <b>MANAGE-binary</b>           | OUTPATIENT       | 81 (36.16%)      | 78 (50.65%)      | 3 (5.88%)       | 0 (0%)                    | <b>1</b>                  | <b>&lt;0.001</b> | 220 |                          |              |  |
| PART or TOTAL                       |                                | 143 (63.84%)     | 76 (49.35%)      | 48 (94.12%)      | 19 (100%)       | <b>10.26 (3.10-33.94)</b> |                           |                  |     |                          |              |  |
| <b>On ACEi/ARB</b>                  | No                             | 150 (66.96%)     | 98 (63.64%)      | 37 (72.55%)      | 15 (78.95%)     |                           |                           |                  |     |                          |              |  |
|                                     | Yes                            | 70 (31.25%)      | 53 (34.42%)      | 14 (27.45%)      | 3 (15.79%)      | 0.82 (0.44-1.52)          | 0.518                     | 216              |     |                          |              |  |
|                                     | Missing                        | 4 (1.79%)        | 3 (1.95%)        | 0 (0%)           | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
| <b>CEIL OF CARE** only 143 obs</b>  | Ward                           | 73 (51.05%)      | 31 (38.27%)      | 34 (73.91%)      | 8 (50.00%)      | <b>1</b>                  |                           |                  |     |                          |              |  |
|                                     | NIV                            | 24 (16.78%)      | 17 (20.99%)      | 5 (10.87%)       | 2 (12.50%)      | <b>0.36 (0.14-0.94)</b>   | <b>0.036</b>              | 141              |     |                          |              |  |
|                                     | Mechanical ventilation         | 46 (32.17%)      | 33 (40.74%)      | 7 (15.22%)       | 6 (37.50%)      | <b>0.25 (0.12-0.56)</b>   | <b>0.001</b>              |                  |     |                          |              |  |
| <b>MAXIMUM BREATHING SUPPORT</b>    | NONE                           | 67 (29.91%)      | 64 (41.56%)      | 0 (0%)           | 3 (15.79%)      | NA                        |                           |                  |     |                          |              |  |
|                                     | Nasal cannula                  | 60 (26.79%)      | 40 (25.97%)      | 14 (27.45%)      | 6 (31.58%)      |                           |                           |                  |     |                          |              |  |
|                                     | Vent/Face mask                 | 32 (14.29%)      | 6 (3.90%)        | 23 (45.10%)      | 3 (15.79%)      |                           |                           |                  |     |                          |              |  |
|                                     | NIV                            | 12 (5.36%)       | 7 (4.55%)        | 4 (7.84%)        | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
|                                     | Mechanical Ventilation         | 9 (4.02%)        | 1 (0.65%)        | 6 (11.77%)       | 2 (10.53%)      |                           |                           |                  |     |                          |              |  |
| <b>Dialysis access</b>              | Missing                        | 44 (19.64%)      | 36 (23.38%)      | 4 (7.84%)        | 4 (21.05%)      |                           |                           |                  |     |                          |              |  |
|                                     | Fistula or AVG                 | 124 (55.36%)     | 89 (57.79%)      | 24 (47.06%)      | 11 (57.90%)     | <b>1</b>                  |                           |                  |     |                          |              |  |
|                                     | Line                           | 98 (43.75%)      | 64 (41.56%)      | 26 (50.98%)      | 8 (42.11%)      | 1.34 (0.77-2.32)          | 0.298                     | 218              |     |                          |              |  |
|                                     | Missing                        | 2 (0.89%)        | 1 (0.65%)        | 1 (1.96%)        | 0 (0%)          |                           |                           |                  |     |                          |              |  |
| <b>Dialysis vintage 5-yr effect</b> | Mean (SD)                      | 4.092 (4.46)     | 3.99 (4.43)      | 4.44 (4.76)      | 3.94 (4.46)     | 1.13 (0.86-1.48)          | 0.393                     | 209              |     |                          |              |  |
|                                     | Median (Q1-Q3)                 | 2.82 (1.11-5.46) | 2.57 (1.05-5.27) | 3.11 (1.17-5.55) | 3.94 (1.2-5.23) |                           |                           |                  |     |                          |              |  |
|                                     | Range                          | 0.003-24.7       | 0.003-24.7       | 0.022-22.9       | 0.22-16.3       |                           |                           |                  |     |                          |              |  |
|                                     | Missing                        | 11 (4.91%)       | 8 (5.20%)        | 2 (3.92%)        | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
| <b>IMMUNO SUPPRESSION</b>           | No                             | 197 (87.95%)     | 135 (87.66%)     | 47 (92.16%)      | 15 (78.95%)     |                           |                           |                  |     |                          |              |  |
|                                     | Yes                            | 23 (10.27%)      | 16 (10.39%)      | 4 (7.84%)        | 3 (15.79%)      | 0.73 (0.27-1.94)          | 0.523                     | 216              |     |                          |              |  |
|                                     | Missing                        | 4 (1.79%)        | 3 (1.95%)        | 0 (0%)           | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
| <b>ITU ADMISSION</b>                | No                             | 207 (92.41%)     | 148 (96.10%)     | 44 (86.28%)      | 15 (78.95%)     |                           |                           |                  |     |                          |              |  |
|                                     | Yes                            | 11 (4.91%)       | 3 (1.95%)        | 6 (11.77%)       | 2 (10.53%)      |                           |                           |                  |     |                          |              |  |
|                                     | Missing                        | 6 (2.68%)        | 3 (1.95%)        | 1 (1.96%)        | 2 (10.53%)      |                           |                           |                  |     |                          |              |  |
| <b>NO PREV TX</b>                   | 0                              | 206 (91.96%)     | 142 (92.21%)     | 47 (92.16%)      | 17 (89.47%)     | <b>1</b>                  |                           |                  |     |                          |              |  |
|                                     | 1-2                            | 14 (6.24%)       | 9 (5.84%)        | 4 (7.84%)        | 1 (5.26%)       | 1.40 (0.54-3.67)          | 0.488                     | 216              |     |                          |              |  |
|                                     | Missing                        | 4 (1.78%)        | 3 (1.95%)        | 0 (0%)           | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
| <b>Transplant WAIT LIST</b>         | No                             | 201 (89.73%)     | 135 (87.66%)     | 48 (94.12%)      | 18 (94.74%)     | <b>1</b>                  |                           |                  |     |                          |              |  |
|                                     | Yes                            | 16 (7.14%)       | 14 (9.09%)       | 2 (3.92%)        | 0 (0%)          | 0.52 (0.123-2.040)        | 0.356                     | 215              |     |                          |              |  |
|                                     | Missing                        | 7 (3.13%)        | 5 (3.25%)        | 1 (1.96%)        | 1 (5.26%)       |                           |                           |                  |     |                          |              |  |
| Symptoms                            | <b>FEVER</b>                   | No               | 58 (25.89%)      | 40 (25.97%)      | 17 (33.33%)     | 1 (5.26%)                 |                           |                  |     |                          |              |  |
|                                     |                                | Yes              | 138 (61.61%)     | 96 (62.34%)      | 31 (60.78%)     | 11 (57.90%)               | 0.72 (0.40-1.29)          | 0.269            | 193 |                          |              |  |
|                                     |                                | Missing          | 28 (12.50%)      | 18 (11.69%)      | 3 (5.88%)       | 7 (36.84%)                |                           |                  |     |                          |              |  |
|                                     | <b>SOB</b>                     | No               | 105 (46.88%)     | 85 (55.20%)      | 17 (33.33%)     | 3 (15.79%)                |                           |                  |     |                          |              |  |
|                                     |                                | Yes              | 92 (41.07%)      | 52 (33.77%)      | 31 (60.78%)     | 9 (47.37%)                | <b>2.32 (1.29-4.17)</b>   | <b>0.005</b>     | 194 |                          |              |  |
|                                     |                                | Missing          | 27 (12.05%)      | 17 (11.04%)      | 3 (5.88%)       | 7 (36.84%)                |                           |                  |     |                          |              |  |
|                                     | <b>DRY COUGH</b>               | No               | 116 (51.79%)     | 84 (54.55%)      | 25 (49.02%)     | 7 (36.84%)                |                           |                  |     |                          |              |  |
|                                     |                                | Yes              | 82 (36.61%)      | 54 (35.07%)      | 23 (45.10%)     | 5 (26.32%)                | 1.31 (0.74-2.29)          | 0.352            | 195 |                          |              |  |

