



# International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC)

*A global federation of clinical research networks, providing a proficient, coordinated, and agile research response to outbreak-prone infectious diseases*

## COVID-19 Report: 19 May 2020

### Summary

The results in this report have been produced using data from the ISARIC COVID-19 database. For information, or to contribute to the collaboration, please contact [ncov@isaric.org](mailto:ncov@isaric.org).

We thank all of the data contributors for collecting standardised data during these extraordinary times. We plan to issue this report of aggregate data weekly for the duration of the SARS-CoV-2/COVID-19 pandemic.

Please note the following caveats. This is a dynamic report which captures new variables and information as our understanding of COVID-19 evolves. Please observe the  $N$  of each result to note newly added variables with fewer data points. Information is incomplete for the many patients who are still being treated. Furthermore, it is likely that that we received more cases of severely ill individuals than those with relatively less severe illness; outcomes from these data, such as the proportion dying, must therefore not be used to infer outcomes for the entire population of people who might become infected. Some patients may be participants in clinical trials of experimental interventions. Many of the included cases are from the United Kingdom. Additional caveats are provided in the in the ‘Caveats’ section below.

Up to the date of this report, data have been entered for **46929** individuals from **355** sites across **36** countries.

The analysis detailed in this report only includes individuals:

1. for whom data collection commenced on or before 05 May 2020. (We have applied a 14-day rule to focus analysis on individuals who are more likely to have a recorded outcome. By excluding patients enrolled during the last 14 days, we aim to reduce the number of incomplete data records and thus improve the generalisability of the results and the accuracy of the outcomes. However, this limits our focus to a restricted cohort despite the much larger volumes of data held in the database.)

### AND

2. who have laboratory-confirmed or clinically-diagnosed SARS-COV-2 infection.

**The cohort satisfying the above criteria has 25849 cases** (97.67% are laboratory-confirmed for SARS-COV-2 infection).

The flow chart in Figure 1 gives an overview of the cohort and outcomes as of 19 May 2020.

## Demographics and presenting features

Of these 25849 cases, 15271 are males and 10493 are females – sex is unreported for 85 cases. The minimum and maximum observed ages were 0 and 104 years respectively. The median age is 72 years.

The observed mean number of days from (first) symptom onset to hospital admission was 13, with a standard deviation (SD) of 7.9 days and a median of 5 days.

The observed mean duration for the number of days from hospital admission to outcome (death or discharge) was 10.5, with SD 10.2 days and a median of 8 days. These estimates are based on all cases which have complete records on length of hospital stay (N = 21270).

The symptoms on admission represent the policy for hospital admission and containment at that time plus, whatever the case definition was. As time passes for most countries these will change. The five most common symptoms at admission were history of fever, shortness of breath, cough, fatigue/malaise, and confusion. Frequencies of symptom prevalence vary with age.

## Outcomes

Outcomes have been recorded for 19983 patients, consisting of 12903 recoveries and 7080 deaths. Follow-up is ongoing for 4112 patients. Outcome records are unavailable for 1754 patients.

**ICU/HDU:** A total of 4752 (18%) patients were admitted at some point of their illness into an intensive care unit (ICU) or high dependency unit (HDU). Of these, 1567 died, 1106 are still in hospital and 1591 have recovered and been discharged.

The observed mean and median durations (in days) from hospital admission to ICU/HDU admission were 2.8 and 1 respectively (SD: 5.9) – estimated from records on cases with complete date records on hospital admission and ICU/HDU entry (N = 4454).

The duration of stay in ICU/HDU had a mean of 9.7 days and a median of 7 (SD: 9.3 days) – estimated on only those cases with complete records for ICU/HDU duration or ICU/HDU start/end dates (N = 3458). Of these 4752 patients who were admitted into ICU/HDU, 1567 died, 1106 are still in hospital and 1591 have recovered and been discharged. Outcome records are unavailable for 488 cases. Approximately 42% of patients with complete records on ICU admission dates were admitted to ICU within the first day of hospital admission. The distribution of the number of days from admission to ICU admission is shown in Figure 11.

## Treatment

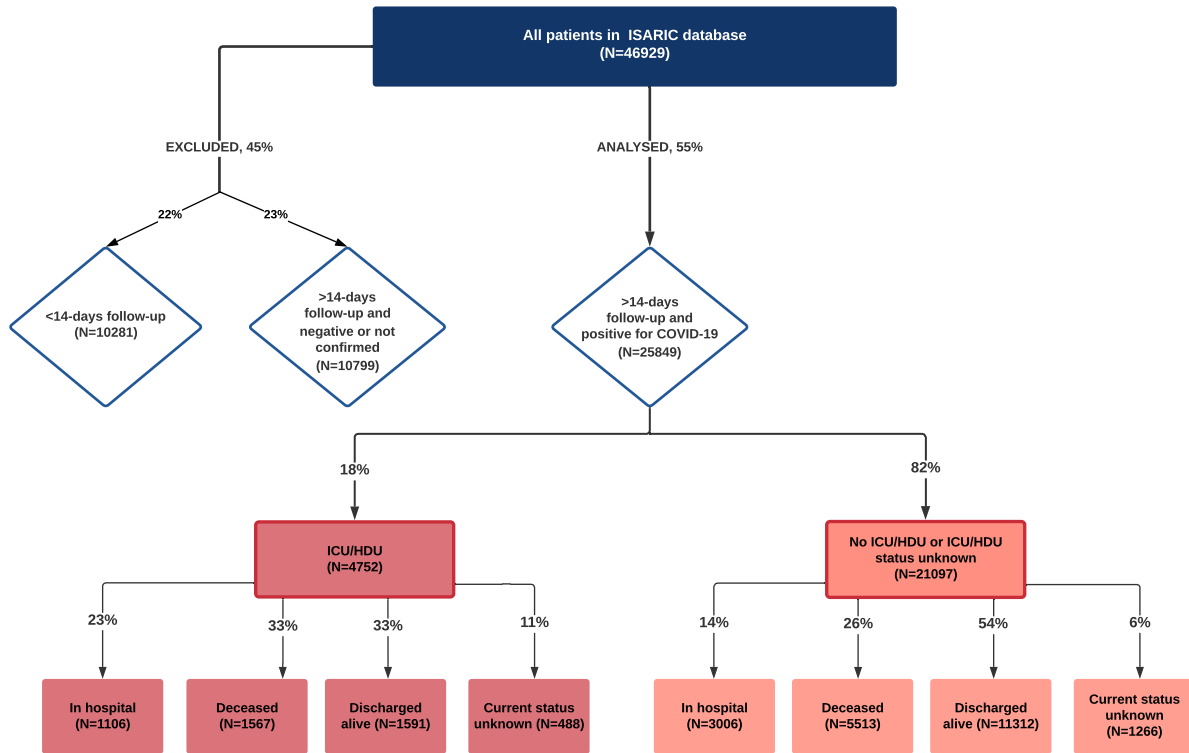
Antibiotics were received by 16820/20114 (83.6%) patients, and 1771/19505 (9.1%) received antivirals. These treatment categories are not mutually exclusive since some patients received multiple treatments. (The denominators differ due to data completeness.) 16760/24861 (67.4%) patients received some degree of oxygen supplementation: of these, 3937/16760 (23.5%) received NIV and 2946/16760 (17.6%) IMV.

Of the patients admitted into ICU/HDU, 3157/3455 (91.4%) received antibiotics and 2582/5164 (50%) antivirals. 4286/4679 (91.6%) received some degree of oxygen supplementation, of which, 2110/4286 (49.2%) received NIV and 2842/4286 (66.3%) IMV.

A total of 3937 patients received non-invasive mechanical ventilation (NIV). The mean and median durations from admission to receiving NIV were 4.2 days and 2 days respectively (SD: 8.3 days) – estimated from records on cases with complete records on dates of hospital admission and NIV onset (N = 3147). The mean and median durations for NIV were 2 days and 0 days respectively (SD: 4 days) – estimated based on only those cases which have complete NIV duration records (N = 1837).

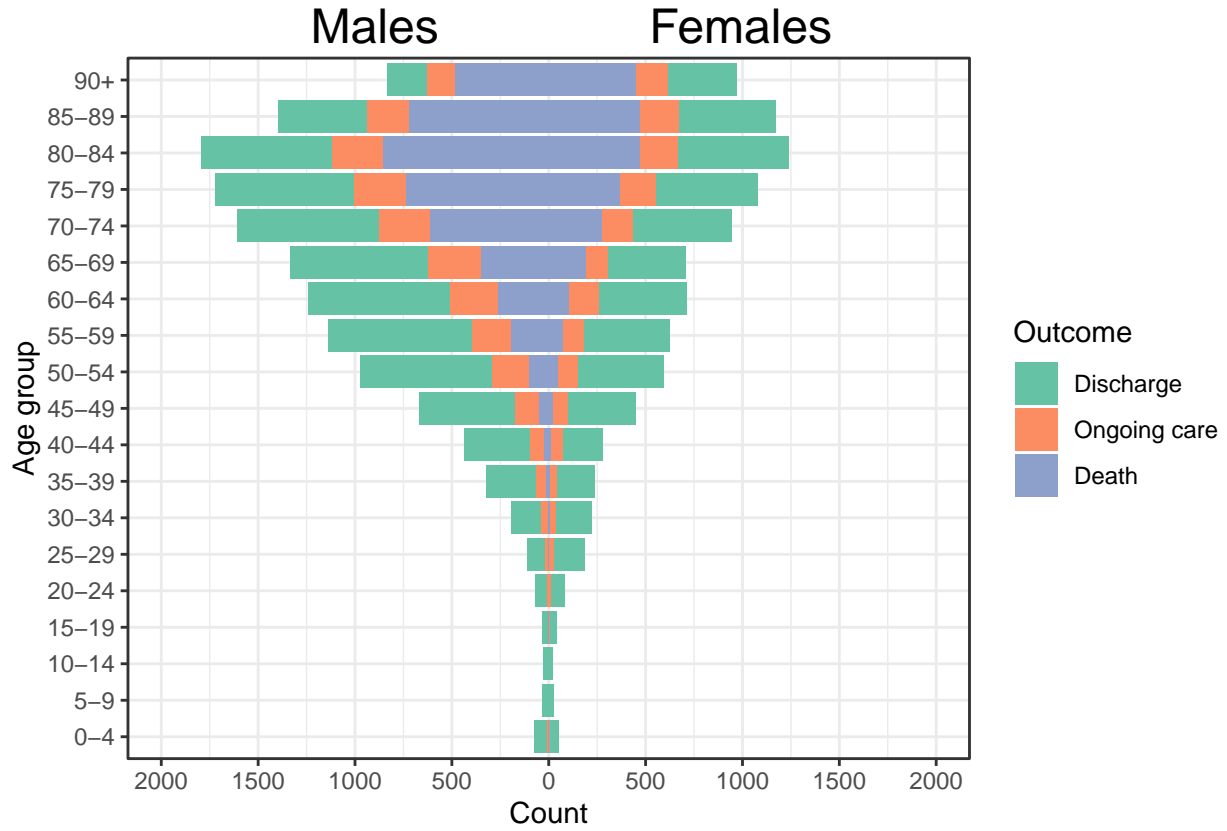
A total of 2946 patients received invasive mechanical ventilation (IMV). The mean and median durations from admission to receiving IMV were 3.2 days and 2 days respectively (SD: 6 days) – estimated from records on cases with complete records on dates of hospital admission and IMV onset (N = 2647). The mean, median and SD for the duration of IMV – estimated based on all 1751 cases with complete records on IMV stays – were 11.2 days, 10 days and 8.2 days respectively.

