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: 20 April 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.

Up to the date of this report, data have been entered for **19809** individuals from **244** sites across **25** countries.

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. Information is incomplete for the many patients who are still being treated. Note that we received more cases of severely ill individuals than people 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.

The analysis detailed in this report only includes individuals for whom data collection commenced on or before 06 April 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 analysis to this restricted cohort despite the much larger volumes of data held in the database.

The cohort comprises **12188** individuals, including 6904 males and 4480 females – sex is unreported for 804 cases. SARS-COV-2 infection has been **confirmed by laboratory testing in 8967 of these individuals**. 3221 individuals are recorded as suspected of SARS-COV-2 infection, without laboratory confirmation at the time of data analysis.

The median age (calculated based on reported age) is 71 years. The minimum and maximum observed ages are 0 and 104 years respectively.

Outcomes have been recorded for 6309 patients, consisting of 3927 recoveries and 2382 deaths. Follow-up is ongoing for 5215 patients. Outcome records are unavailable for 664 patients.

The observed mean duration for the number of days from hospital admission to outcome (death or discharge) is 8.7, with a standard deviation (SD) of 8.6 days and a median of 6 days. These estimates are based on all cases which have complete records on length of hospital stay (N = 6801).

The observed mean number of days from (first) symptom onset to hospital admission is 10.9, with a SD of 7.4 days and a median of 5 days.

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 four most common symptoms at admission were fatigue and malaise alongside cough, history of fever and shortness of breath.

1483 patients received non-invasive mechanical ventilation (NIV). The mean and median durations from admission to receiving NIV are 4.5 days and 2 days respectively (SD: 9.4 days) – estimated from records on cases with complete records on dates of hospital admission and NIV onset (N = 1281).

The mean and median durations for NIV are 1.8 days and 0.5 days respectively (SD: 3 days) – estimated based on only those cases which have complete NIV duration records (N = 627).

2416 patients were admitted at some point of their illness into an intensive care unit (ICU) or high dependency unit (HDU). The observed mean and median durations (in days) from hospital admission to ICU/HDU admission are 3.3 and 1 respectively (SD: 7.4) – estimated from records on cases with complete date records on hospital admission and ICU/HDU entry (N = 2317).

The duration of stay in ICU/HDU has a mean of 6.6 days and a median of 5 (SD: 6.2 days) – estimated on only those cases with complete records for ICU/HDU duration or ICU/HDU start/end dates (N = 1108). Of these 2416 patients who were admitted into ICU/HDU, 622 died, 1051 are still in hospital and 444 have recovered and been discharged. Outcome records are unavailable for 299 cases.

1488 patients received invasive mechanical ventilation (IMV). The mean and median durations from admission to receiving IMV are 3.2 days and 2 days respectively (SD: 6.8 days) – estimated from records on cases with complete records on dates of hospital admission and IMV onset (N = 1333).

The mean, median and SD for the duration of IMV – estimated based on all 663 cases with complete records on IMV stays – are 9.7 days, 9 days and 6.4 days respectively.

Of 6014 patients with a recorded outcome and details of treatments received, 67.7% received an antibiotic and 9.7% received antivirals. These treatment categories are not mutually exclusive since some patients received multiple treatments. 57.6% of patients received some degree of oxygen supplementation: of these, 25.1% received NIV and 16.9% IMV.

Of 1056 patients admitted into ICU/HDU with a recorded outcome and details of treatments, 76.5% received antibiotics and 25.0% antivirals; and 90.0% received some degree of oxygen supplementation, of which 38.1% was NIV and 59.2% IMV.

Patient Characteristics

Figure 1: Age and sex distribution of patients. Bar fills are outcome (death/discharge/ongoing care) at the time of report.