|  |  |                    |                    |                    |                   |                          |                         |              |                         |                  |  |
|--|--|--------------------|--------------------|--------------------|-------------------|--------------------------|-------------------------|--------------|-------------------------|------------------|--|
|  |  | Missing            | 26 (11.61%)        | 16 (10.39%)        | 3 (5.88%)         | 7 (36.84%)               |                         |              |                         |                  |  |
|  | <b>PRODUCTIVE<br/>COUGH</b>  | No                 | 160 (71.43%)       | 111 (72.08%)       | 39 (76.47%)       | 10 (52.63%)              | 1.14 (0.57-2.26)        | 0.710        | 194                     |                  |  |
|  |  | Yes                | 37 (16.52%)        | 25 (16.23%)        | 10 (19.61%)       | 2 (10.53%)               |                         |              |                         |                  |  |
|  |  | Missing            | 27 (12.05%)        | 18 (11.69%)        | 2 (3.92%)         | 7 (36.84%)               |                         |              |                         |                  |  |
|  | <b>HEADACHE</b>  | No                 | 176 (78.57%)       | 122 (79.22%)       | 44 (86.27%)       | 10 (52.63%)              | 0.76 (0.27-2.10)        | 0.593        | 193                     |                  |  |
|  |  | Yes                | 20 (8.93%)         | 14 (9.09%)         | 4 (7.84%)         | 2 (10.53%)               |                         |              |                         |                  |  |
|  |  | Missing            | 28 (12.50%)        | 18 (11.69%)        | 3 (5.88%)         | 7 (36.84%)               |                         |              |                         |                  |  |
|  | <b>VOMITING</b>  | No                 | 166 (74.11%)       | 118 (76.62%)       | 39 (76.47%)       | 9 (47.37%)               | 1.29 (0.63-2.65)        | 0.483        | 193                     |                  |  |
|  |  | Yes                | 30 (13.39%)        | 18 (11.69%)        | 9 (17.65%)        | 3 (15.79%)               |                         |              |                         |                  |  |
|  |  | Missing            | 28 (12.50%)        | 18 (11.69%)        | 3 (5.88%)         | 7 (36.84%)               |                         |              |                         |                  |  |
|  | <b>ACHES<br/>&amp; PAINS</b>                                       | No                 | 157 (70.10%)       | 110 (71.43%)       | 38 (74.51%)       | 9 (47.37%)               | 1.06 (0.53-2.15)        | 0.861        | 193                     |                  |  |
|  |  | Yes                | 39 (17.42%)        | 26 (16.88%)        | 10 (19.61%)       | 3 (15.79%)               |                         |              |                         |                  |  |
|  |  | Missing            | 28 (12.50%)        | 18 (11.69%)        | 3 (5.88%)         | 7 (36.84%)               |                         |              |                         |                  |  |
|  | <b>DIARHOEA</b>  | No                 | 165 (73.66%)       | 113 (73.38%)       | 43 (84.31%)       | 9 (47.37%)               | 0.60 (0.24-1.51)        | 0.275        | 192                     |                  |  |
|  |  | Yes                | 30 (13.39%)        | 23 (14.94%)        | 5 (9.80%)         | 2 (10.53%)               |                         |              |                         |                  |  |
|  |  | Missing            | 29 (12.95%)        | 18 (11.69%)        | 3 (5.88%)         | 8 (42.11%)               |                         |              |                         |                  |  |
|  | <b>SYMPTOMS</b>  | No                 | 186 (83.04%)       | 127 (82.47%)       | 47 (92.16%)       | 12 (63.16%)              | 0.37 (0.05-2.95)        | 0.350        | 193                     |                  |  |
|  |  | Yes                | 10 (4.46%)         | 9 (5.84%)          | 1 (1.96%)         | 0 (0%)                   |                         |              |                         |                  |  |
|  |  | Missing            | 28 (12.50%)        | 18 (11.69%)        | 3 (5.88%)         | 7 (36.84%)               |                         |              |                         |                  |  |
| <b>Blood analyses</b>  | <b>Haemoglobin (g/L)</b>   | Mean (SD)          | 105.04 (15.28)     | 104.13 (13.74)     | 108.49 (18.383)   | 103.06 (17.38)           | 1.10 (0.99-1.22)        | 0.092        | 210                     |                  |  |
|  |  | Median (Q1-Q3)     | 105 (97-114)       | 105 (96-113)       | 107 (99-120)      | 102.5 (91-116)           |                         |              |                         |                  |  |
|  |  | Range              | 70-145             | 73-145             | 70-141            | 72-136                   |                         |              |                         |                  |  |
|  |  | Missing            | 11 (4.91%)         | 5 (3.25%)          | 2 (3.92%)         | 18 (94.74%)              |                         |              |                         |                  |  |
|  | <b>CRP (mg/L)<br/>(10-unit SHR effect)</b>                         | Mean (SD)          | 103.62 (101.8)     | 89.26 (92.13)      | 140.76 (116.6)    | 115.14 (110.2)           | <b>1.03 (1.01-1.05)</b> | <b>0.005</b> | 198                     |                  |  |
|  |  | Median (Q1-Q3)     | 74 (31.8-129.3)    | 65 (28-103.8)      | 113 (47-212)      | 76.4 (38.7-183)          |                         |              |                         |                  |  |
|  |  | Range              | 1.1-596.5          | 1.1-596.5          | 4.4-471           | 6-368                    |                         |              |                         |                  |  |
|  |  | Missing            | 23 (10.27%)        | 18 (11.69%)        | 4 (7.84%)         | 1 (5.26%)                |                         |              |                         |                  |  |
|  | <b>CRP<br/>(log scale)</b>   | Mean (SD)          | 4.074 (1.20)       | 3.91 (1.29)        | 4.51 (1.10)       | 4.203 (1.22)             | <b>1.44 (1.07-1.93)</b> | <b>0.015</b> | 198                     |                  |  |