**Figure 1:** Overview of cohort and outcomes as of 19 May 2020.

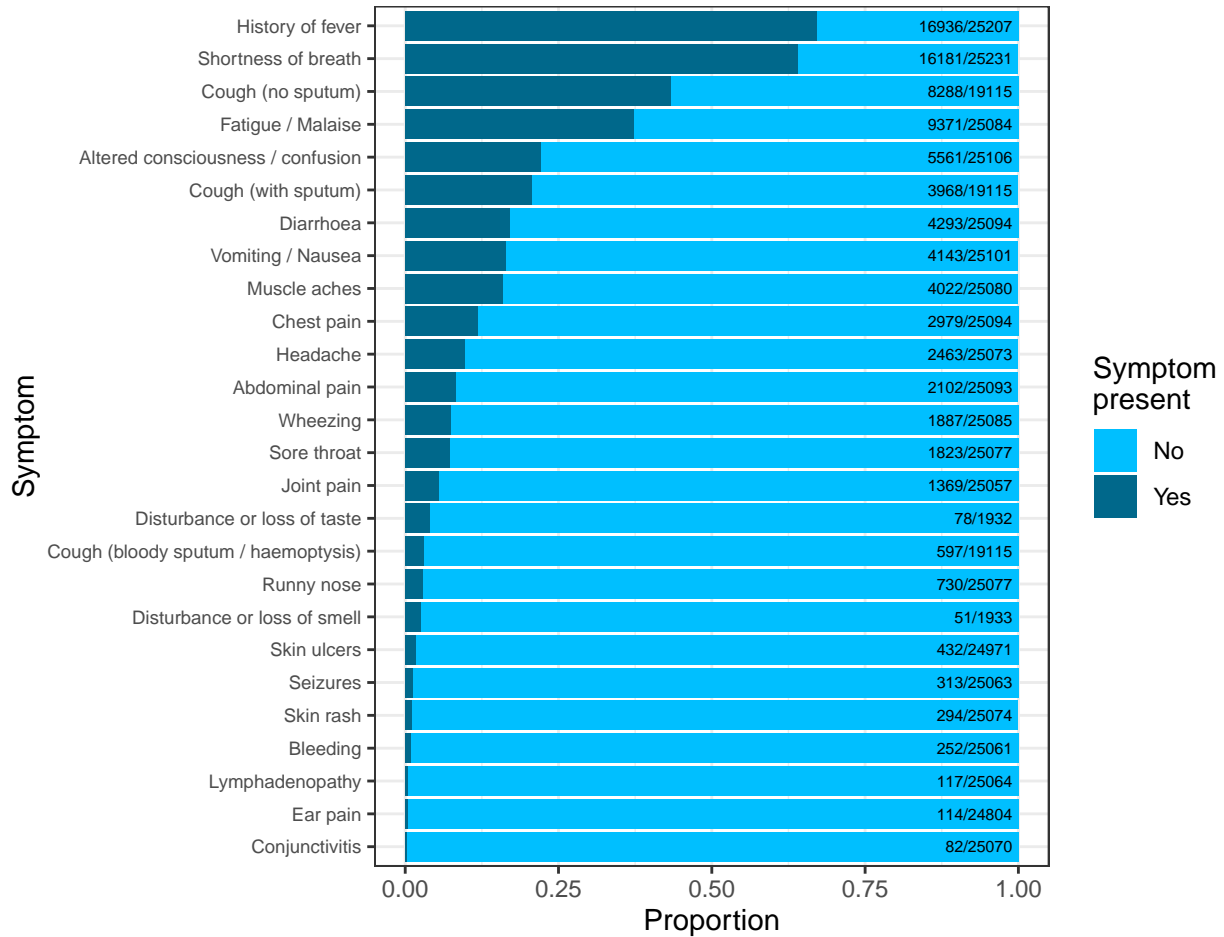


# Patient Characteristics

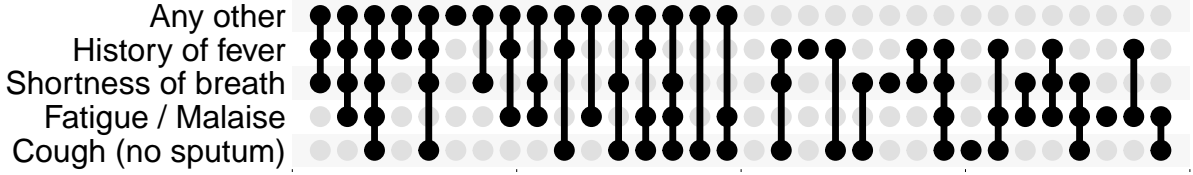
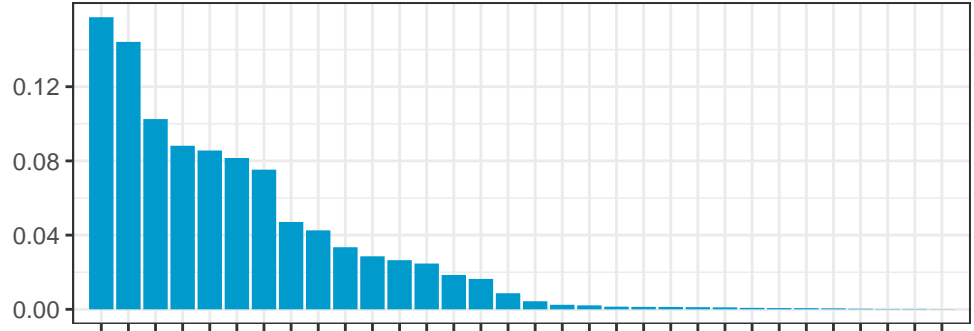
**Figure 2:** Age and sex distribution of patients. Bar fills are outcome (death/discharge/ongoing care) at the time of report.



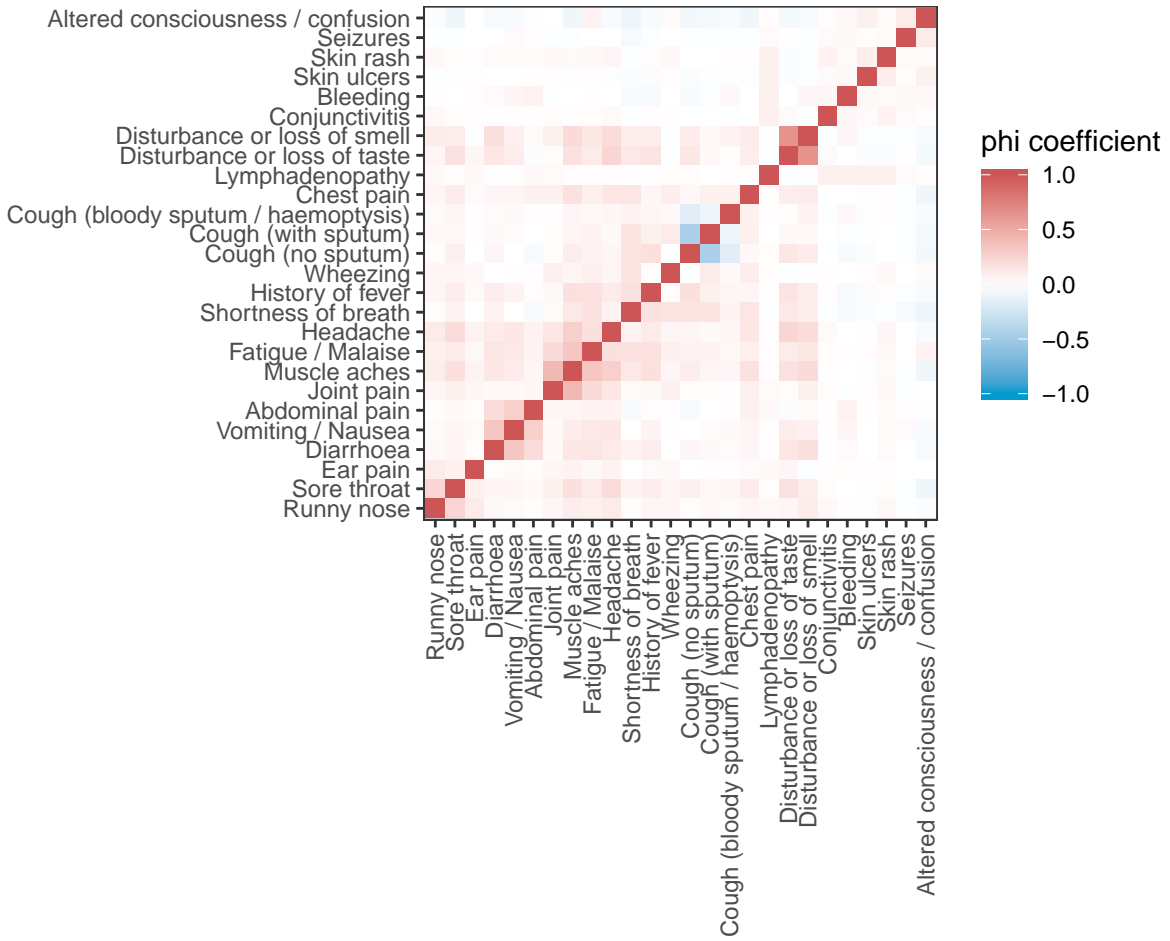
**Figure 3: Top:** Frequency of symptoms seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this symptom over the number of patients for whom presence or absence of this symptom was recorded. **Middle:** The distribution of combinations of the four most common symptoms, amongst all patients for whom these data were recorded. Filled and empty circles below the x-axis indicate the presence or absence of each comorbidity. The “Any other” category contains all remaining symptoms in the top plot. **Bottom:** Heatmap for correlation between symptoms. Fill colour is the phi correlation coefficient for each pair of symptoms, calculated amongst patients with recorded presence or absence of both.



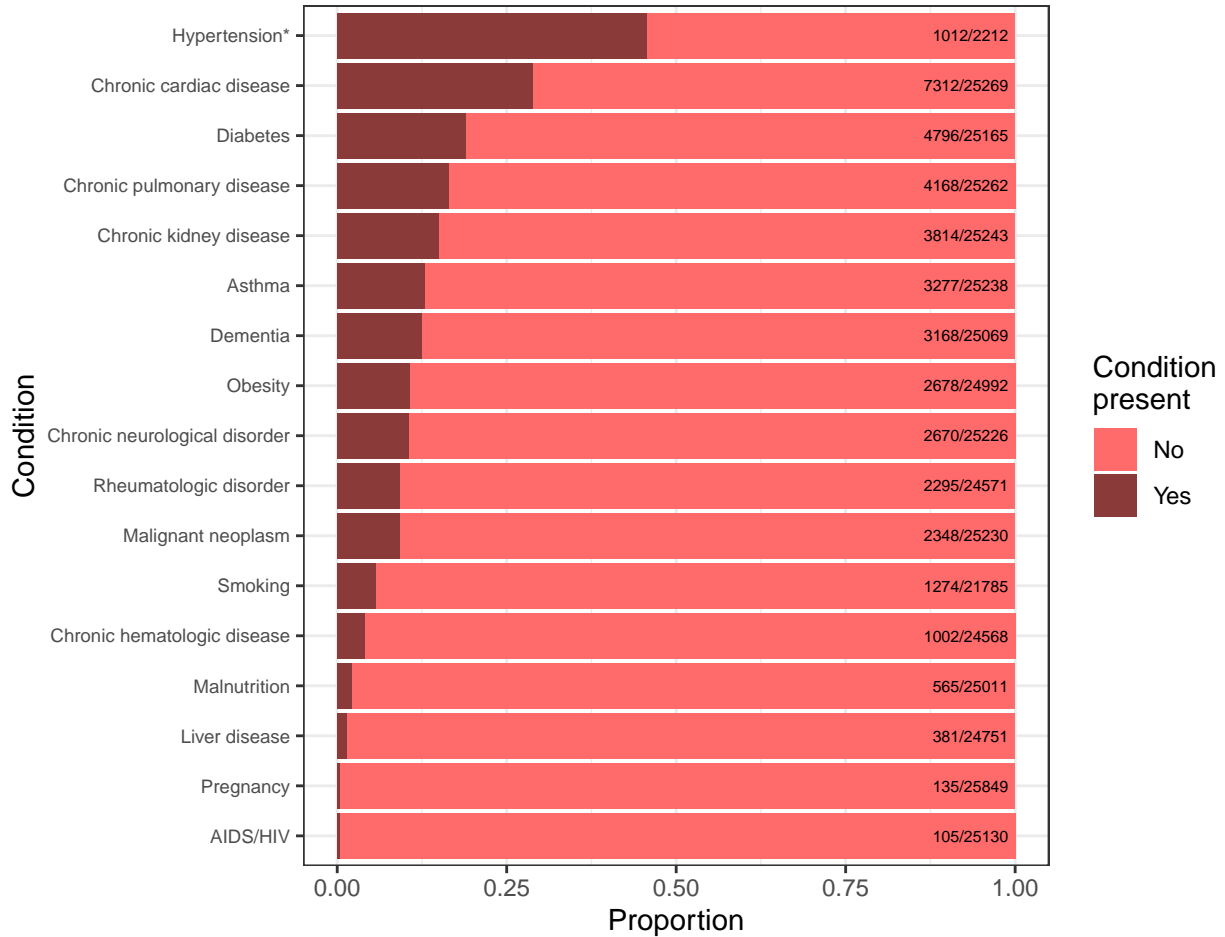
Proportion of patients



Symptoms present at admission

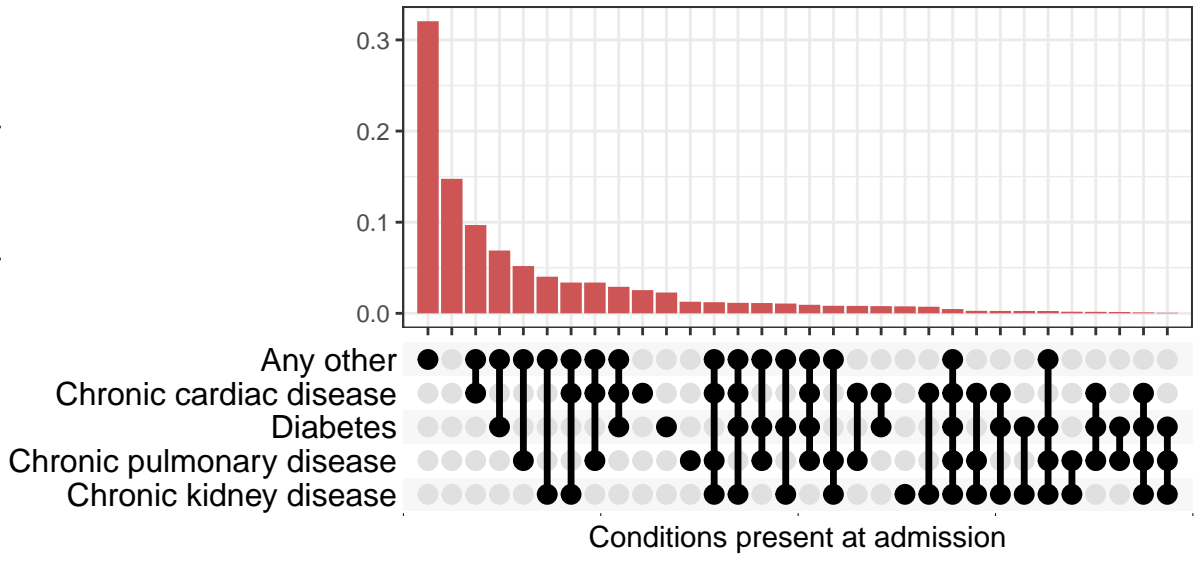


**Figure 4: Top:** Frequency of comorbidities or other concomitant conditions seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this comorbidity over the number of patients for whom presence or absence of this comorbidity was recorded. **Bottom:** The distribution of combinations of the four most common such conditions, amongst all patients for whom these data were recorded. Filled and empty circles below the x-axis indicate the presence or absence of each comorbidity. The “Any other” category contains all remaining conditions in the top plot, and any others recorded as free text by clinical staff. 16% of individuals had no comorbidities reported on admission (some due to missing data).