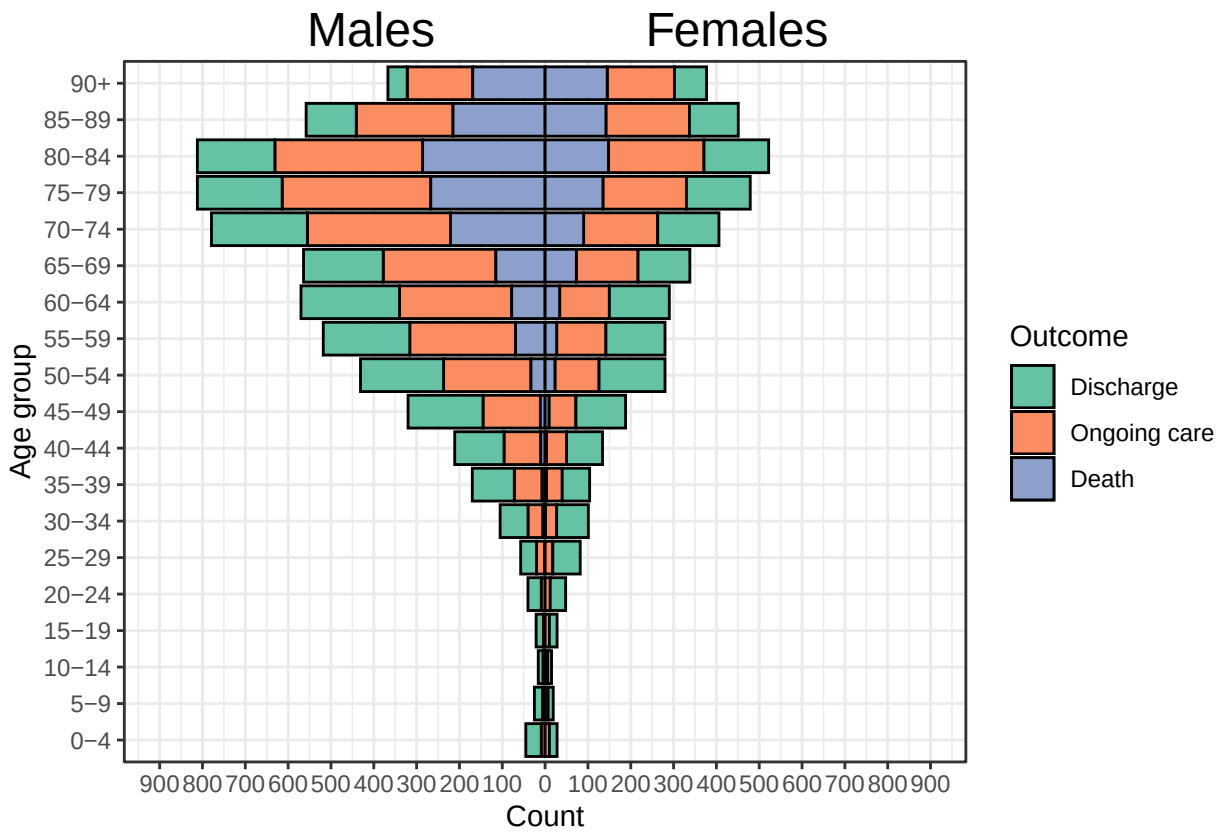
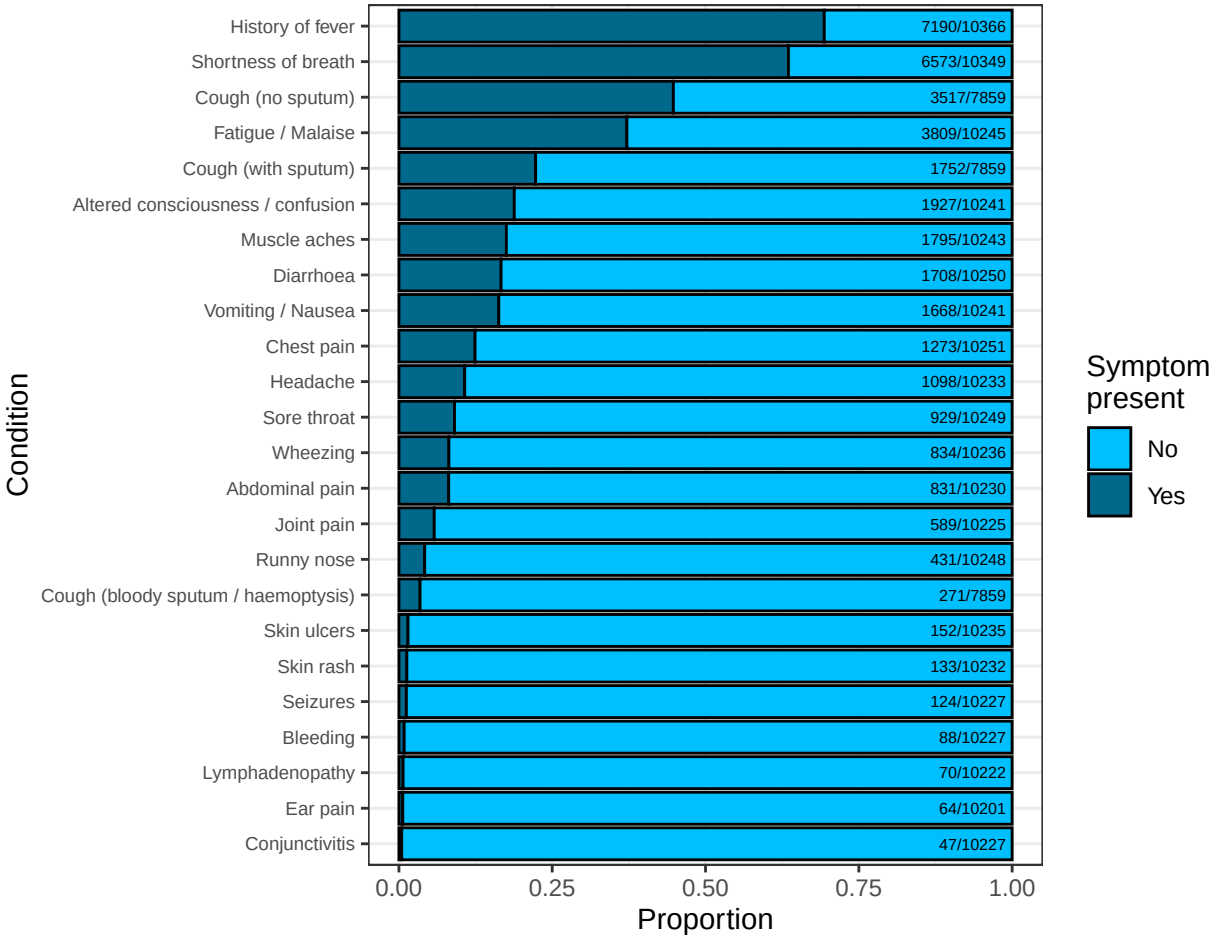
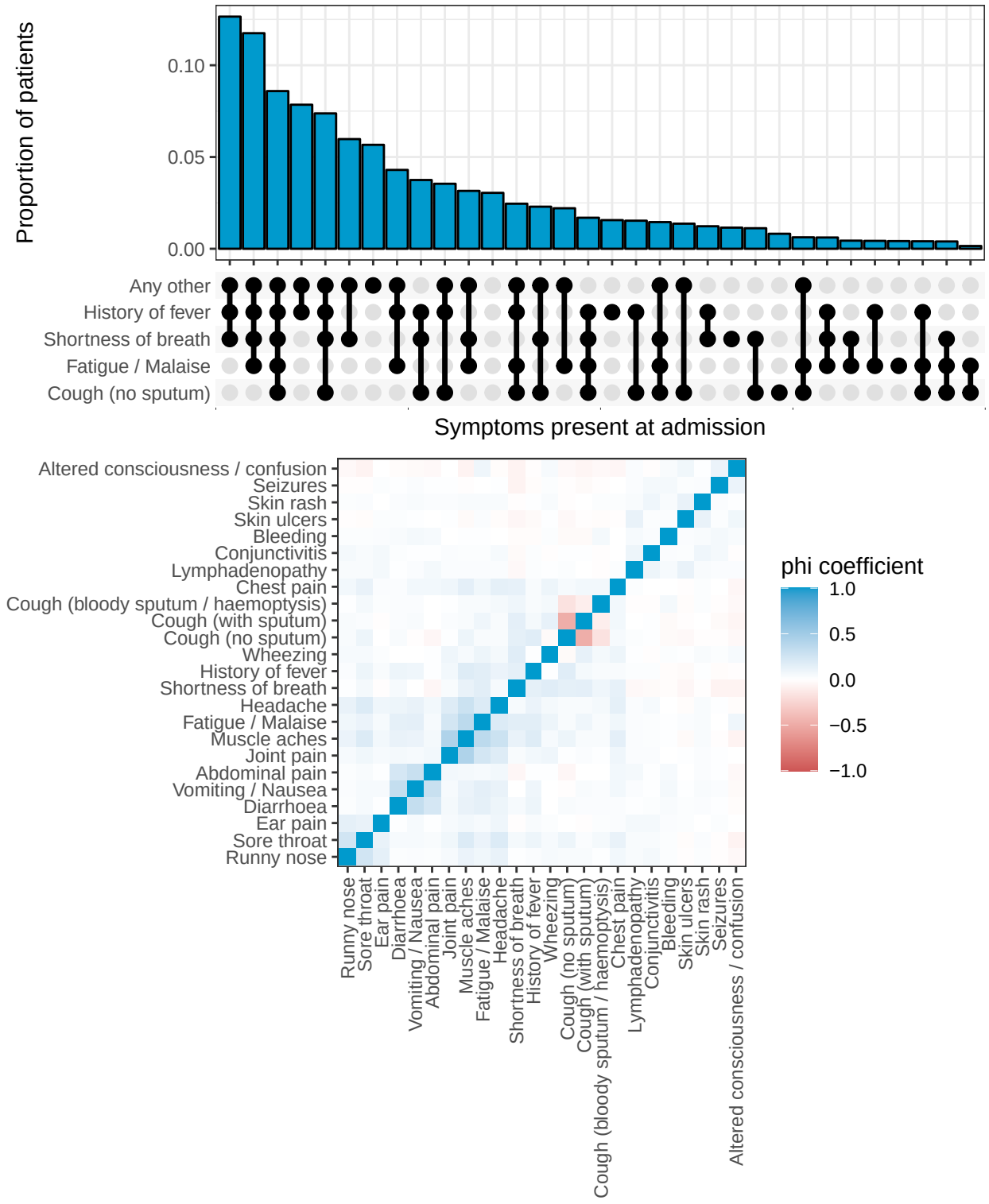