|  |  | Median (Q1-Q3)     | 4.30 (3.46-4.86)   | 4.17 (3.33-4.64)   | 4.73 (3.85-5.36)  | 4.32 (3.7-5.21)          |                         |              |                         |                  |  |
|  |  | Range              | 0.095-6.39         | 0.095-6.39         | 1.48-6.15         | 1.97-5.91                |                         |              |                         |                  |  |
|  |  | Missing            | 23 (10.27%)        | 18(11.69%)         | 4 (7.84%)         | 1 (5.26%)                |                         |              |                         |                  |  |
|  | <b>WHITE CELL COUNT<br/>original scale<br/>(5-unit effect)</b>     | Mean (SD)          | 6.16 (3.175)       | 5.65 (3.029)       | 7.39 (3.158)      | 6.92 (3.476)             | <b>1.70 (1.22-2.37)</b> | <b>0.002</b> | 210                     |                  |  |
|  |  | Median (Q1-Q3)     | 5.38 (3.9-7.43)    | 5.1 (3.5-6.6)      | 6.9 (5.22-9.7)    | 6.16 (4.27-8.1)          |                         |              |                         |                  |  |
|  |  | Range              | 1.65-18.9          | 1.65-18.9          | 1.8-15.3          | 2.3-15.2                 |                         |              |                         |                  |  |
|  | <b>WHITE CELL COUNT<br/>(log scale)</b>                            | Mean (SD)          | 1.70 (0.49)        | 1.62 (.50)         | 1.90 (0.47)       | 1.82 (0.50)              | <b>2.53 (1.45-4.42)</b> | <b>0.001</b> | 210                     |                  |  |
|  |  | Median (Q1-Q3)     | 1.68 (1.36-2.01)   | 1.63 (1.25-1.89)   | 1.93 (1.65-2.27)  | 1.81 (1.45-2.1)          |                         |              |                         |                  |  |
|  |  | Range              | 0.5-2.94           | 0.50-2.94          | .59-2.73          | 0.83-2.72                |                         |              |                         |                  |  |
|  |  | Missing            | 11 (4.91%)         | 8 (5.20%)          | 2(3.92%)          | 1 (5.26%)                |                         |              |                         |                  |  |
|  | <b>NEUTROPHIL COUNT<br/>(x10<sup>9</sup>/L)<br/>original scale</b> | Mean (SD)          | 4.67 (2.99)        | 4.22 (2.88)        | 5.91 (3.02)       | 4.98 (2.97)              | <b>1.80 (1.26-2.56)</b> | <b>0.001</b> | 210                     |                  |  |
|  |  | Median (Q1-Q3)     | 3.8(2.6-5.93)      | 3.5 (2.3-5.2)      | 5.4 (3.57-7.9)    | 4.52 (3-6.1)             |                         |              |                         |                  |  |
|  |  | Range              | 0.68-17.5          | 0.68-17.5          | 1.1-13.9          | 1.2-12.6                 |                         |              |                         |                  |  |
| <b>NEUTROPHIL COUNT<br/>(log scale)</b>                            | Mean (SD)  | 1.36 (0.61)        | 1.26 (0.59)        | 1.64 (0.56)        | 1.43 (0.64)       | <b>2.30 (1.45-3.66)</b>  | <b>&lt;0.001</b>        | 210          |                         |                  |  |
|  | Median (Q1-Q3)   | 1.34 (0.96-1.78)   | 1.25 (0.83-1.65)   | 1.67 (1.27-2.07)   | 1.51 (1.1-1.81)   |                          |                         |              |                         |                  |  |
|  | Range  | -0.39-2.86         | -0.39-2.86         | 0.10-2.63          | 0.18-2.53         |                          |                         |              |                         |                  |  |
|  | Missing  | 11 (4.91%)         | 8 (5.20%)          | 2 (3.92%)          | 1 (5.26%)         |                          |                         |              |                         |                  |  |
| <b>LYMPHOCYTE COUNT<br/>(x10<sup>9</sup>/L)<br/>original scale</b> | Mean (SD)  | 0.903(0.49)        | 0.889 (0.403)      | 0.815 (0.56)       | 1.27 (0.73)       | 0.59 (0.23-1.53)         | 0.276                   | 210          |                         |                  |  |
|  | Median (Q1-Q3)   | 0.8 (.58-1.1)      | 0.8 (0.6-1.1)      | 0.7 (0.4-1)        | 1.2 (0.8-1.6)     |                          |                         |              |                         |                  |  |
|  | Range  | 0.1-3.6            | 0.2-2.3            | 0.1-3.4            | 0.4-3.6           |                          |                         |              |                         |                  |  |
| <b>LYMPHOCYTE COUNT<br/>(log scale)</b>                            | Mean (SD)  | -0.23 (0.52)       | -0.22(0.45)        | -0.39 (0.63)       | 0.10 (0.54)       | <b>0.52 (0.31-0.86)</b>  | <b>0.012</b>            | 210          |                         |                  |  |
|  | Median (Q1-Q3)   | -0.22 (-0.54-0.10) | -0.22 (-1.08-0.70) | -0.36 (-0.92-0.00) | 0.18 (-0.22-0.47) |                          |                         |              |                         |                  |  |
|  | Range  | -1.3-1.28          | -1.61-0.83         | -2.30-1.22         | -0.92-1.28        |                          |                         |              |                         |                  |  |
|  | Missing  | 11 (4.91%)         | 8 (5.20%)          | 2 (3.92%)          | 1 (5.26%)         |                          |                         |              |                         |                  |  |
| <b>NEUT/LYMP ratio</b>   | Mean (SD)  | 6.9 (8.4)          | 5.7 (4.97)         | 11.6 (14.3)        | 4.8 (3.2)         | <b>1.03 (1.017-1.05)</b> | <b>&lt;0.001</b>        | 210          | <b>1.03 (1.01-1.04)</b> | <b>&lt;0.001</b> |  |
|  | Median (Q1-Q3)   | 4.7 (3.1-7.8)      | 4.30 (2.9-6.7)     | 7.2 (4.2-13.4)     | 4.1 (2.1-7.4)     |                          |                         |              |                         |                  |  |
|  | Range  | 0.7-93             | 0.9-32             | 0.7-93             | 0.9-11.98         |                          |                         |              |                         |                  |  |
| <b>NEUT/LYMP ratio</b>   | Mean (SD)  | 1.59 (.80)         | 1.47 (.71)         | 2.03 (.90)         | 1.33 (0.73)       | <b>2.10 (1.54-2.87)</b>  | <b>&lt;0.001</b>        | 210          |                         |                  |  |