\*Caution when interpreting this result as the sample size is small due to it being a new variable in the dataset.

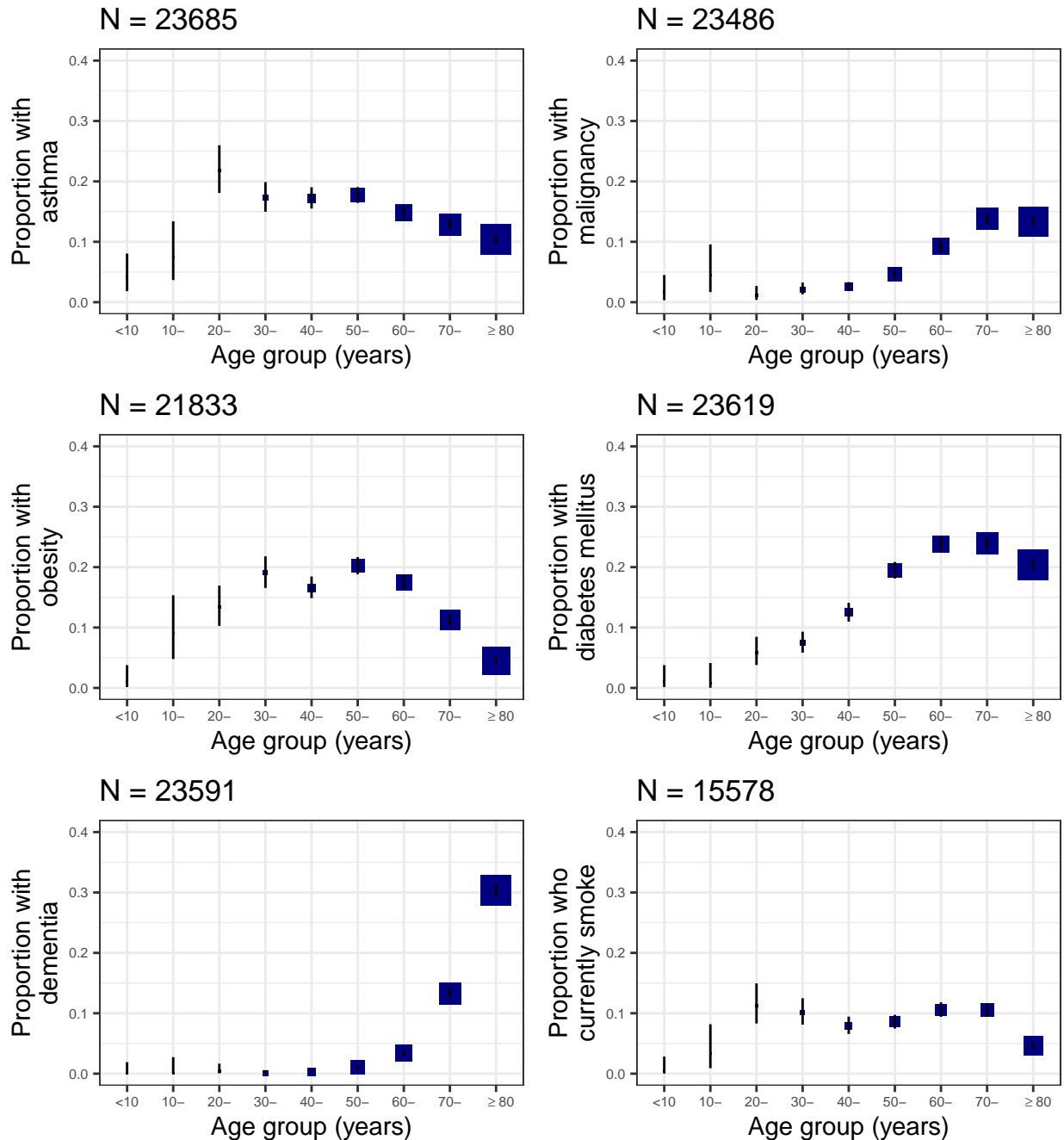
Proportion of patients



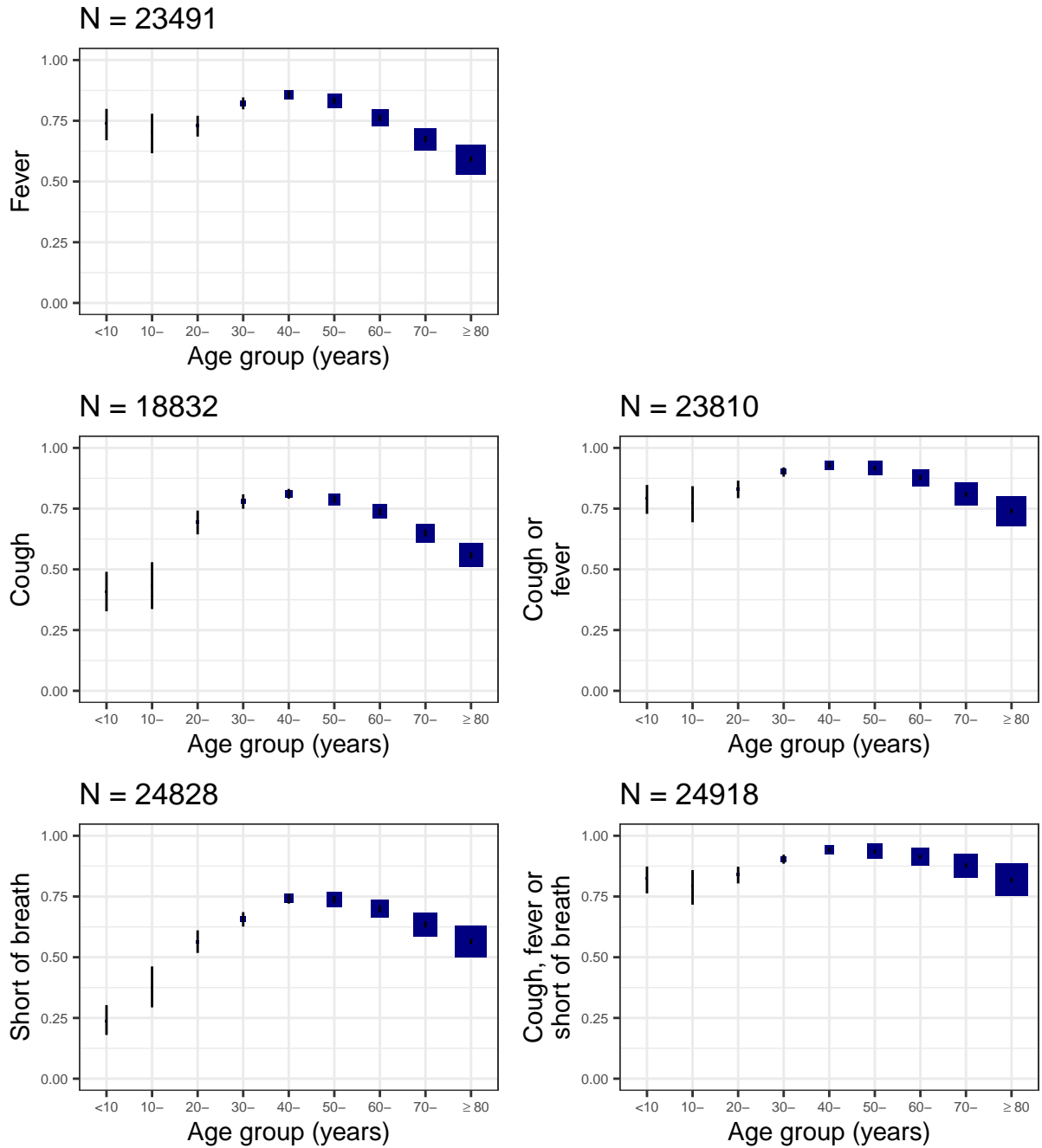


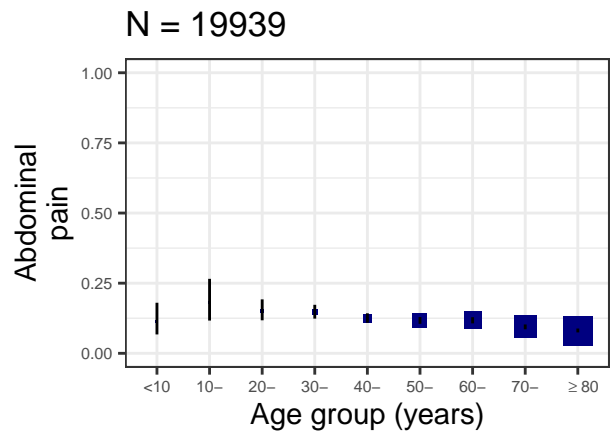
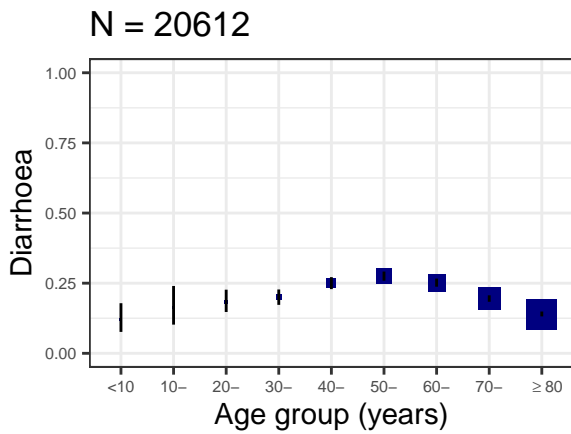
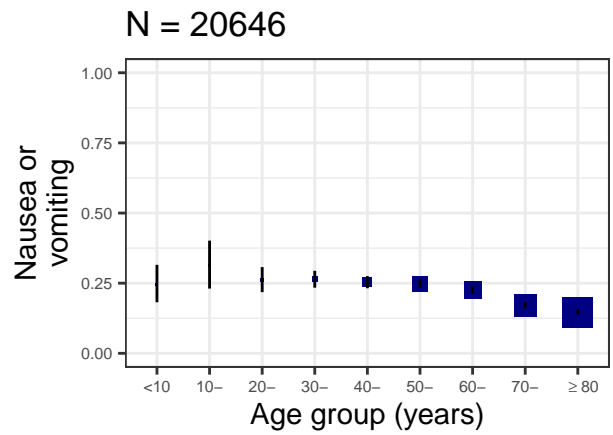
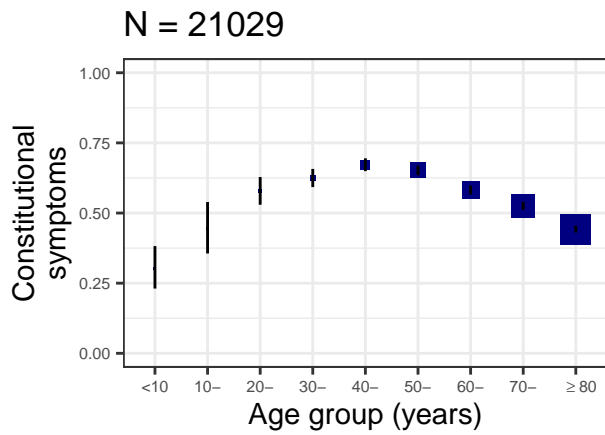
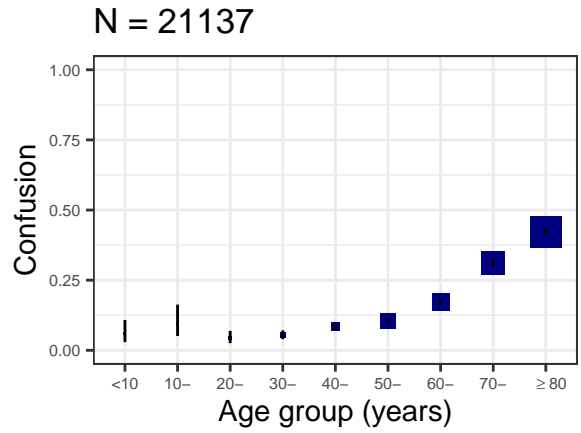
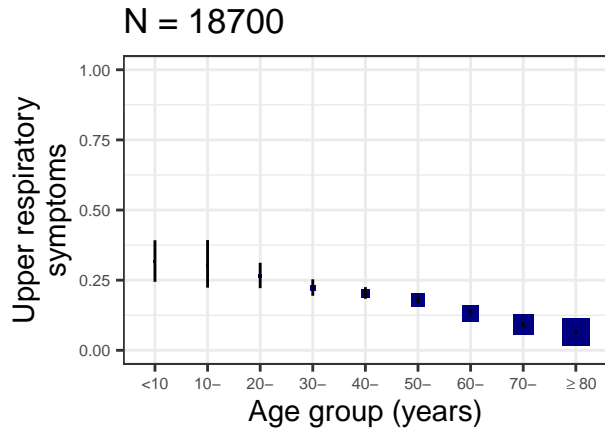
## Variables by age

**Figure 5:** Comorbidities stratified by age group. Boxes show the proportion of individuals with each comorbidity, with error bars showing 95% confidence intervals. The size of each box is proportional to the number of individuals represented. N is the number of individuals included in the plot (this varies between plots due to data completeness).