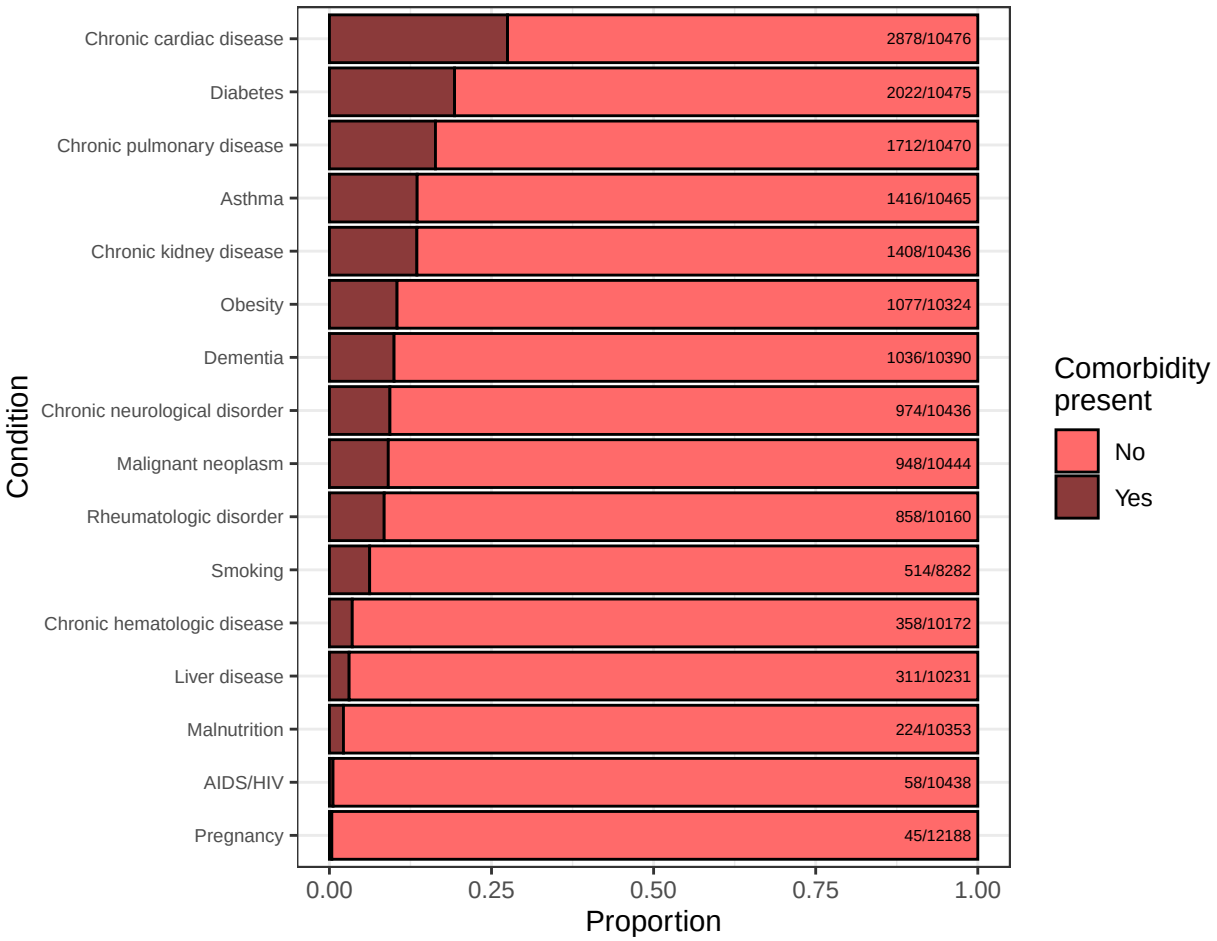
Figure 2: Top: Frequency of symptoms seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this symptom over the number of patients for whom presence or absence of this symptom was recorded. Middle: The distribution of combinations 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.*

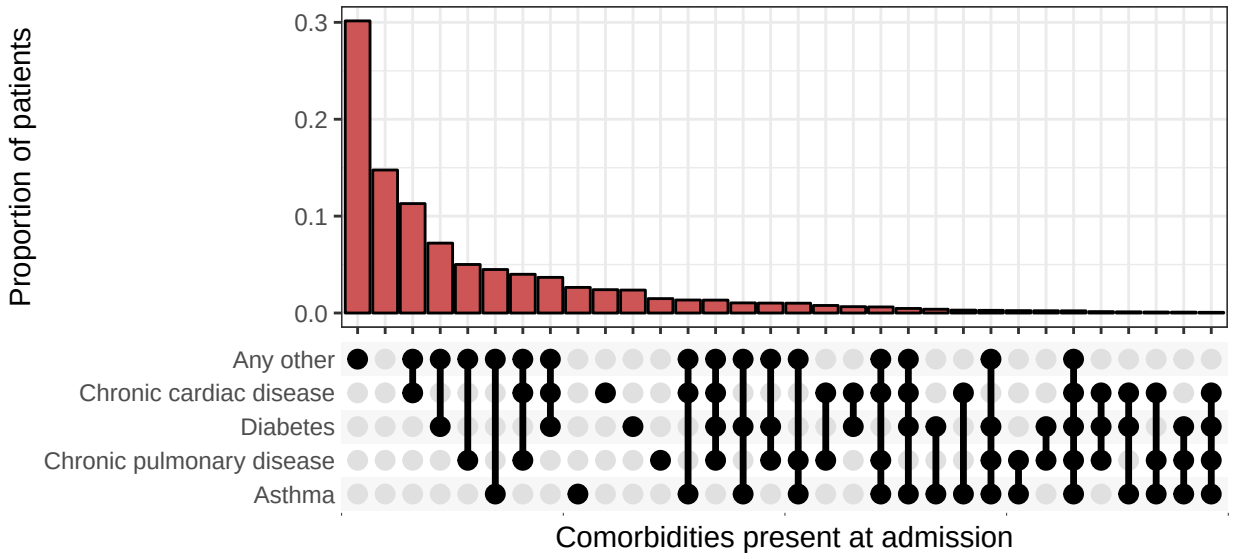




* We are working to gain a greater understanding of patients reported as having no presenting symptoms.

Figure 3: Top: Frequency of comorbidities 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 comorbidities, 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 comorbidities in the top plot, and any other comorbidities recorded as free text by clinical staff.




Proportion of patients
0.3
0.2
0.1
0.0
Any other
Chronic cardiac disease
Diabetes
Chronic pulmonary disease
Asthma
Comorbidities present at admission

Variables by age

Figure 4: Comorbidities stratified by age group. Numbers on the plot show the number with the comorbidity and the number in the age group (numbers are not displayed if <5). Denominators vary between plots due to data completeness.