|  |                        |                |                  |                  |                  |                  |                         |              |     |  |  |
|--|------------------------|----------------|------------------|------------------|------------------|------------------|-------------------------|--------------|-----|--|--|
|  | <b>(log scale)</b>     | Median (Q1-Q3) | 1.54 (1.12-2.05) | 1.46 (1.05-1.91) | 1.98 (1.43-2.60) | 1.40 (0.76-1.99) |                         |              |     |  |  |
|  |                        | Range          | -0.31-4.53       | -0.13-3.47       | -0.31-4.53       | -0.07-2.48       |                         |              |     |  |  |
|  |                        | Missing        | 11 (4.91%)       | 8 (5.20%)        | 2 (3.92%)        | 1 (5.26%)        |                         |              |     |  |  |
|  | <b>ALBUMIN (g/L)</b>   | Mean (SD)      | 33.66 (6.32)     | 34.25 (6.01)     | 31.88 (7.14)     | 33 (6.26)        | <b>0.80 (0.64-1.01)</b> | <b>0.059</b> | 200 |  |  |
|  | <b>(5-unit effect)</b> | Median (Q1-Q3) | 34 (30-38)       | 35 (31-39)       | 33 (29-37)       | 33.5 (29-35)     |                         |              |     |  |  |
|  |                        | Range          | 13-47            | 16-47            | 13-45            | 22-43            |                         |              |     |  |  |
|  |                        | Missing        | 20 (8.93%)       | 7 (4.55%)        | 8 (15.69%)       | 5 (26.32%)       |                         |              |     |  |  |