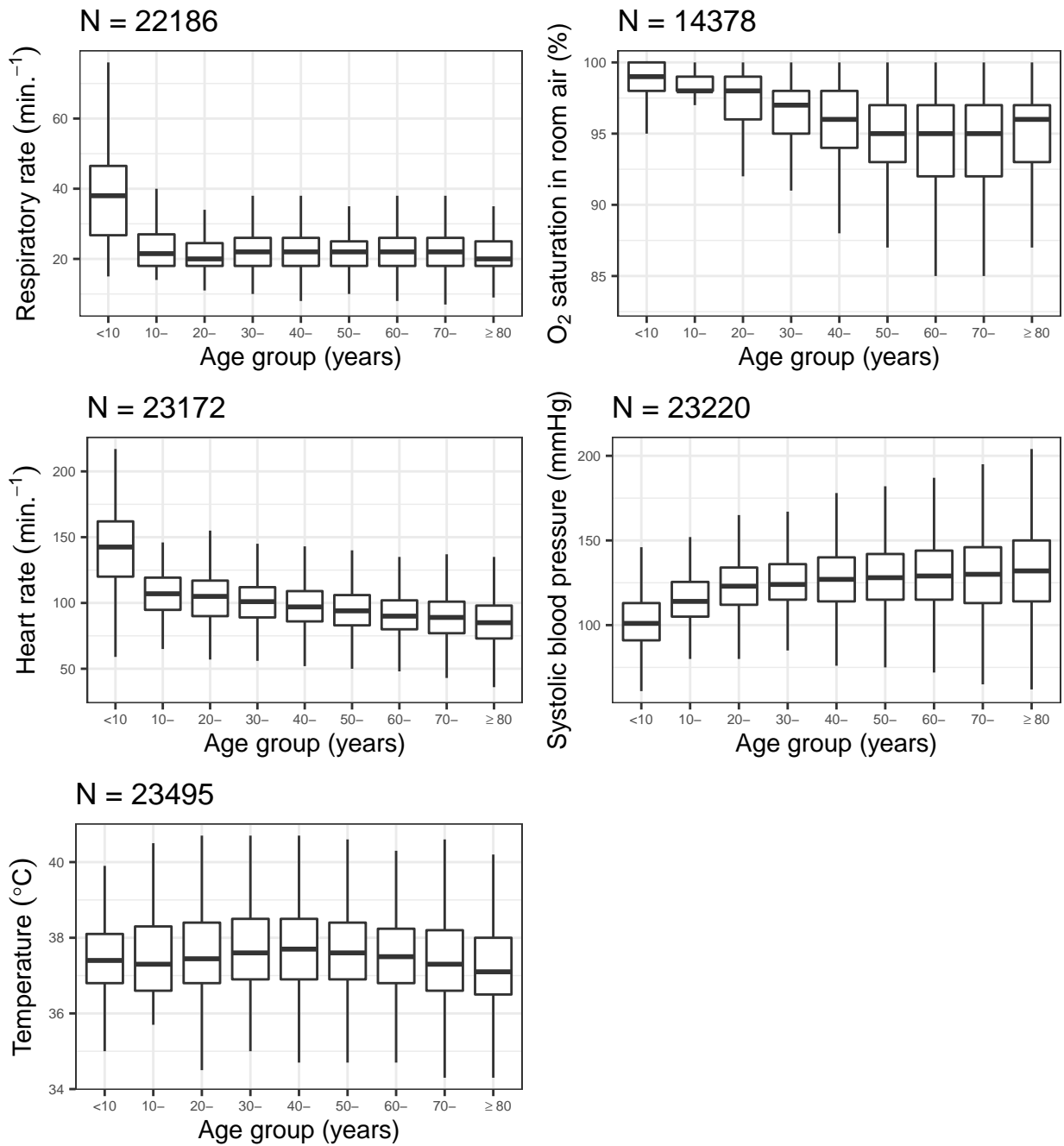


**Figure 6:** Symptoms recorded at hospital presentation stratified by age group. Boxes show the proportion of individuals with each symptom, with error bars showing 95% confidence intervals. The size of each box is proportional to the number of individuals represented. N is the number of individuals included in the plot (this varies between plots due to data completeness). **Top:** Left-hand column shows symptoms of fever, cough and shortness of breath, and right-hand column shows the proportions experiencing at least one of these symptoms. **Bottom:** The following symptoms are grouped: upper respiratory is any of runny nose, sore throat or ear pain; constitutional is any of myalgia, joint pain, fatigue or headache.

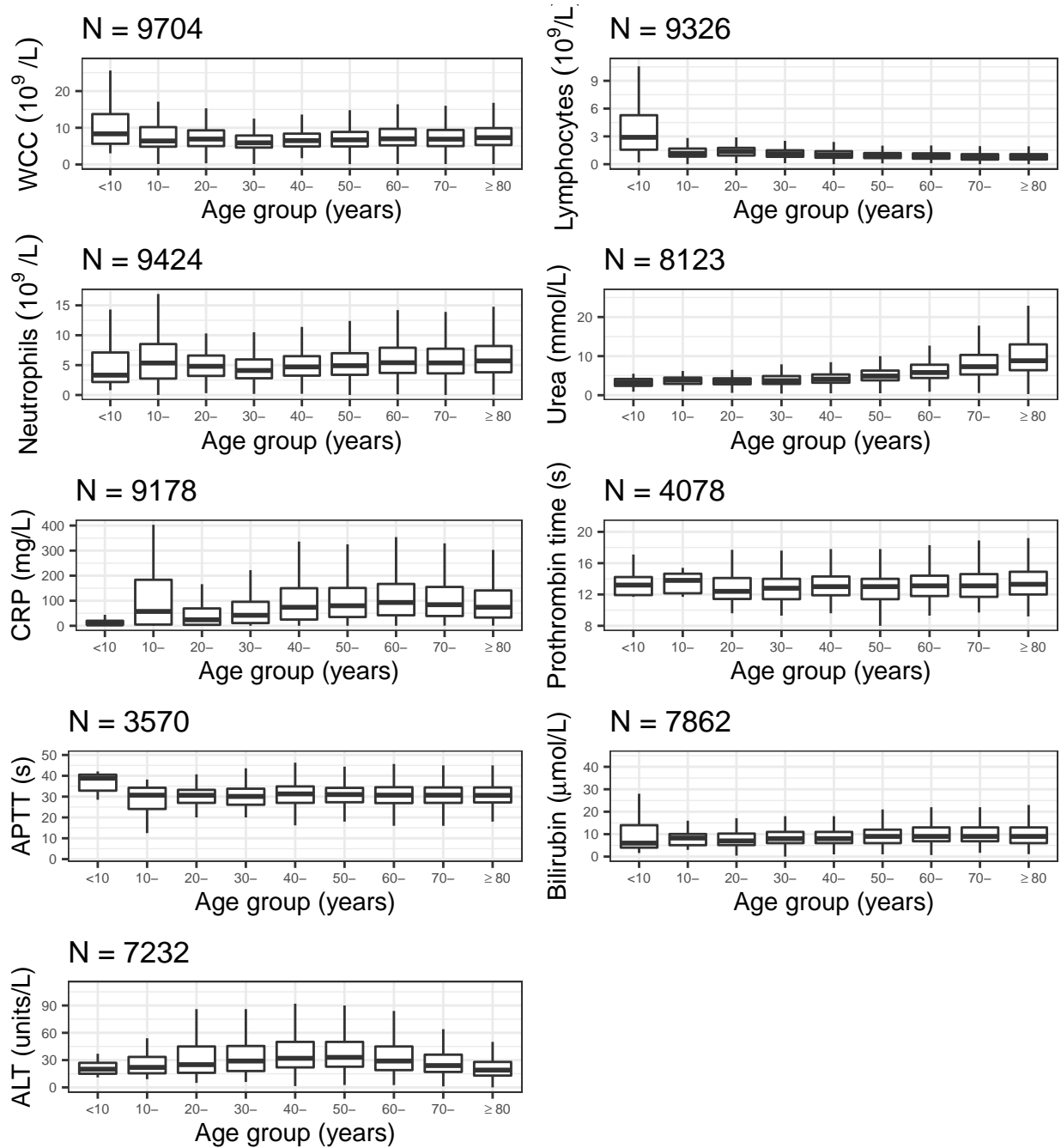




**Figure 7:** Box and whisker plots for observations at hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness).

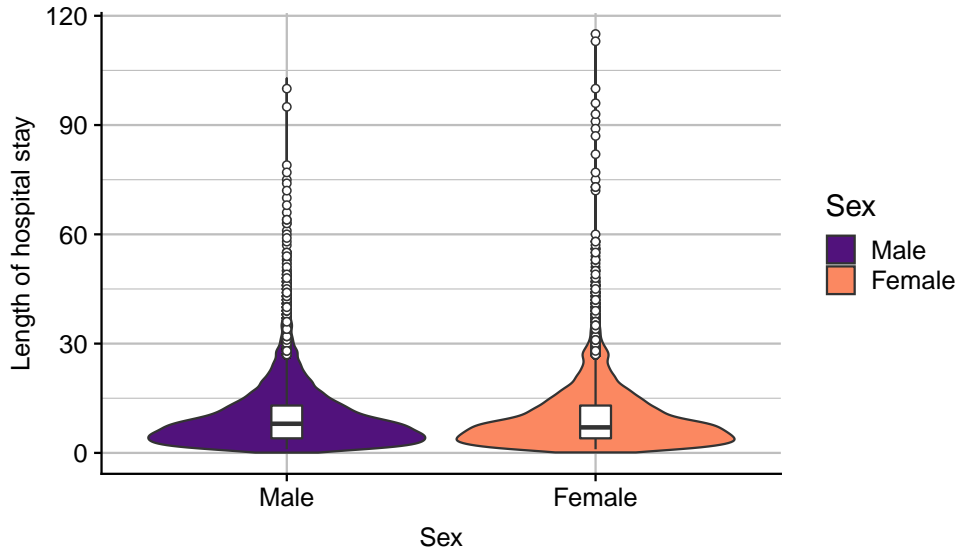


**Figure 8:** Box and whisker plots for laboratory results within 24 hours of hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness). ALT, Alanine transaminase; APTT, Activated partial thromboplastin time; CRP, C-reactive protein; WCC, white cell count



## Hospital stays and outcomes

**Figure 9:** Distribution of length of hospital stay, according to sex. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest. White dots are outliers.



**Figure 10:** Distribution of length of hospital stay, according to patient age group. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest. White dots are outliers.