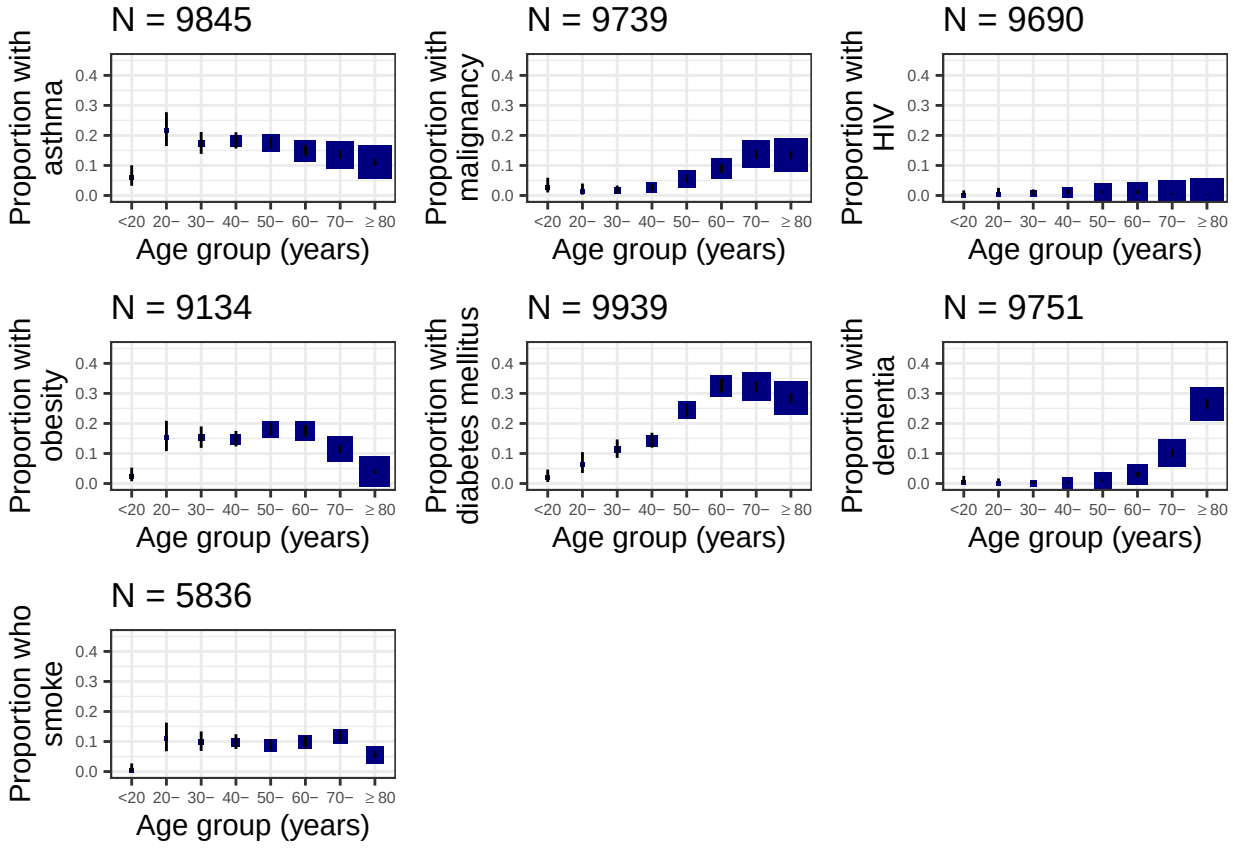


Figure 5: Symptoms recorded at hospital presentation stratified by age group. Numbers on the plot show the number reporting the symptoms and the number in the age group (numbers are not displayed if <5). Denominators vary between plots due to data completeness.

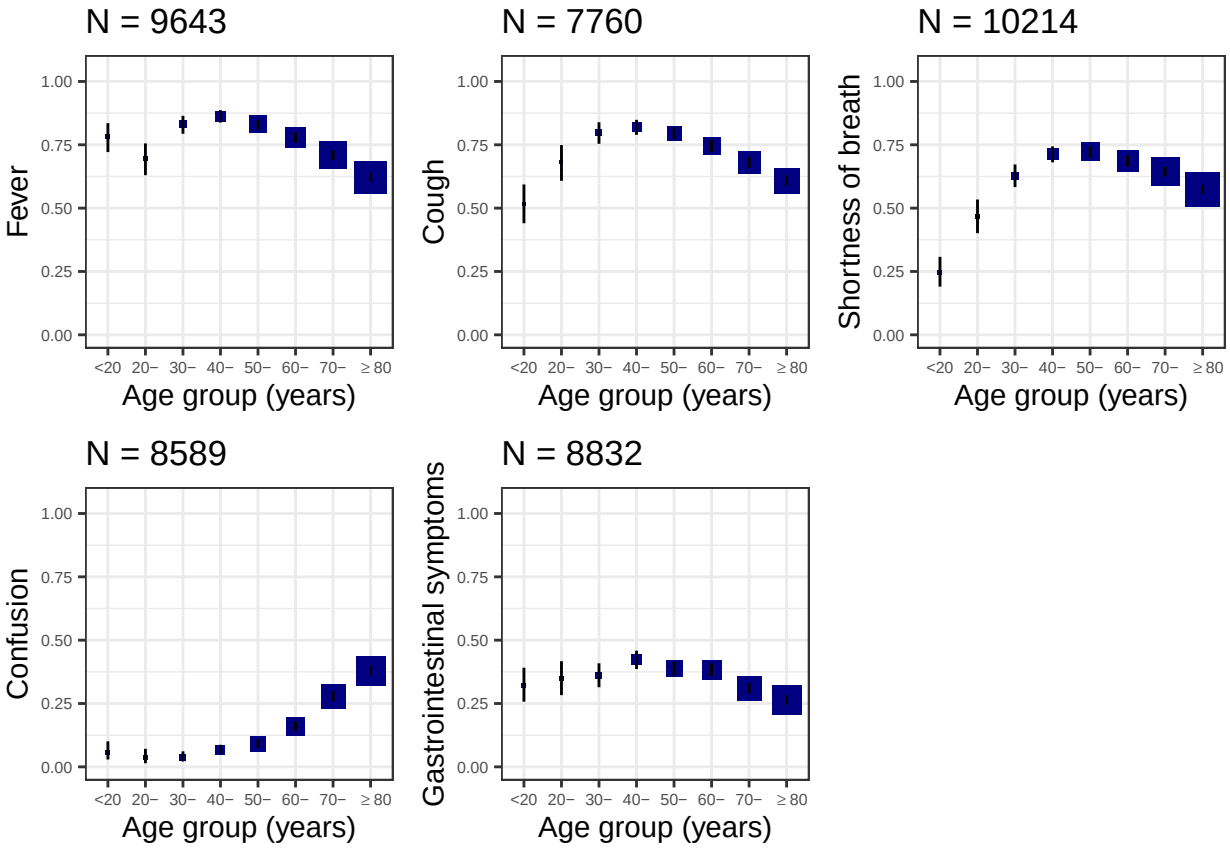


Figure 6: Box and whisker plots for observations at hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness).