Table 1: Demographic, clinical characteristics and hospital management features of all 224 SARS-CoV-2 positive patients from St George's, King's and St Helier hospitals in London collected between 29<sup>th</sup> February and 15<sup>th</sup> May.

Legend: The two columns on the right represent the univariate and adjusted effects of the corresponding raw variable on the SHR of death vs. discharged alive and the p-values tests the null hypothesis that that SHR is 1. A SHR value greater than 1 indicates a harmful effect whilst a value less than 1 indicates a protective effect of the corresponding variable on the left. The last column represents the most parsimonious model derived from the data.

Abbreviations: angiotensin-converting-enzyme inhibitors (ACEi); angiotensin II receptor blockers (ARB); arteriovenous graft (AVG); non-invasive ventilation (NIV). Neutrophil/lymphocyte (NEUT/LYMP)



Table 2

| Variable          | Summary | Hemodialysis population |           |              |           |                     |                  | Peritoneal dialysis population |           |              |          |                     |             |
|-------------------|---------|-------------------------|-----------|--------------|-----------|---------------------|------------------|--------------------------------|-----------|--------------|----------|---------------------|-------------|
|                   |         | St. Helier's            | King's    | St. George's | Pooled    | SARS-CoV-2 positive | P-value          | St. Helier's                   | King's    | St. George's | Pooled   | SARS-CoV-2 positive | P-value     |
| <b>Total</b>      | Number  | 846                     | 597       | 294          | 1737      | 224                 |                  | 98                             | 90        | 40           | 228      | 10                  |             |
| <b>Gender</b>     | Male    | 61.9%                   | 59%       | 58.5%        | 1048(60%) | 133(59%)            | <b>0.753</b>     | 55.1%                          | 60%       | 60%          | 132(58%) | 8 (80%)             | <b>.198</b> |
|                   | Female  | 28.1%                   | 41%       | 41.5%        | 689(40%)  | 91(41 %)            |                  | 44.9%                          | 40%       | 40%          | 96(42%)  | 2(20%)              |             |
| <b>Ethnicity</b>  | White   | 60%                     | 40%       | 29.9%        | 834(48%)  | 85(38%)             | <b>0.001</b>     | 75.5%                          | 37.8%     | 47.5%        | 127(56%) | 5(50%)              | <b>.754</b> |
|                   | Other   | 35.3%                   | 59.9%     | 66%          | 903(52%)  | 139(62%)            |                  | 21.4%                          | 62.2%     | 42.5%        | 101(44%) | 5(50%)              |             |
|                   | Missing | 4.7%                    | 0.01%     | 4.1%         |           |                     |                  | 3.1%                           | 0%        | 10%          |          |                     |             |
| <b>Age(years)</b> | Median  | 68.7                    | 63.4      | 66.6         | 66.5      | 65                  | <b>.384</b>      | 67.1                           | 56.8      | 62.5         | 62.2     | 69.5                | <b>.137</b> |
|                   | Q1-Q2   | 56.4-77.7               | 53.0-75.1 | 54.6-75.6    |           | 57-77               |                  | 57.7-76.5                      | 45.5-72.4 | 50.9-73.8    |          | 59-75               |             |
| <b>Diabetes</b>   | No      |                         |           |              | 1360(78%) | 103(46%)            | <b>&lt;0.001</b> |                                |           |              | 185(81%) | 4(40%)              | <b>.004</b> |
|                   | Yes     | 11.9%                   | 35.5%     | 21.8%        | 377(22%)  | 120 (54%)           |                  | 5.1%                           | 28.9%     | 30%          | 43(19%)  | 6(60%)              |             |

Table 2 Comparisons between COVID patients characteristics and the whole sample of ICDH/PD patients across the 3 hospitals.

Legend: The pooled proportions and numbers are weighted averages across the three hospitals.

Table 3

|                 | Total RRT | Hemodialysis population |            |       |                     |         | Peritoneal dialysis population |            |       |                     |         |
|-----------------|-----------|-------------------------|------------|-------|---------------------|---------|--------------------------------|------------|-------|---------------------|---------|
|                 |           | Total ICHD              | SARS-CoV-2 | Death | Case Fatality Ratio | p-value | Total PD                       | SARS-CoV-2 | Death | Case Fatality Ratio | p-value |
| All 3 Hospitals |           | 1737                    | 224        | 51    | 23%(17%,28%)        | -       | 98                             | 10         | 6     | 30%                 | -       |
| London          | 14394     |                         | 1021       | 219   | 21%(19%,24%)        | 0.67    |                                | 44         | 12    | 27%                 | 0.257   |
| England         | 56201     |                         | 2134       | 502   | 24%(22%,25%)        | 0.80    |                                | 78         | 25    | 32%                 | 0.299   |
| UK              | 66612     |                         | 2326       | 553   | 24%(22%,26%)        | 0.74    |                                | 84         | 26    | 31%                 | 0.289   |

Table 3 Local and national cumulative numbers as reported until 15<sup>th</sup> May by the UK Renal Registry.

Legend: The p-values are consistent with no difference between the case-fatality ratio in our sample and those in London, England and UK. Our data suggest some evidence that the case fatality ratio is higher in PD than in HD (51/224) and PD (6/10) patients (p=0.015 according to Fisher's exact test).