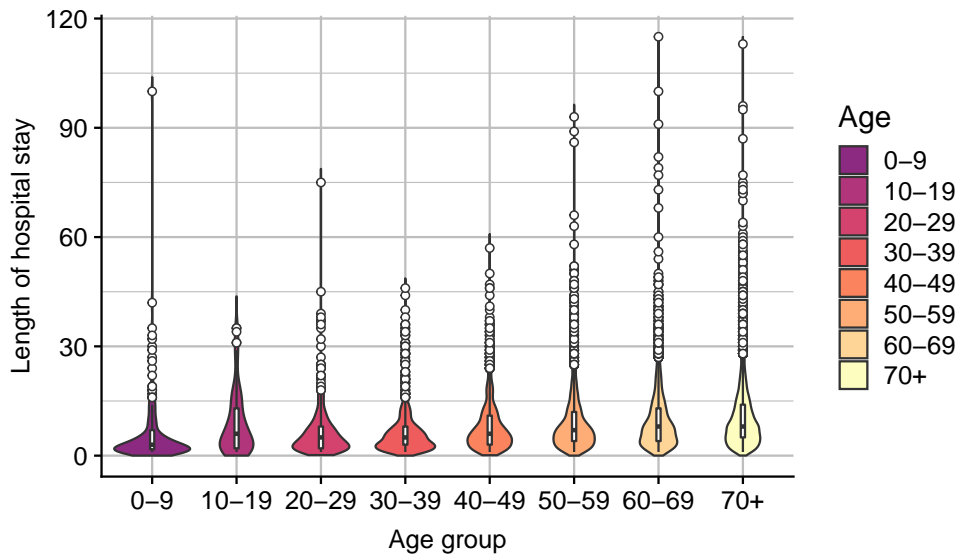
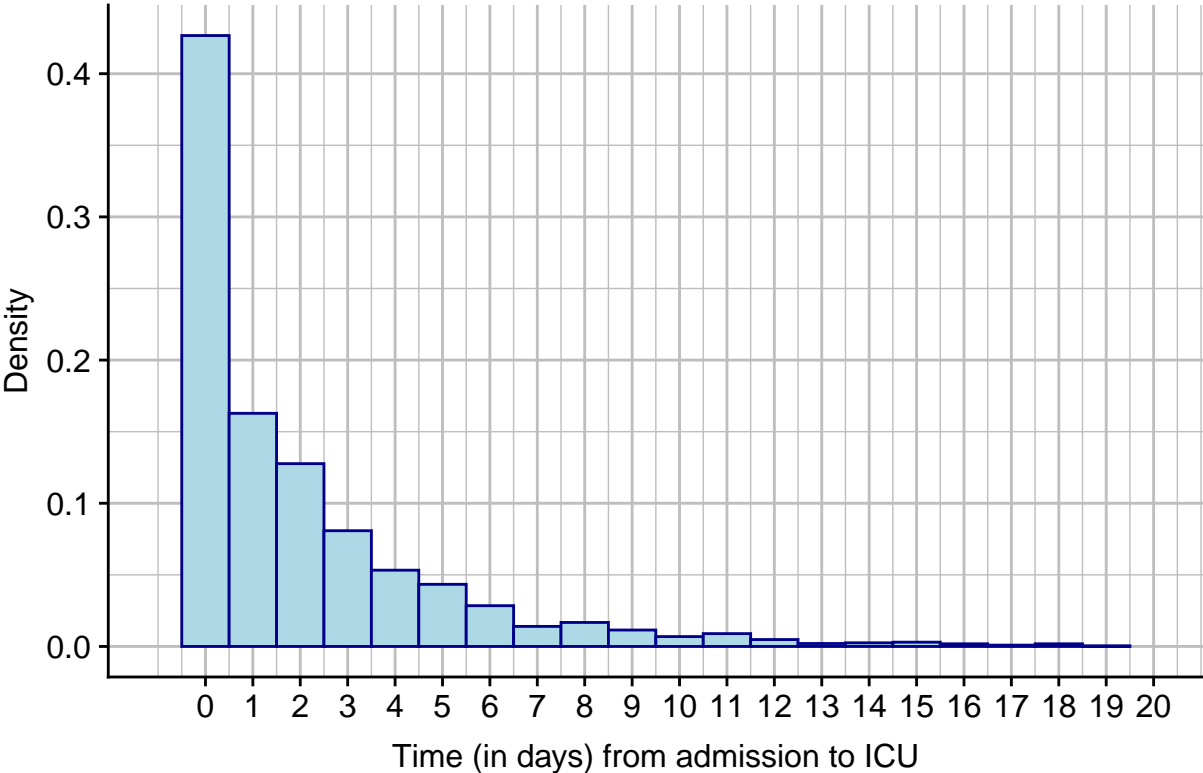
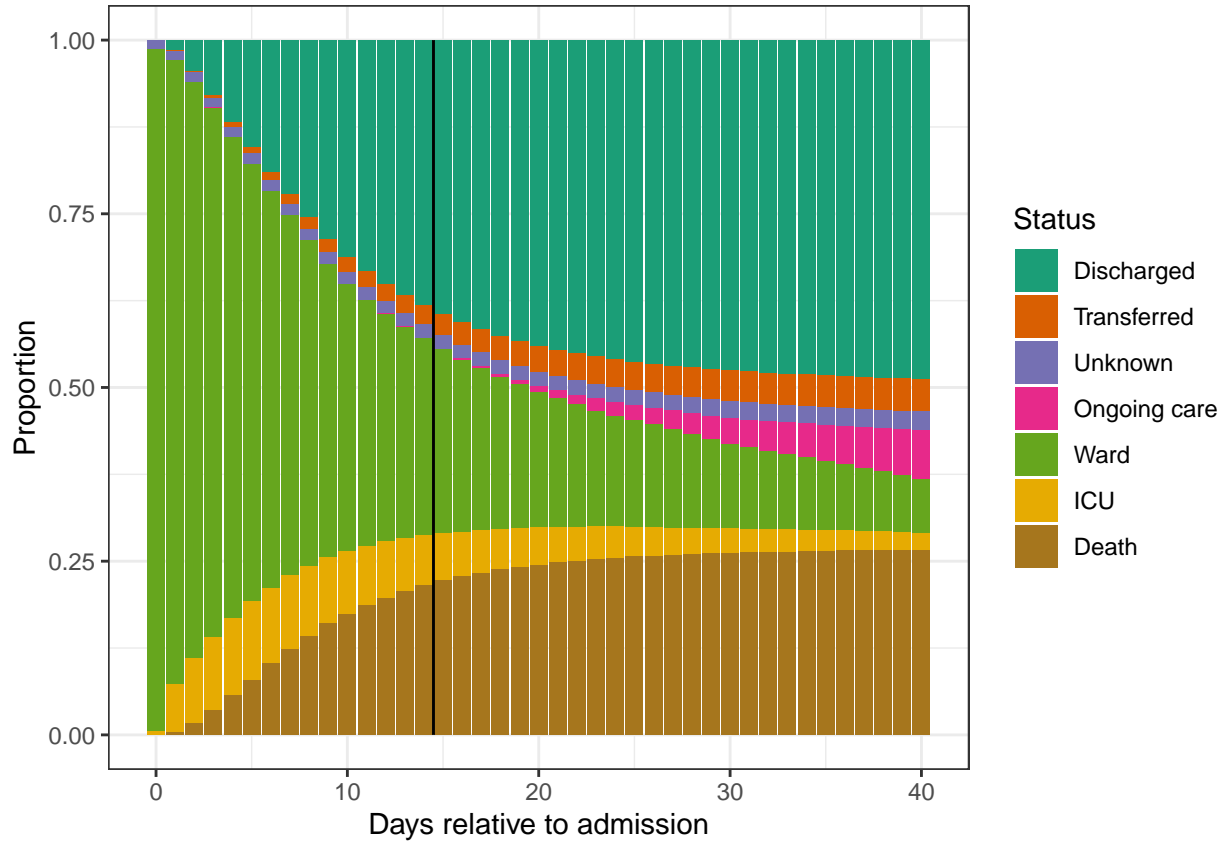


Figure 11: Distribution of time (in days) from hospital admission to ICU admission, excluding outliers.

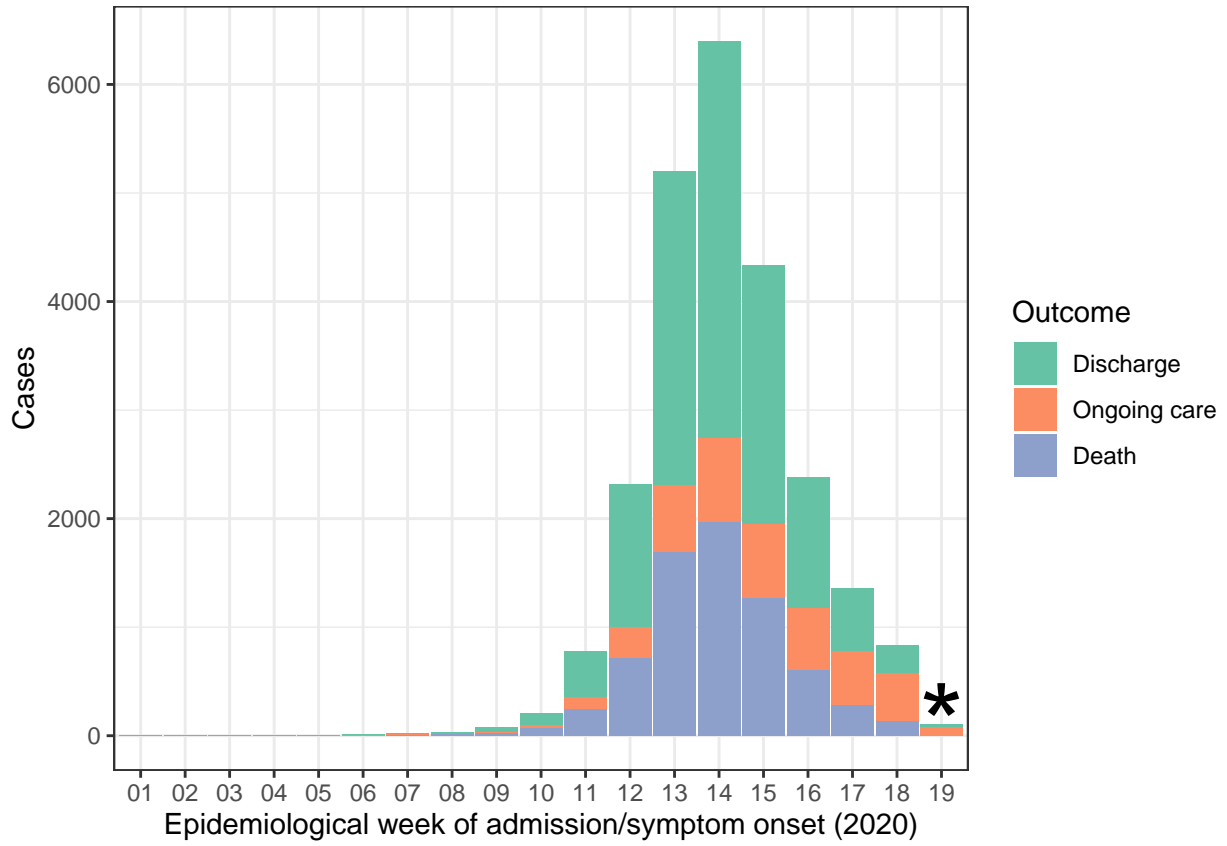


**Figure 12:** The distribution of patient status by number of days after admission. Patients with “unknown” status have left the site at the time of report but have unknown outcomes due to missing data. Patients still on site at the time of report appear in the “ongoing care” category for days which are in the future at that time. (For example, a patient admitted 7 days before the date of report and still on site by the date of the report would be categorised as “ongoing care” for days 8 and later.) The black line marks the end of 14 days; due to the cut-off, only a small number of patients appear in the “ongoing care” category left of this line.