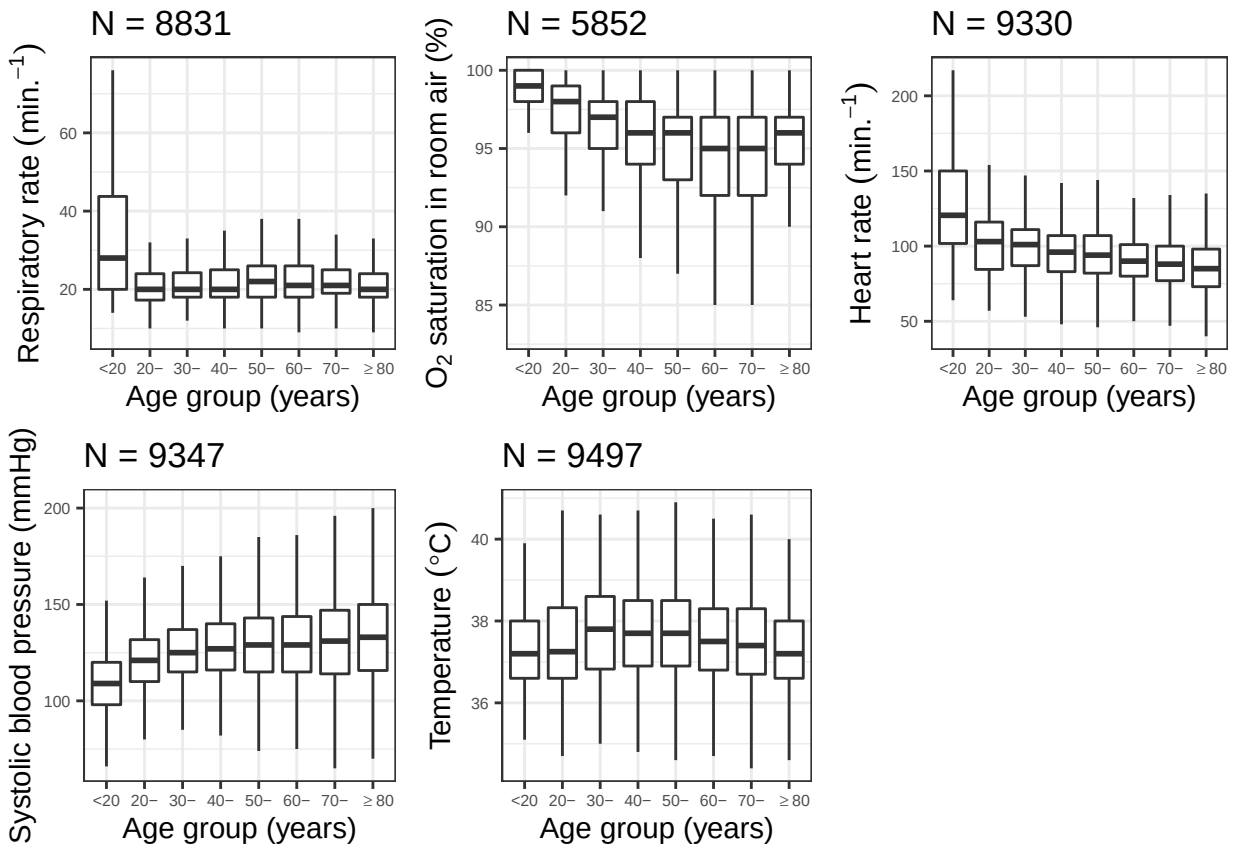
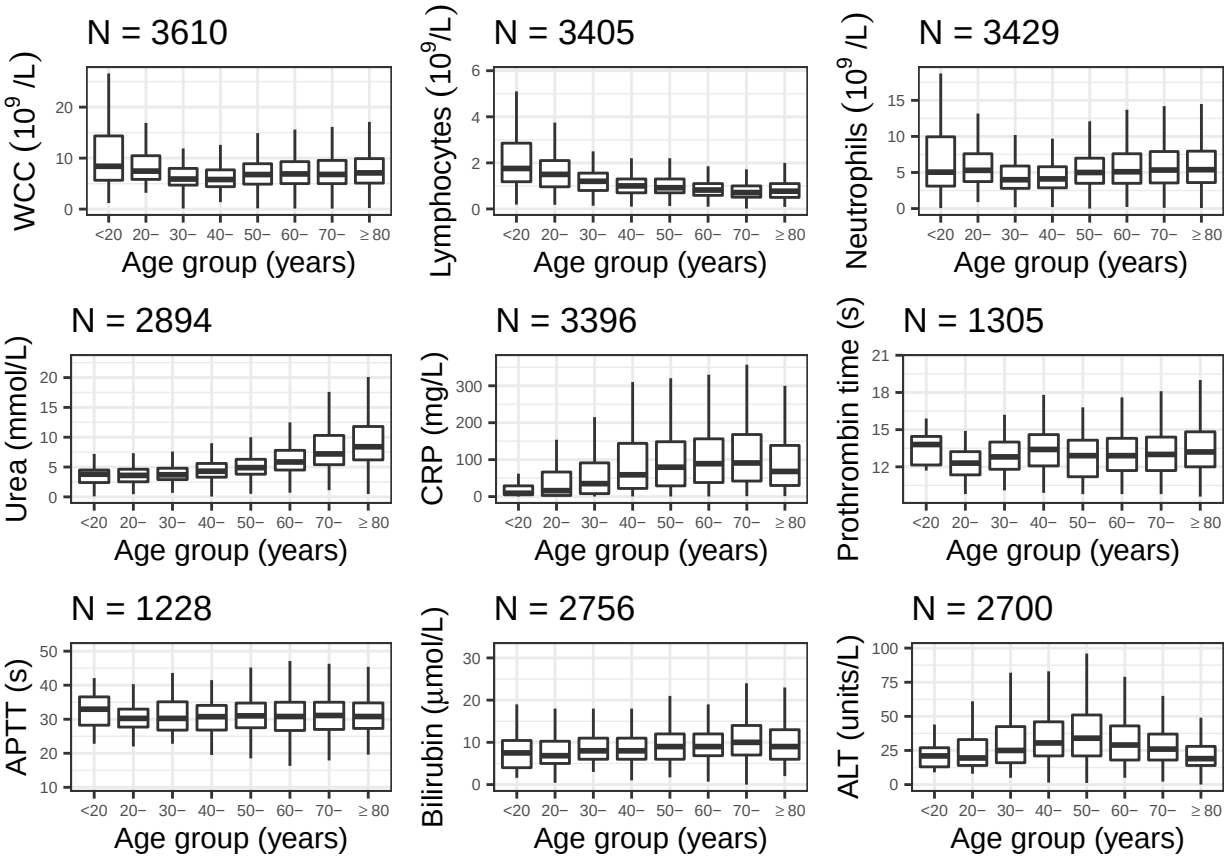


Figure 7: Box and whisker plots for laboratory results within 24 hours of hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness). ALT, Alanine transaminase; APTT, Activated partial thromboplastin time; CRP, C-reactive protein; WCC, white cell count



Hospital stays and outcomes

Figure 8: 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.