Table 4

| Variable                        | Category/Summary | CEILING OF CARE |                 |                    |                 |         | ICU admission   |                 |           |         |
|---------------------------------|------------------|-----------------|-----------------|--------------------|-----------------|---------|-----------------|-----------------|-----------|---------|
|                                 |                  | ALL (143)       | WARD (73)       | OPTIFLOW/CPAP (24) | INTUBATION (46) | p-value | NO (207)        | YES (11)        | Miss (6)  | p-value |
| GENDER                          | Male             | 84(58.7%)       | 46(63.0%)       | 9(37.5%)           | 29(63.0%)       | 0.068   | 121(58.5)       | 8(72.7)         | 4 (66.7%) | 0.348   |
|                                 | Female           | 59(41.3 %)      | 27(37.0%)       | 15(62.5%)          | 17(37.0%)       |         | 86(41.6)        | 3(27.3)         | 2(33.3%)  |         |
| ETHNICITY (binary)              | White            | 58(38%)         | 28(38.4%)       | 13(54.2%)          | 17(36.9%)       | 0.327   | 78(37.7)        | 5(45.6)         | 2(33.3)   | 0.605   |
|                                 | Other            | 85(62%)         | 45(61.6%)       | 11(45.8%)          | 29(63.1%)       |         | 129(62.3)       | 6(54.6)         | 4(66.7)   |         |
| SMOKING status                  | Never            | 94 (41.9%)      | 23(31.5%)       | 11(45.8%)          | 19(41.3 %)      | 0.284   | 86(41.6)        | 4(36.4)         | 4(66.7)   | 0.715   |
|                                 | Ever             | 71 (31.7%)      | 28(38.4%)       | 10(41.7%)          | 11(13.9%)       |         | 66(31.9)        | 4(36.4)         | 1 (16.7)  |         |
|                                 | Missing          | 59 (26.3%)      | 22(30.1%)       | 3(12.5%)           | 16(34.8%)       |         | 55(26.6)        | 3(27.3)         | 1(16.7)   |         |
| AGE at admission (5 yrs effect) | Mean (SD)        | 66.8(14.5)      | 74.8(8.9)       | 65.9(12.0)         | 54.6(14.3)      | <0.001  | 66.7(14.0)      | 49.9(12.5)      | 4 (66.7%) | 0.0004  |
|                                 | Median (Q1-Q3)   | 70(59-78)       | 77(70-81)       | 67(57-72.5)        | 57(44-62)       |         | 68(58-77)       | 53(40-61)       | 2(33.3%)  |         |
|                                 | Range            | 25-90           | 37-90           | 33-87              | 25-85           |         | 26-90           | 25-63           |           |         |
| BMI (kg/m <sup>2</sup> )        | Mean (SD)        | 27.6(7.7)       | 25.8(4.9)       | 28.1 (8.9)         | 30.6(9.8)       | 0.1263  | 28.5(7.6)       | 31.7 (9.9)      |           | 0.296   |
|                                 | Median (Q1-Q3)   | 25.9(22.3-30.1) | 25.8(21.4-29.6) | 25.3(22.6-29.0)    | 27.8(23.2-36.5) |         | 26.2(23.1-30.7) | 29.9(24.9-35.4) |           |         |
|                                 | Range            | 16.5-57.8       | 16.7-38.2       | 16.5-51.7          | 18.4-52.7       |         | 16.5-57.8       | 21.0-49.2       |           |         |
|                                 | Missing          | 21(14.5%)       | 9(12%)          | 9(12.5%)           | 9(20%)          |         | 21(10%)         | 54(5.5%)        |           |         |
| WHO Performance status binary   | 0-2              | 76 (53.2 %)     | 22(30.1 %)      | 17(70.8%)          | 37(80.4%)       | <0.001  | 120(58%)        | 8(72.7%)        | 6(100%)   | 0.40    |
|                                 | 3-4              | 66 (46.2 %)     | 51(69.9%)       | 7(29.2 %)          | 8(17.4 %)       |         | 80(38.7%)       | 3(27.3%)        | 0(0%)     |         |
|                                 | Missing          | 1(0.7%)         | 0(0%)           | 0(0 %)             | 1(2.2 %)        |         | 7(3.4%)         | 0(0%)           | 0(0%)     |         |
| NEUT/LYMP ratio (log scale)     | Mean (SD)        | 1.74(.78)       | 1.67(.79)       | 1.96(.68)          | 1.75(.81)       | 0.233   | 1.54(.76)       | 2.46(.87)       |           | 0.0006  |
|                                 | Median (Q1-Q3)   | 1.67(1.25-2.14) | 1.63(1.12-2.13) | 1.98(1.43-2.44)    | 1.59(1.25-2.14) |         | 1.53(1.07-1.99) | 2.14(1.83-2.90) |           |         |
|                                 | Range            | -.07-4.53       | -.07-3.52       | .65-2.59           | .22-4.53        |         | -.31-3.52       | 1.47-4.53       |           |         |
|                                 | Missing          | 2(1.4%)         | 0(0%)           | 1(4%)              | 1(2%)           |         | 11(5%)          | 0(0%)           |           |         |
| Hist of cancer                  | No               | 121 (84.62%)    | 62 (84.93%)     | 19 (79.17%)        | 40 (86.96%)     | 0.688   | 176(85.02%)     | 10(90.91%)      | 3 (50%)   | 0.999   |
|                                 | Yes              | 22(15.38%)      | 11 (15.07%)     | 5 (20.83%)         | 6 (13.04%)      |         | 29(14.01%)      | 1(9.09%)        | 3(50%)    |         |
|                                 | Missing          | 0(0%)           | 0(0%)           | 0(0%)              | 0(0%)           |         | 2(0.97%)        | 0(0%)           | 0(0%)     |         |
| Hypertension                    | No               | 27(18.88%)      | 10 (13.70%)     | 6 (25%)            | 11 (23.91%)     | 0.269   | 37(17.87%)      | 3(27.27%)       | 1(16.67%) | 0.430   |
|                                 | Yes              | 116(81.12%)     | 63 (86.30%)     | 18 (75%)           | 35 (76.09%)     |         | 169(81.64%)     | 8(72.73%)       | 5(83.33%) |         |
|                                 | Missing          | 0(0%)           | 0(0%)           | 0(0%)              | 0(0%)           |         | 1(0.48%)        | 0(0%)           | 0(0%)     |         |
| DIABETES                        | No               | 72(50.35%)      | 32 (43.84%)     | 13 (54.17%)        | 27 (58.70%)     | 0.264   | 91(43.96%)      | 10(90.91%)      | 2(33.33%) | 0.003   |
|                                 | Yes              | 71 (49.65%)     | 41 (56.16%)     | 11 (45.83%)        | 19 (41.30%)     |         | 115(55.56%)     | 1(9.09%)        | 4(66.67%) |         |
|                                 | Missing          | 0(0%)           | 0(0%)           | 0(0%)              | 0(0%)           |         | 1(0.48%)        | 0(0%)           | 0(0%)     |         |
| HFrEF                           | No               | 118 (83.10%)    | 54 (73.97%)     | 22 (91.67%)        | 42 (93.33%)     | 0.013   | 164(79.23%)     | 11(100%)        | 6(100%)   | 0.224   |
|                                 | Yes              | 25(16.90%)      | 20 (26.03%)     | 2 (8.33%)          | 3 (6.67%)       |         | 40(19.32%)      | 0(0%)           | 0(0%)     |         |
|                                 | Missing          | 0(0%)           | 0(0%)           | 0(0%)              | 0(0%)           |         | 3(1.45%)        | 0(0%)           | 0(0%)     |         |
| CHR LUNG DISEASE                | No               | 102 (71.33%)    | 51 (69.86%)     | 15 (62.50%)        | 36 (78.26%)     | 0.379   | 154(74.40%)     | 10(90.91%)      | 4(66.67%) | 0.300   |
|                                 | Yes              | 41 (28.67%)     | 22 (30.14%)     | 9 (37.50%)         | 10 (21.74%)     |         | 53(25.60%)      | 1(9.09%)        | 2(33.33%) |         |
| Ischaemic heart disease         | No               | 94 (65.73%)     | 43 (58.90%)     | 15 (62.50%)        | 36 (78.26%)     | 0.083   | 144(69.57%)     | 9(81.82%)       | 4(66.67%) | 0.518   |
|                                 | Yes              | 49 (34.27%)     | 30 (41.10%)     | 9 (37.50%)         | 10 (21.74%)     |         | 60(28.99%)      | 2(18.18%)       | 2(33.33%) |         |
|                                 | Missing          | 0(0%)           | 0(0%)           | 0(0%)              | 0(0%)           |         | 3(1.45%)        | 0(0%)           | 0(0%)     |         |
| Cerebrovascular disease         | No               | 106 (74.13%)    | 46 (63.01%)     | 18 (75.00%)        | 42 (91.30%)     | 0.003   | 156(75.36%)     | 11(100%)        | 6 (100%)  | 0.073   |
|                                 | Yes              | 37 (25.87%)     | 27 (36.99%)     | 6 (25.00%)         | 4 (8.70%)       |         | 49(23.67%)      | 0(0%)           | 0(0%)     |         |
|                                 | Missing          | 0 (0%)          | 0 (0%)          | 0 (0%)             | 0 (0%)          |         | 0 (0%)          | 0 (0%)          | 0 (0%)    |         |