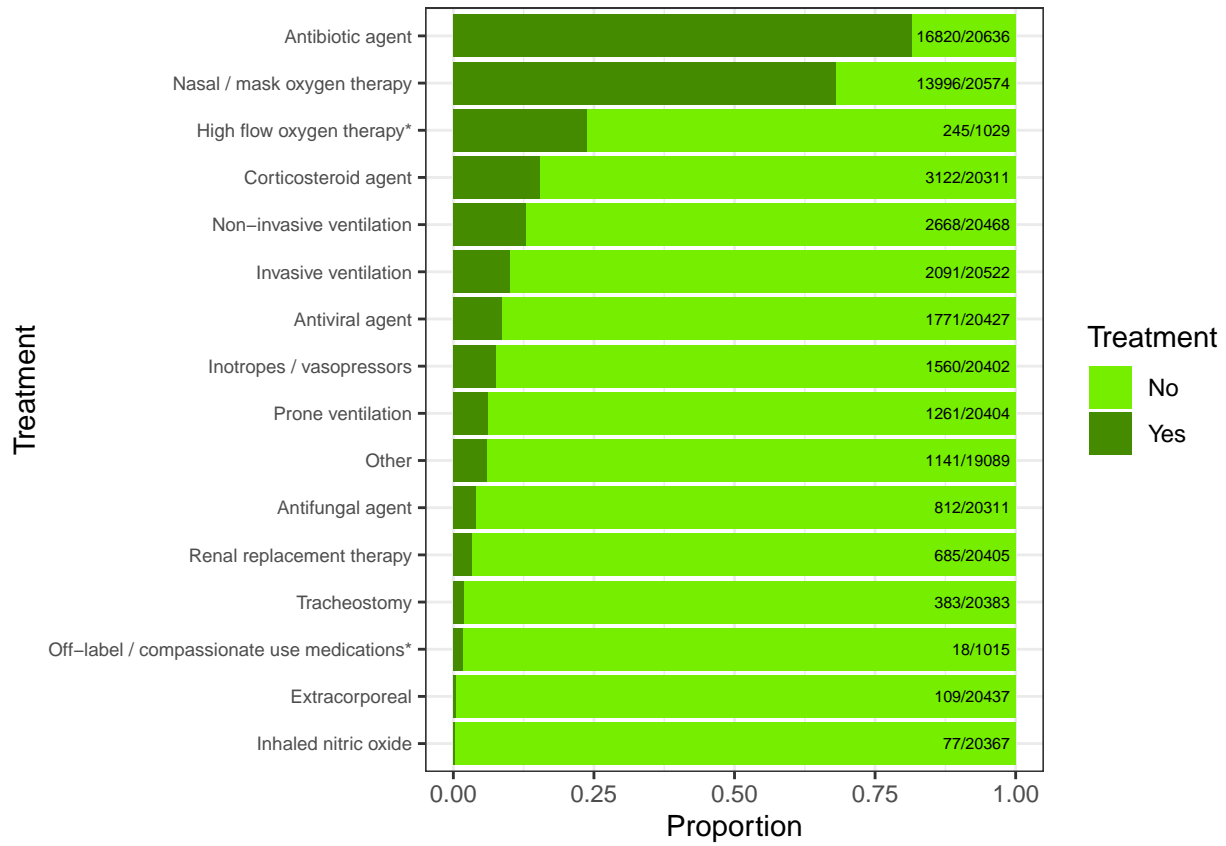


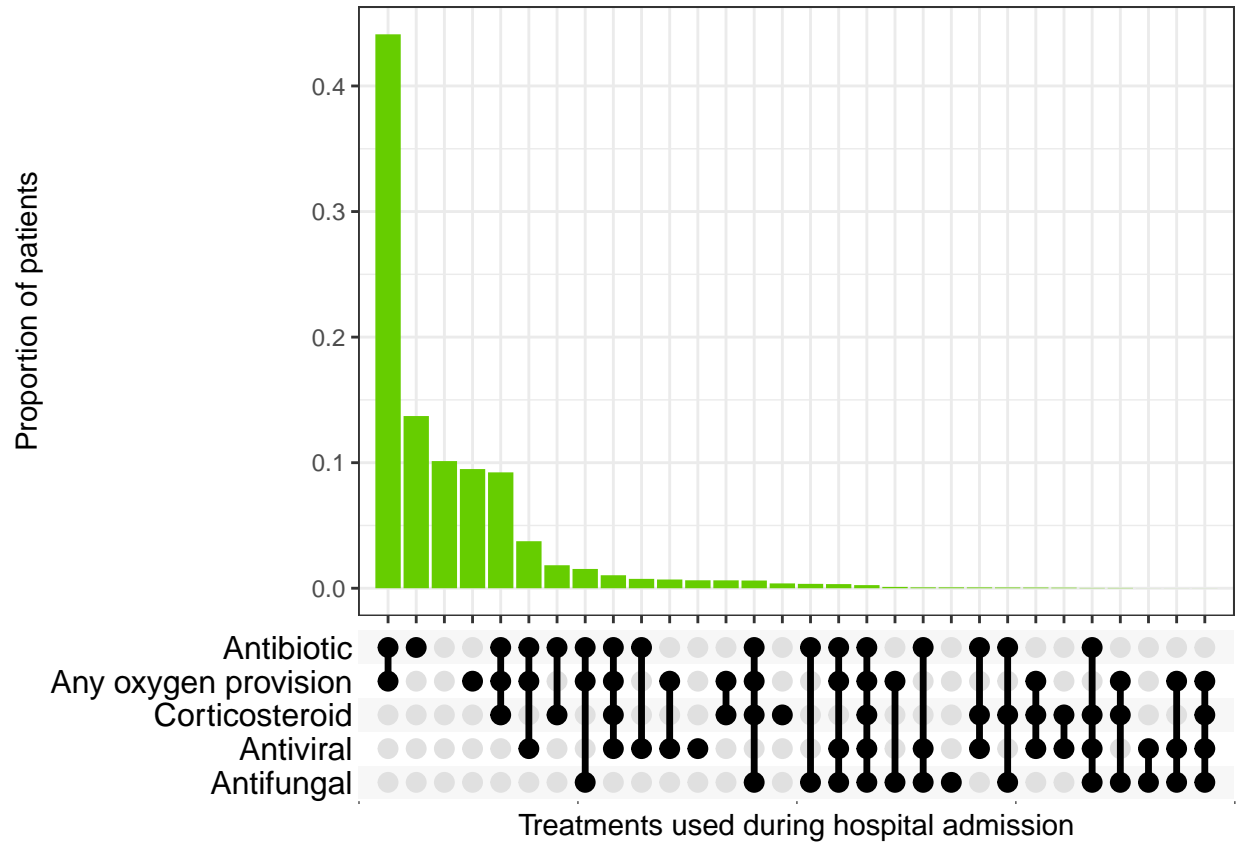
**Figure 13:** Patient numbers and outcomes by epidemiological week (of 2020) of admission (or, for patients infected in hospital, of symptom onset). The rightmost bar, marked with an asterisk, represents an incomplete week (due to the 14-day cutoff).



# Treatment

**Figure 14: Top:** Treatments used. This only includes patients for whom this information was recorded. **Bottom:** The distribution of combinations of antimicrobial treatments and steroids administered during hospital stay, across all patients with completed hospital stay and recorded treatment data. Filled and empty circles below the x-axis indicate treatments that were and were not administered.

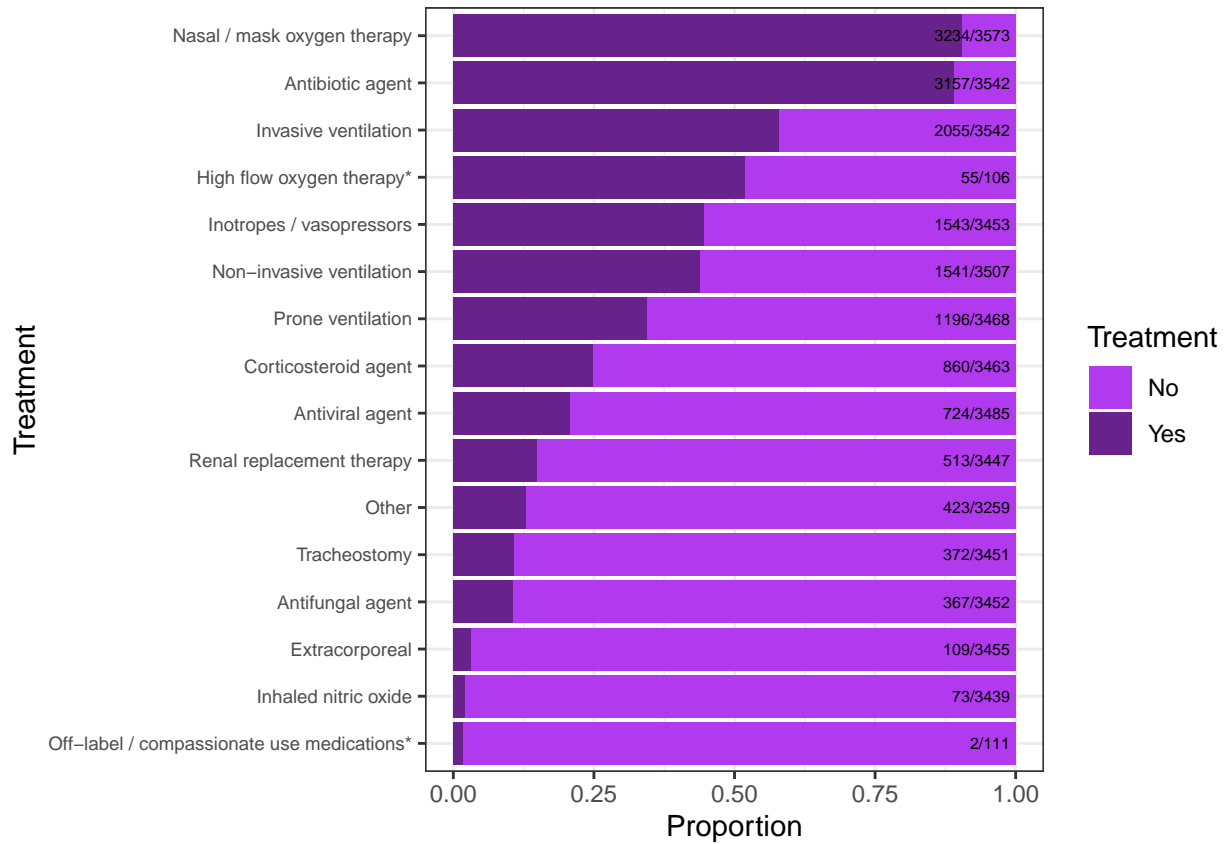


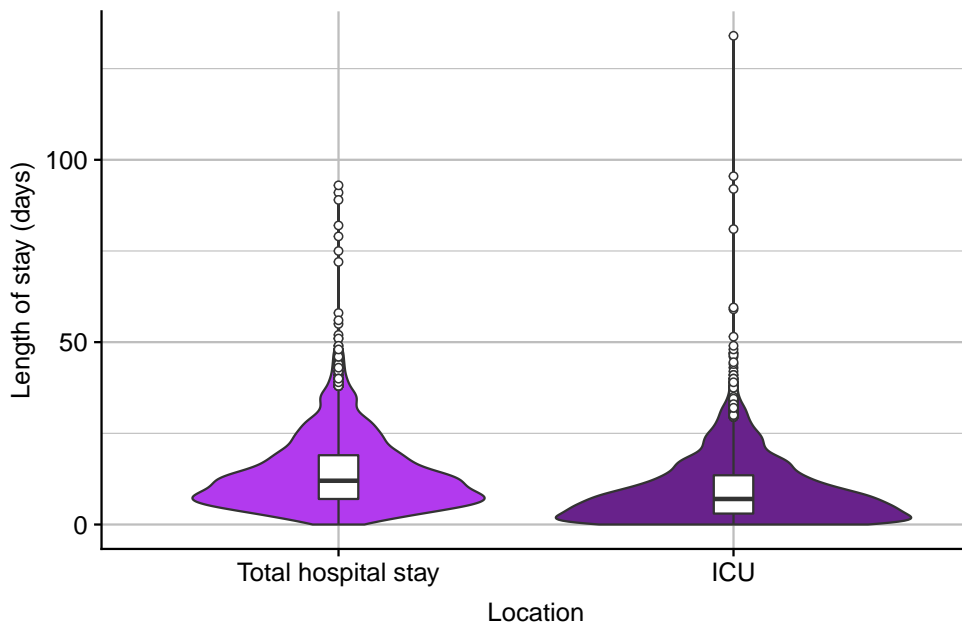
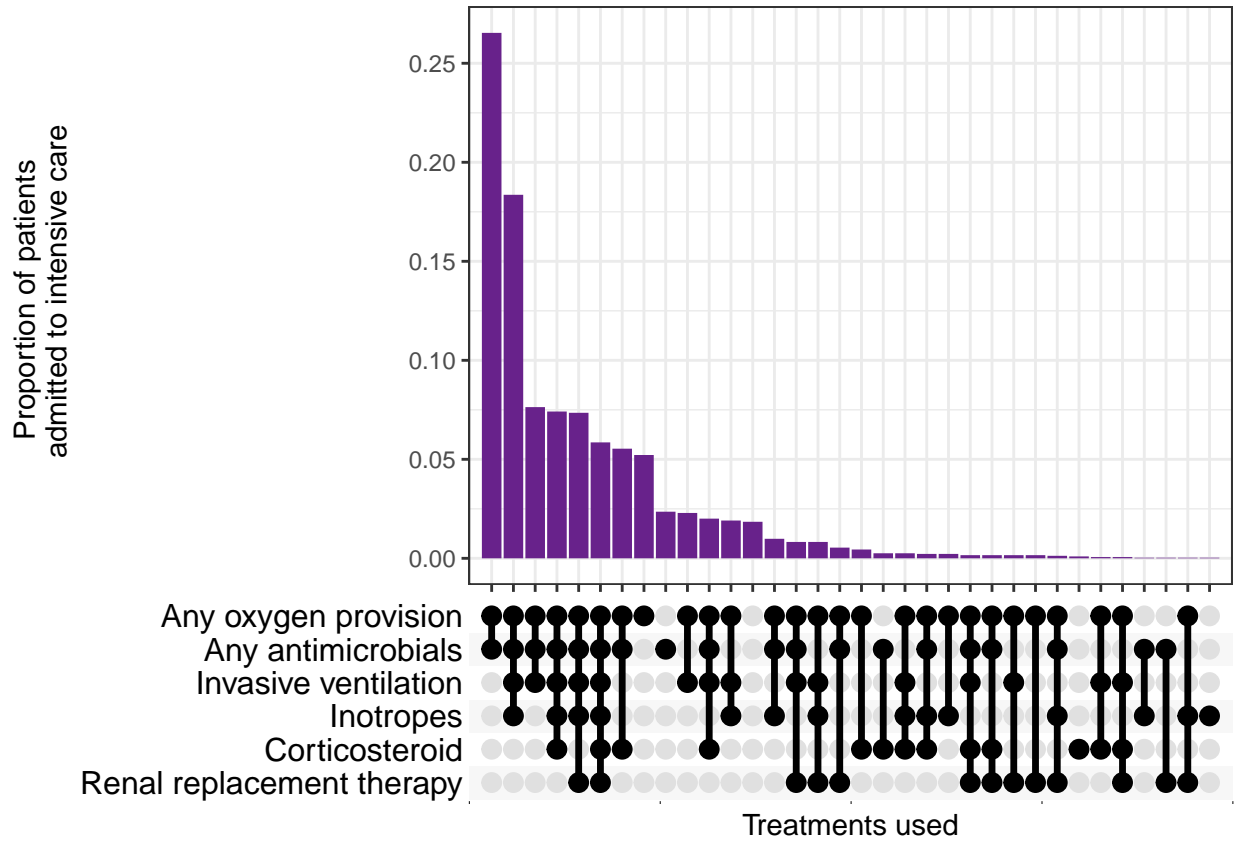


\*Caution when interpreting this result as the sample size is small due to it being a new variable in the dataset.

## Intensive Care and High Dependency Unit Treatments

**Figure 15: Top:** Treatments used amongst patients admitted to the ICU. This only includes patients for whom this information was recorded. **Middle:** The distribution of combinations of treatments administered during ICU/HDU stay. Filled and empty circles below the x-axis indicate treatments that were and were not administered respectively. **Bottom:** Distribution of lengths of stay for patients who were admitted to ICU/HDU: total length of stay for this group and length of stay within intensive care. This only includes cases with reported completed stays. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest.