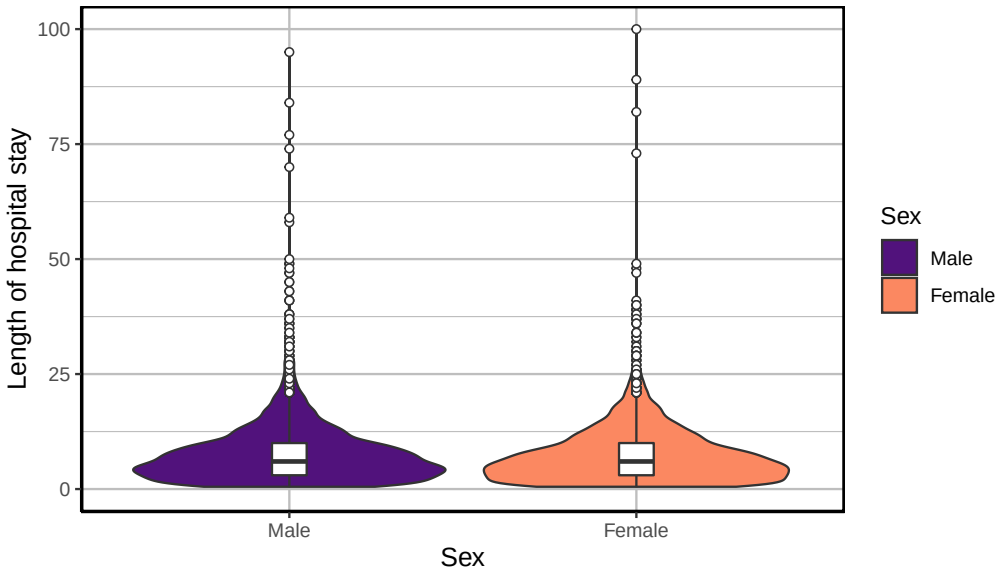


Figure 9: Distribution of length of hospital stay, according to patient age group. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest.

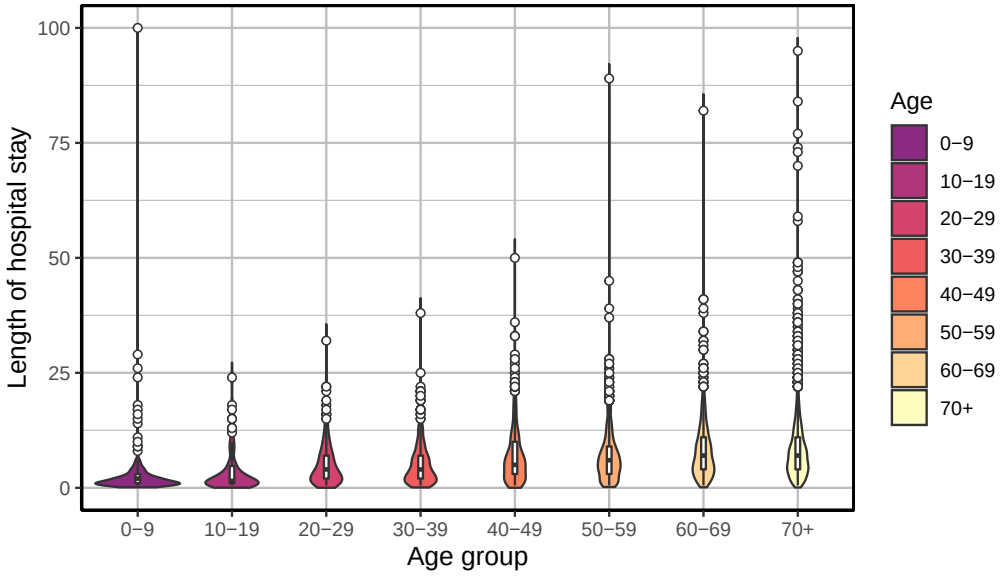
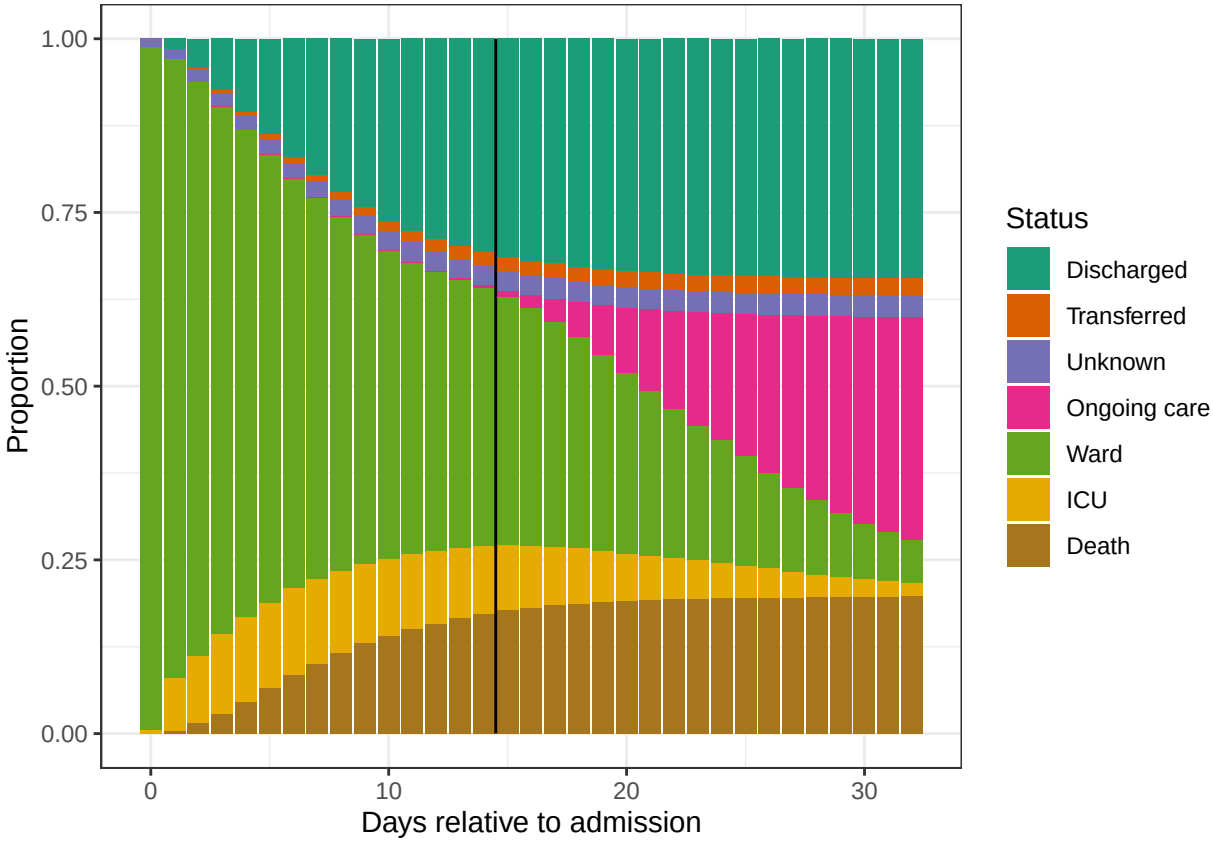
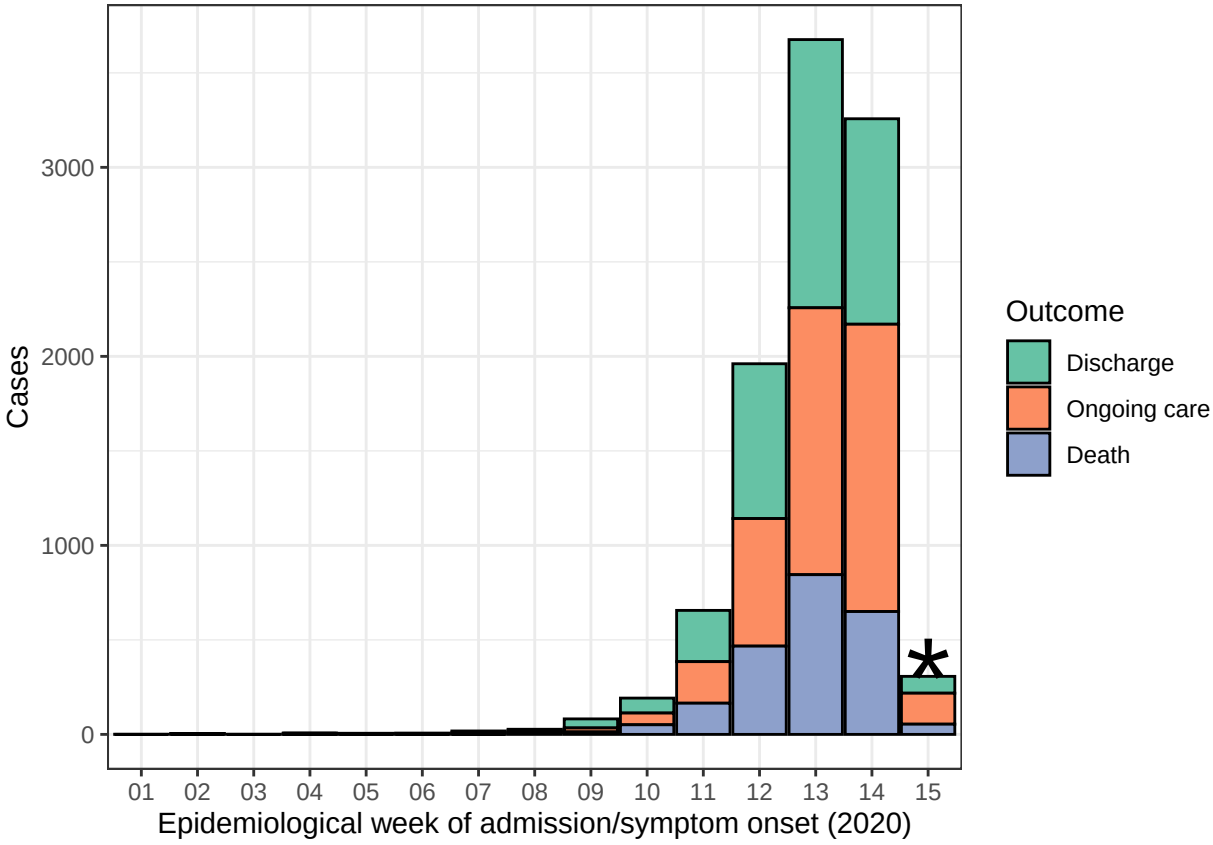