Table 4: Impact of Clinical Variable and comorbidity on Ceiling of care or ICU

Legend: \*Tests are conducted on complete data

## Figure Title and Legends

Figure 1 The age dependent case fatality ratio and the daily time series of hospital admissions and deaths in COVID-19 positive hemodialysis patients.

Figure 2 The predicted daily cumulative incidence of death and hospital discharge of HD COVID positive patients. Legend The curves indicate a short and fast dynamics of death and a long time to discharge.

Figure 3 The dynamics of hospital death and hospital discharge in association with neutrophil/lymphocytes ratio. Legend: High levels of this ratio are associated with high risk of in-care deaths in COVID-19 positive hemodialysis patients. Low values of this ratio are associated with rapid and high probability of hospital discharge.

Figure 4 Meta-analyses for the pooled case-fatality ratio based on existing research with and without current London study

Figure 1

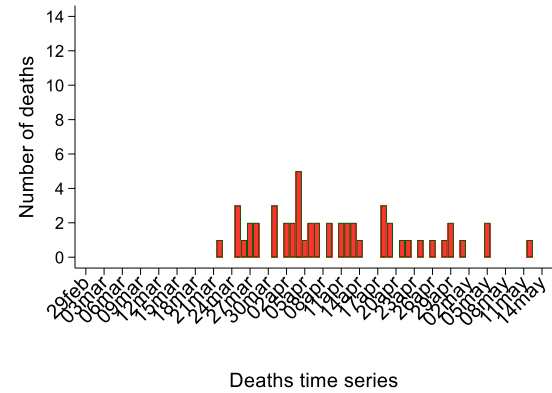
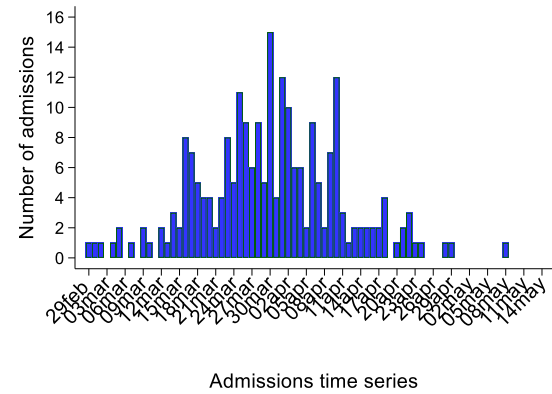
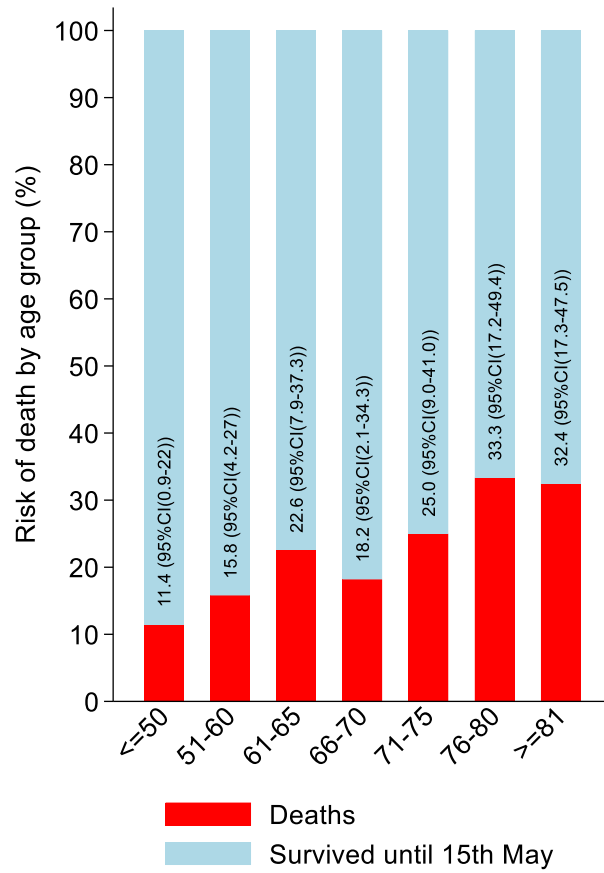