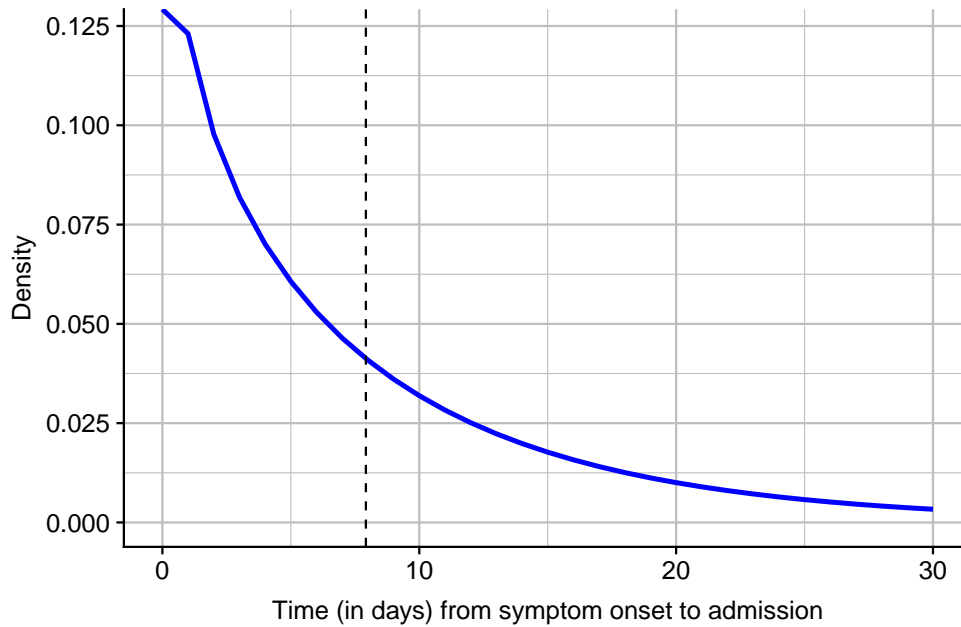




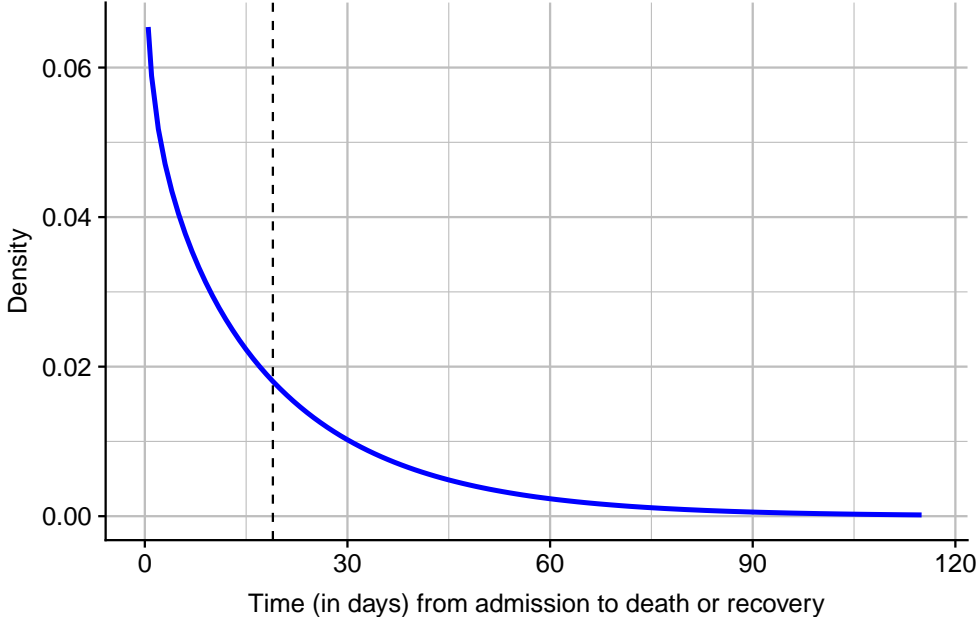
\*Caution when interpreting this result as the sample size is small due to it being a new variable in the dataset.

## Statistical Analysis

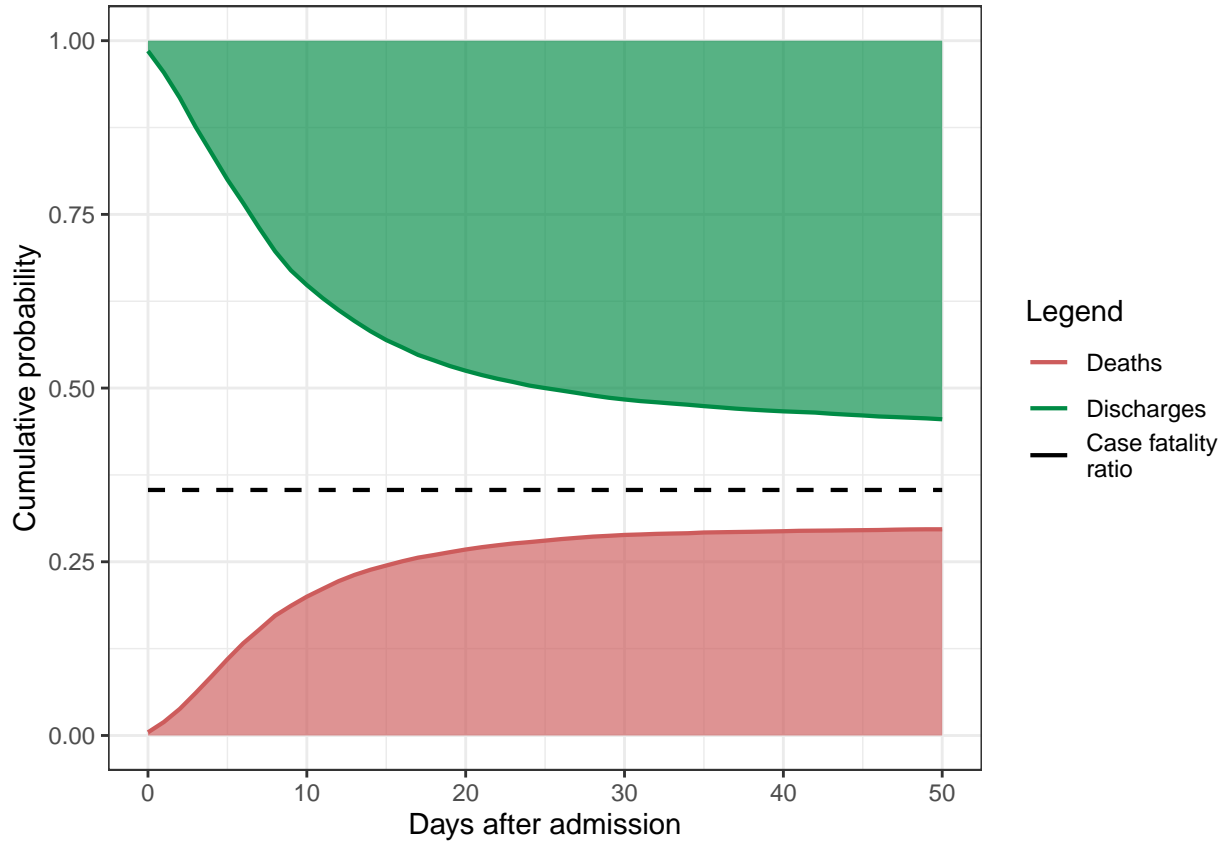
**Figure 16:** Distribution of time from symptom onset to admission. The blue curve is the Gamma distribution fit to the data. The black dashed line indicates the position of the expected mean. The expected mean estimate here differs from the observed mean indicated in the summary text due to the differences in estimation: the mean shown in the figure below is the mean of the fitted Gamma distribution whereas the observed mean (in the summary text) is the arithmetic mean.



**Figure 17:** Distribution of time from admission to an outcome - either death or recovery (discharge). The blue curve is the Gamma distribution fit to the data. The black dashed line indicates the position of the expected mean. The expected mean differs from the observed mean in that it accounts for unobserved outcomes.



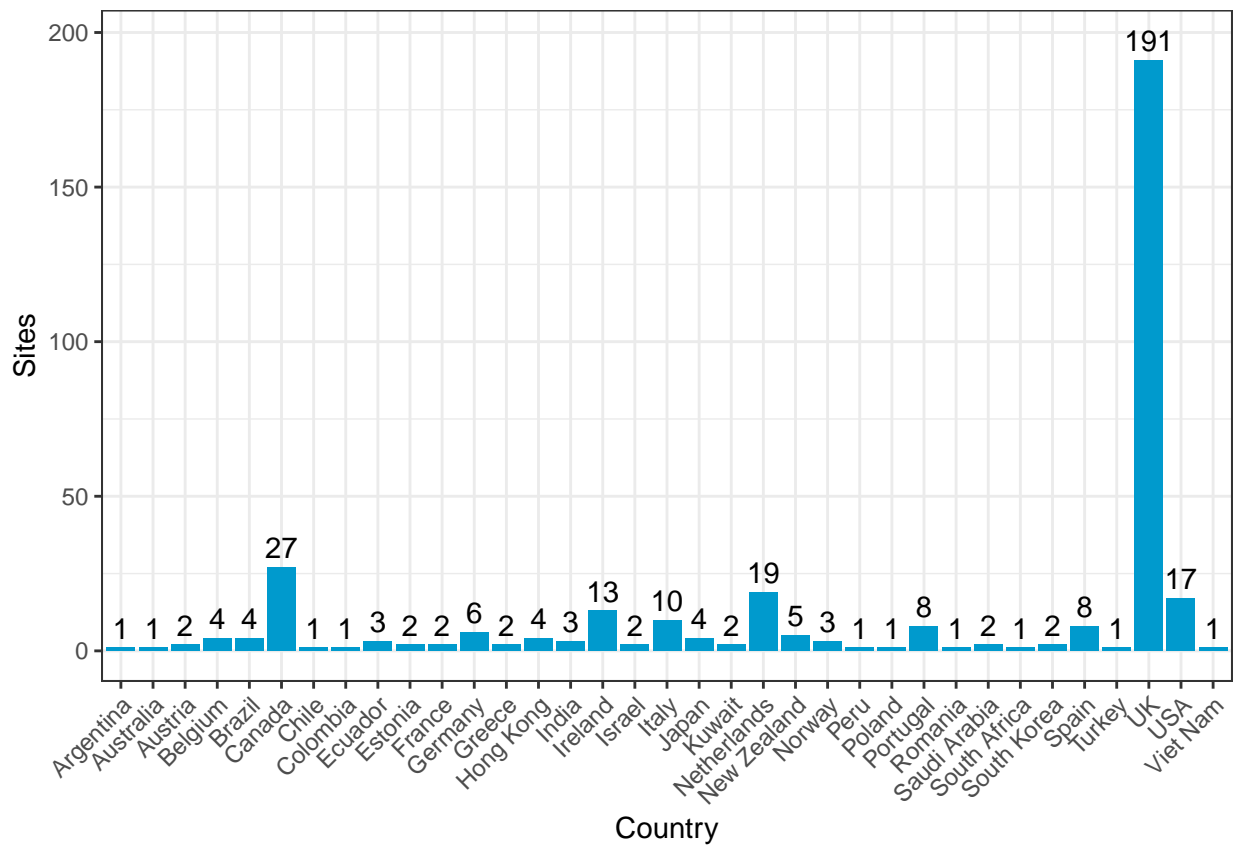
**Figure 18:** Probabilities of death (red curve) and recovery (green curve) over time. The black line indicates the case fatality ratio (CFR). The method used here considers all cases, irrespective of whether an outcome has been observed. For a completed epidemic, the curves for death and recovery meet. Estimates were derived using a nonparametric Kaplan-Meier-based method proposed by Ghani *et al.* (2005). The point estimate of the CFR is 0.35 (95% CI: 0.34-0.36).



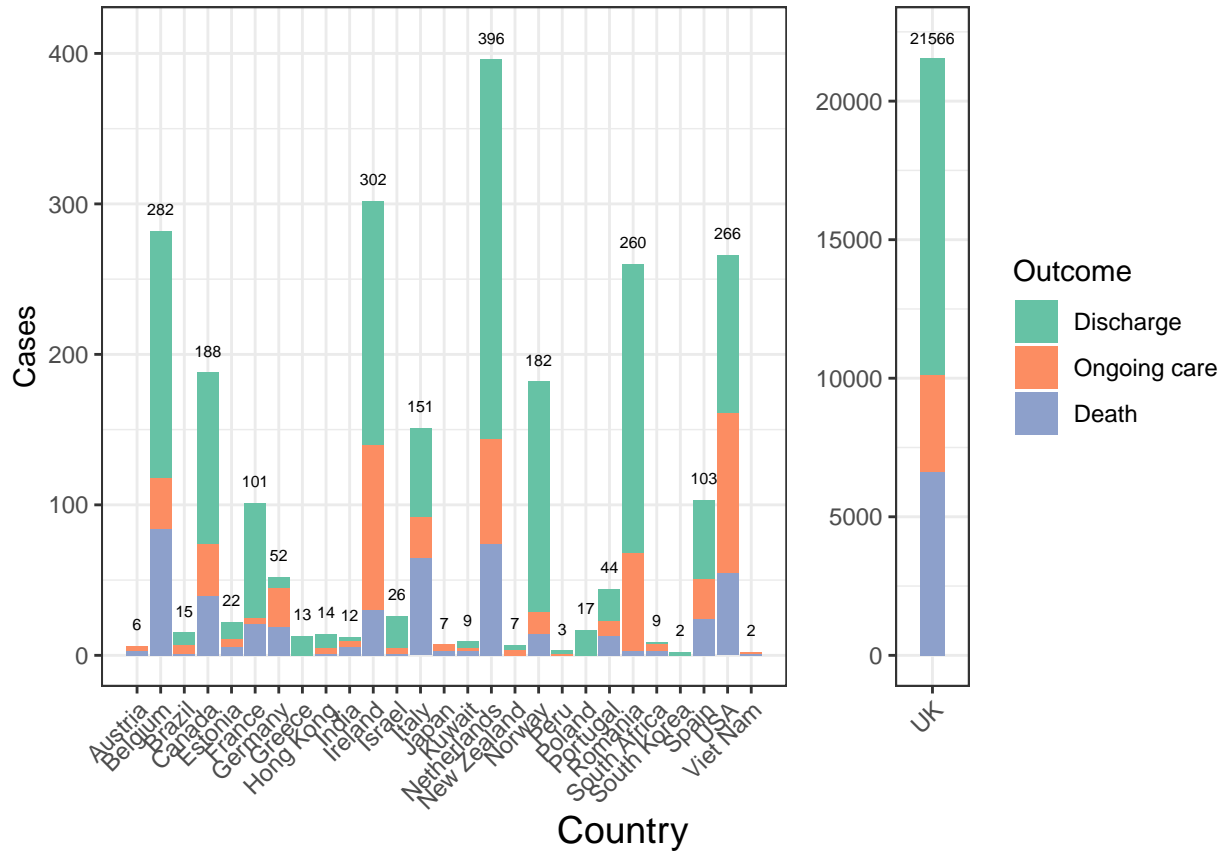


# Country Comparisons

Figure 19: Number of sites per country.