Figure 10: The distribution of patient status by number of days after admission. Patients with "Unknown" status have left the site at the time of report but have unknown outcomes due to missing data. Patients still on site at the time of report appear in the ongoing "ongoing care" for days which are in the future at that time. (For example, a patient admitted 7 days before the date of report and still on site at 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.*



* We are working to gain a greater understanding of the patient pathway for individuals recorded as having extremely long hospital stays.

Figure 11: 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 12: Treatments used. This only includes patients for whom this information was recorded.

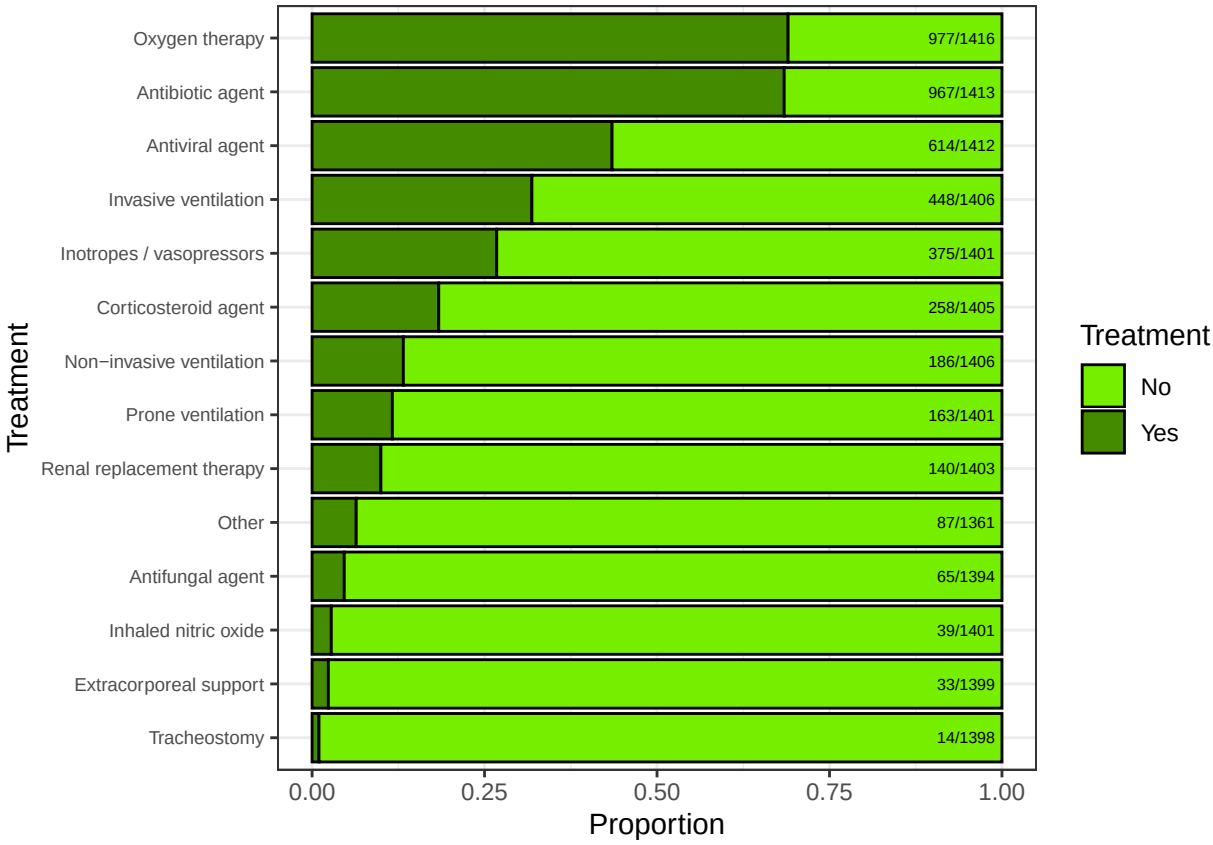
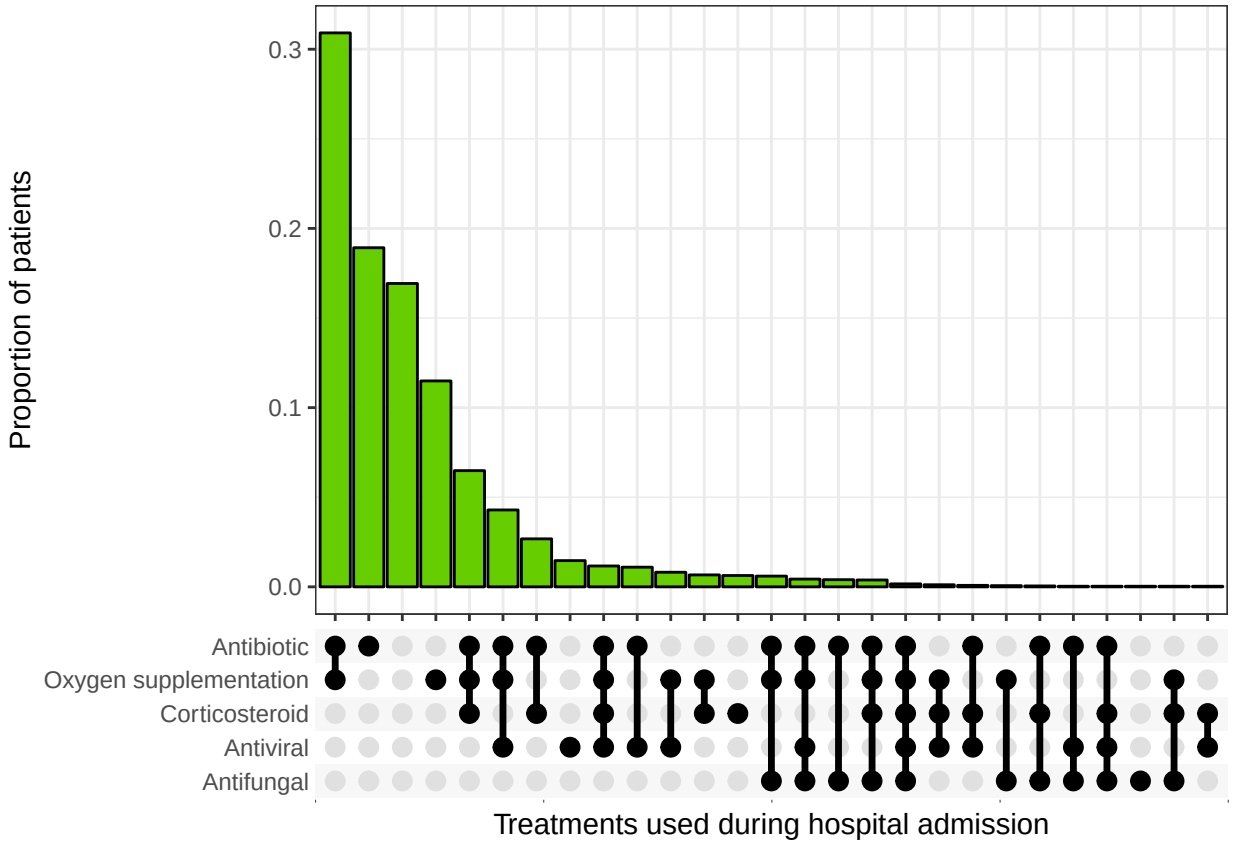