Figure 2

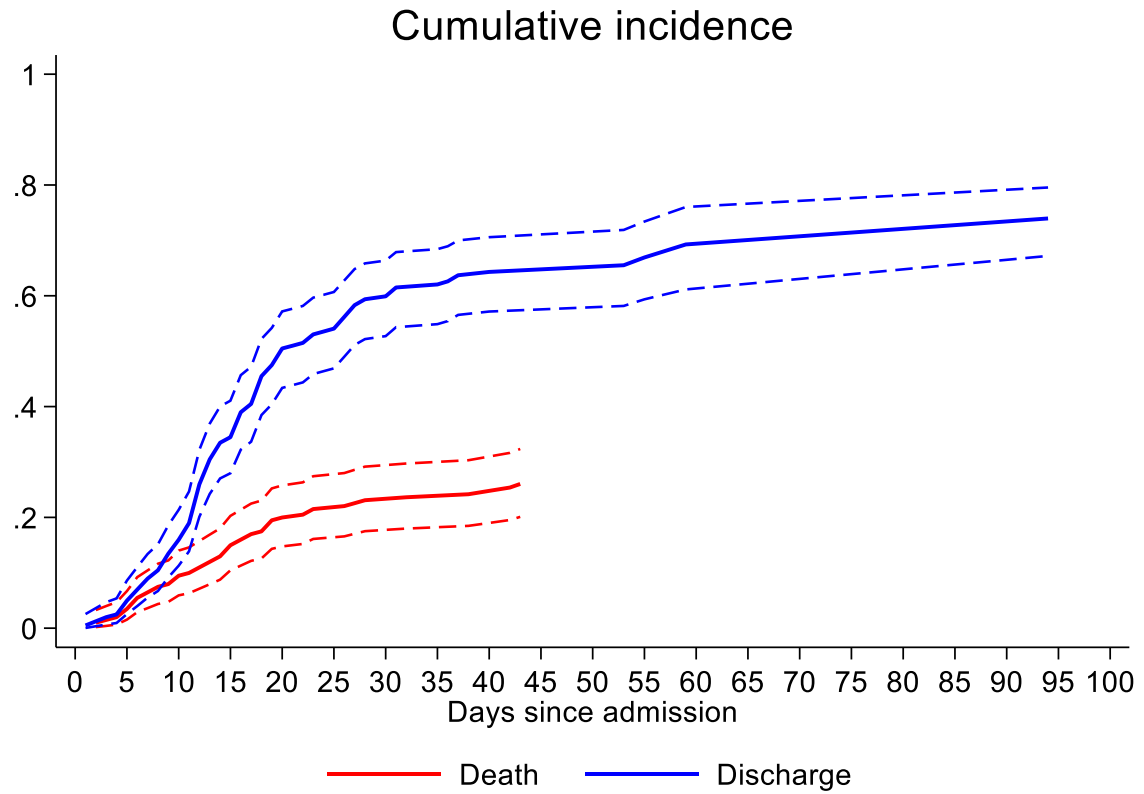
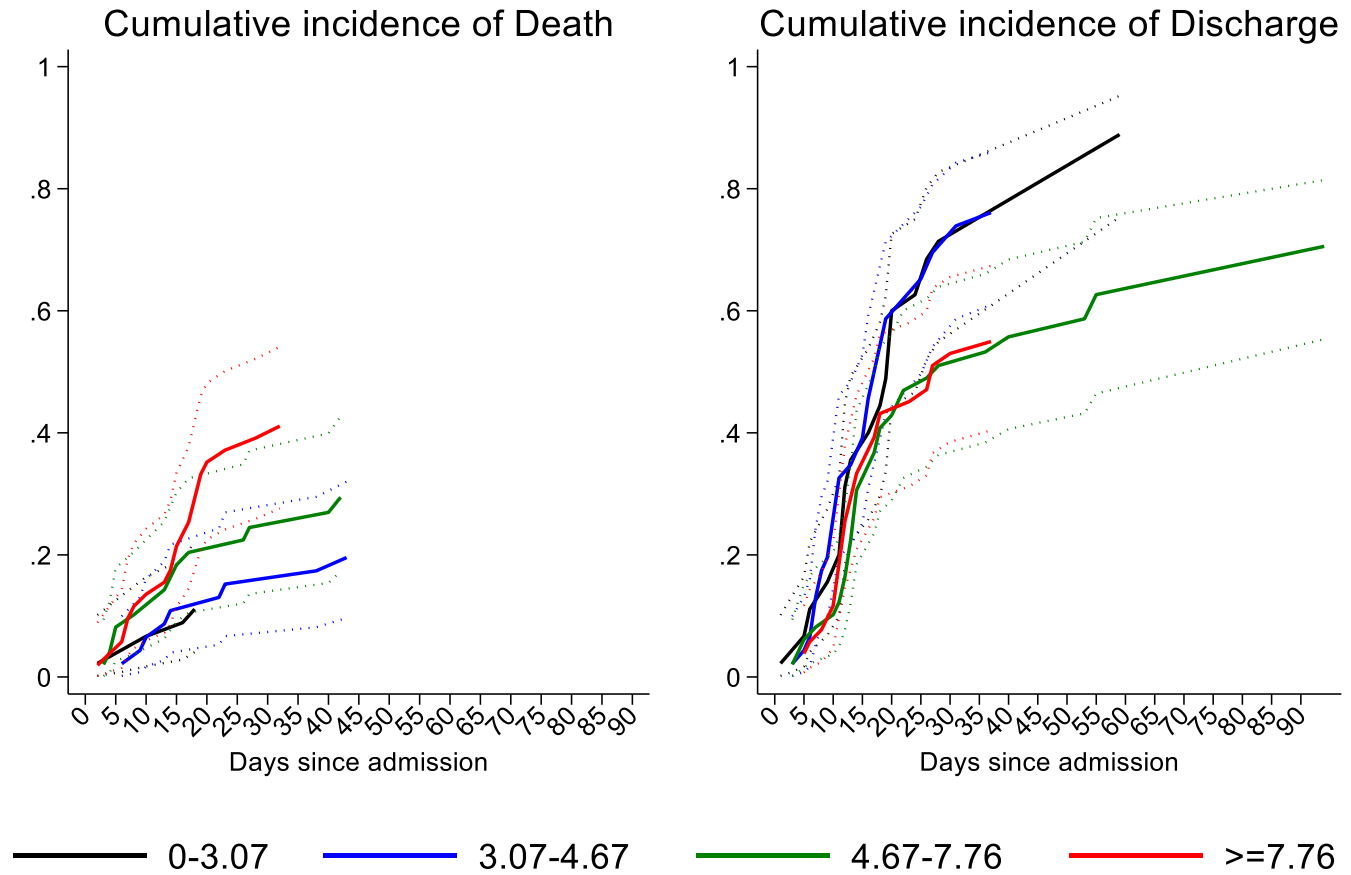


Figure 3

Figure 3: Neutrophil/Lymphocyte ratio



# Figure 4