**Figure 20:** Distribution of patients by country and outcome.



## Background

In response to the emergence of novel coronavirus (COVID-19), ISARIC launched a portfolio of resources to accelerate outbreak research and response. These include data collection, analysis and presentation tools which are freely available to all sites which have requested access to these resources. All data collection tools are designed to address the most critical public health questions, have undergone extensive review by international clinical experts, and are free for all to use. Resources are available on the [ISARIC website](#).

The [ISARIC-WHO COVID-19 Case Record Form \(CRF\)](#) enables the collection of standardised clinical data to inform patient management and public health response. These forms should be used to collect data on suspected or confirmed cases of COVID-19. The CRF is available in multiple languages and is now in use across dozens of countries and research consortia, who are contributing data to these reports.

To support researchers to retain control of the data and samples they collect, ISARIC also hosts a data platform, where data can be entered to a web-based REDCap data management system, securely stored, and used to produce regular reports on their sites as above. Data contributors are invited to input on the methods and contents of the reports, and can also contribute to the aggregated data platform which aggregates site-specific data from all other sites across the world who are using this system. For more information, visit the ISARIC website.

All decisions regarding data use are made by the institutions that enter the data. ISARIC keeps contributors informed of any plans and welcomes their input to promote the best science and the interests of patients, institutions and public health authorities. Feedback and suggestions are welcome at [ncov@isaric.org](mailto:ncov@isaric.org).

## Methods

Patient details were submitted electronically by participating sites to the ISARIC database. Relevant background and presenting symptoms were recorded on the day of study recruitment. Daily follow-up was then completed until recovery or death. A final form was completed with details of treatments received and outcomes. All categories that represent fewer than five individuals have been suppressed to avoid the potential for identification of participants.

Graphs have been used to represent the age distribution of patients by sex and status (dead, recovered & still in hospital), the prevalence of individual symptoms on admission, comorbidities on admission, the length of hospital stay by sex and age group and the distribution of patient statuses by time since admission. In addition, the number of cases recruited by country and site, as well as the case count by status, has been represented.

Using a non-parametric Kaplan-Meier-based method (Ghani *et al.*, 2005), the case-fatality ratio (CFR) was estimated, as well as probabilities for death and recovery. This method estimates the CFR with the formula  $a/(a + b)$ , where  $a$  and  $b$  are the values of the cumulative incidence function for deaths and recoveries respectively, estimated at the last observed time point. In a competing risk context (i.e. where there are multiple endpoints), the cumulative incidence function for an endpoint is equal to the product of the hazard function for that endpoint and the survival function assuming a composite endpoint. It is worth noting that this method assumes that future deaths and recoveries will occur with the same relative probabilities as have been observed so far. Binomial confidence intervals for the CFR were obtained by a normal approximation (See Ghani *et al.*, (2005)).

To obtain estimates for the distributions of time from symptom onset to hospital admission and the time from admission to outcome (death or recovery), Gamma distributions were fitted to the observed data, accounting for unobserved outcomes. Parameters were estimated by a maximum likelihood procedure and confidence intervals for the means and variances were obtained by bootstrap.

All analysis were performed using the R statistical software (R Core Team, 2019).

## Caveats

Patient data are collected and uploaded from start of admission, however a complete patient data set is not available until the episode of care is complete. This causes a predictable lag in available data influenced by the duration of admission which is greatest for the sickest patients, and accentuated during the up-phase of the outbreak.

These reports provide regular outputs from the ISARIC COVID-19 database. We urge caution in interpreting unexpected results. We have noted some unexpected results in the report, and are working with sites that submitted data to gain a greater understanding of these.

## Summary Tables

Proportions are presented in parentheses and have been rounded to two decimal places.

**Table 1:** Patient Characteristics

<b>Description</b>	<b>Value</b>
Size of cohort	25849
<b>By sex</b>	
Male	15271 (0.59)
Female	10493 (0.41)
Unknown	85 (0)
<b>By outcome status</b>	
Dead	7080 (0.27)
Recovered (discharged alive)	12903 (0.5)
Still in hospital	4112 (0.16)
Transferred to another facility	1303 (0.05)
Unknown	451 (0.02)
<b>By age group</b>	
0-9	195 (0.01)
10-19	137 (0.01)
20-29	462 (0.02)
30-39	1018 (0.04)
40-49	1919 (0.07)
50-59	3546 (0.14)
60-69	4280 (0.17)
70+	13886 (0.54)
Unknown	406 (0.02)
<b>Admitted to ICU/HDU?</b>	
Yes	4752 (18)
No/Unknown	21097 (82)

**Table 2:** Outcome by age and sex.

Variable	Still in hospital	Death	Discharge	Transferred	Unknown
<b>Age</b>					
0-9	25 (0.01)	2 (0)	162 (0.01)	4 (0)	2 (0)
10-19	15 (0)	4 (0)	110 (0.01)	7 (0.01)	1 (0)
20-29	57 (0.01)	14 (0)	379 (0.03)	9 (0.01)	3 (0.01)
30-39	153 (0.04)	38 (0.01)	786 (0.06)	25 (0.02)	16 (0.04)
40-49	325 (0.08)	120 (0.02)	1384 (0.11)	64 (0.05)	26 (0.06)
50-59	607 (0.15)	424 (0.06)	2314 (0.18)	132 (0.1)	69 (0.15)
60-69	792 (0.19)	915 (0.13)	2300 (0.18)	203 (0.16)	70 (0.16)
70+	2070 (0.5)	5475 (0.77)	5247 (0.41)	848 (0.65)	246 (0.55)
<b>Sex</b>					
Male	2424 (0.59)	4503 (0.64)	7316 (0.57)	767 (0.59)	261 (0.58)
Female	1673 (0.41)	2553 (0.36)	5547 (0.43)	533 (0.41)	187 (0.41)
Unknown	1 (0)	12 (0)	22 (0)	1 (0)	2 (0)

**Table 3:** Prevalence of Symptoms

Symptoms	Present	Absent	Unknown
History of fever	16936 (0.66)	6934 (0.27)	1979 (0.08)
Shortness of breath	16181 (0.63)	9040 (0.35)	628 (0.02)
Cough	12853 (0.5)	6262 (0.24)	6734 (0.26)
Fatigue / Malaise	9371 (0.36)	10544 (0.41)	5934 (0.23)
Altered consciousness / confusion	5561 (0.22)	15918 (0.62)	4370 (0.17)
Diarrhoea	4293 (0.17)	16659 (0.64)	4897 (0.19)
Vomiting / Nausea	4143 (0.16)	16834 (0.65)	4872 (0.19)
Muscle aches	4022 (0.16)	14550 (0.56)	7277 (0.28)
Chest pain	2979 (0.12)	17317 (0.67)	5553 (0.21)
Headache	2463 (0.1)	15988 (0.62)	7398 (0.29)
Abdominal pain	2102 (0.08)	18154 (0.7)	5593 (0.22)
Wheezing	1887 (0.07)	17315 (0.67)	6647 (0.26)
Sore throat	1823 (0.07)	16345 (0.63)	7681 (0.3)
Joint pain	1369 (0.05)	16400 (0.63)	8080 (0.31)
Runny nose	730 (0.03)	17076 (0.66)	8043 (0.31)
Skin ulcers	432 (0.02)	18707 (0.72)	6710 (0.26)
Seizures	313 (0.01)	20017 (0.77)	5519 (0.21)
Skin rash	294 (0.01)	18933 (0.73)	6622 (0.26)
Bleeding	252 (0.01)	19776 (0.77)	5821 (0.23)
Lymphadenopathy	117 (0)	18695 (0.72)	7037 (0.27)
Ear pain	114 (0)	17439 (0.67)	8296 (0.32)
Conjunctivitis	82 (0)	18750 (0.73)	7017 (0.27)

**Table 4:** Prevalence of Comorbidities

Comorbidities	Present	Absent	Unknown
Chronic cardiac disease	7312 (0.28)	16914 (0.65)	1623 (0.06)
Diabetes	4796 (0.19)	19185 (0.74)	1868 (0.07)
Chronic pulmonary disease	4168 (0.16)	19982 (0.77)	1699 (0.07)
Chronic kidney disease	3814 (0.15)	20225 (0.78)	1810 (0.07)
Asthma	3277 (0.13)	20765 (0.8)	1807 (0.07)
Dementia	3168 (0.12)	20633 (0.8)	2048 (0.08)
Obesity	2678 (0.1)	19346 (0.75)	3825 (0.15)
Chronic neurological disorder	2670 (0.1)	21210 (0.82)	1969 (0.08)
Malignant neoplasm	2348 (0.09)	21491 (0.83)	2010 (0.08)
Rheumatologic disorder	2295 (0.09)	20866 (0.81)	2688 (0.1)
Smoking	1274 (0.05)	12058 (0.47)	12517 (0.48)
Hypertension	1012 (0.04)	1069 (0.04)	23768 (0.92)
Chronic hematologic disease	1002 (0.04)	22188 (0.86)	2659 (0.1)
Malnutrition	565 (0.02)	22220 (0.86)	3064 (0.12)
Liver disease	381 (0.01)	22955 (0.89)	2513 (0.1)
Pregnancy	135 (0.01)	25146 (0.97)	568 (0.02)

**Table 5:** Prevalence of Treatments

The counts presented for treatments include all cases, not only cases with complete details of treatments (as expressed in the summary).

Treatments	Present	Absent	Unknown
Antibiotic agent	16820 (0.65)	3294 (0.13)	5735 (0.22)
Oxygen therapy	16760 (0.65)	8101 (0.31)	988 (0.04)
Nasal / mask oxygen therapy	13996 (0.54)	5858 (0.23)	5995 (0.23)
Non-invasive ventilation	3937 (0.15)	20791 (0.8)	1121 (0.04)
Corticosteroid agent	3122 (0.12)	16250 (0.63)	6477 (0.25)
Invasive ventilation	2946 (0.11)	21831 (0.84)	1072 (0.04)
Antiviral agent	1771 (0.07)	17734 (0.69)	6344 (0.25)
Inotropes / vasopressors	1560 (0.06)	17652 (0.68)	6637 (0.26)
Prone ventilation	1261 (0.05)	17853 (0.69)	6735 (0.26)
Other	1141 (0.04)	16276 (0.63)	8432 (0.33)
Antifungal agent	812 (0.03)	18563 (0.72)	6474 (0.25)
Renal replacement therapy	685 (0.03)	18562 (0.72)	6602 (0.26)
Tracheostomy	383 (0.01)	18762 (0.73)	6704 (0.26)
Extracorporeal membrane oxygenation (ECMO)	310 (0.01)	24428 (0.95)	1111 (0.04)

**Table 6:** Key time variables.

Unlike the observed mean, the estimation process of the **expected mean** accounts for all cases, irrespective of whether an outcome has been observed. The expected mean is ‘NA’ for those variables for which parameter estimation could not be performed, due to the high proportion of unobserved end dates. The interquartile range is abbreviated ‘IQR’.

Time (in days)	Mean (observed)	SD (observed)	Median (observed)	IQR (observed )	Expected mean (95% CI)
Length of hospital stay	10.5	10.2	8	9	19 (17.9, 20.4)
Symptom onset to admission	13	7.9	5	9	7.9 (7.5, 8.7)
Admission to ICU entry	2.8	5.9	1	3	3.7 (3.5, 4.1)
Duration of ICU	9.7	9.3	7	11	NA
Admission to IMV	3.2	6	2	4	3.9 (3.7, 4.3)
Duration of IMV	11.2	8.2	10	10	NA
Admission to NIV	4.2	8.3	2	5	4.9 (4.6, 5.3)
Duration of NIV	2	4	0	5	NA

## Acknowledgements

This report is made possible through the efforts and expertise of the staff collecting data at our partner institutions across the globe, and the ISARIC Team. For a list of partners and team members, please visit <https://isaric.tghn.org/covid-19-data-management-hosting-contributors/>.

## References

1. A. C. Ghani, C. A. Donnelly, D. R. Cox, J. T. Griffin, C. Fraser, T. H. Lam, L. M. Ho, W. S. Chan, R. M. Anderson, A. J. Hedley, G. M. Leung (2005). Methods for Estimating the Case Fatality Ratio for a Novel, Emerging Infectious Disease, *American Journal of Epidemiology*, 162(5), 479 - 486. doi:10.1093/aje/kwi230.
2. R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.