Figure 13: The distribution of combinations of antimicrobial treatments and steroids administered during hospital stay, across all patients with completed hospital stay and recorded treatment data. Filled and empty circles below the x-axis indicate treatments that were and were not administered.



Intensive Care and High Dependency Unit Treatments

Figure 14: Treatments used amongst patients admitted to the ICU. This only includes patients for whom this information was recorded.

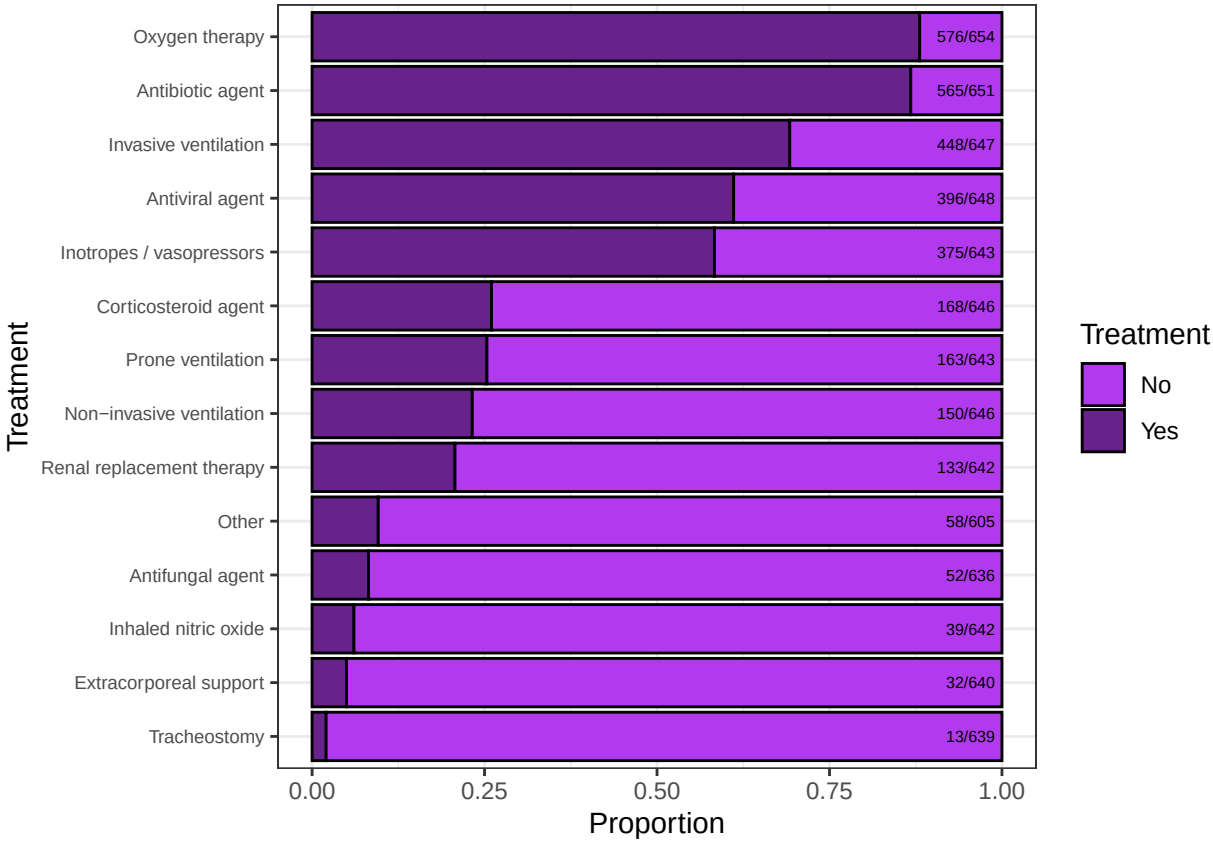
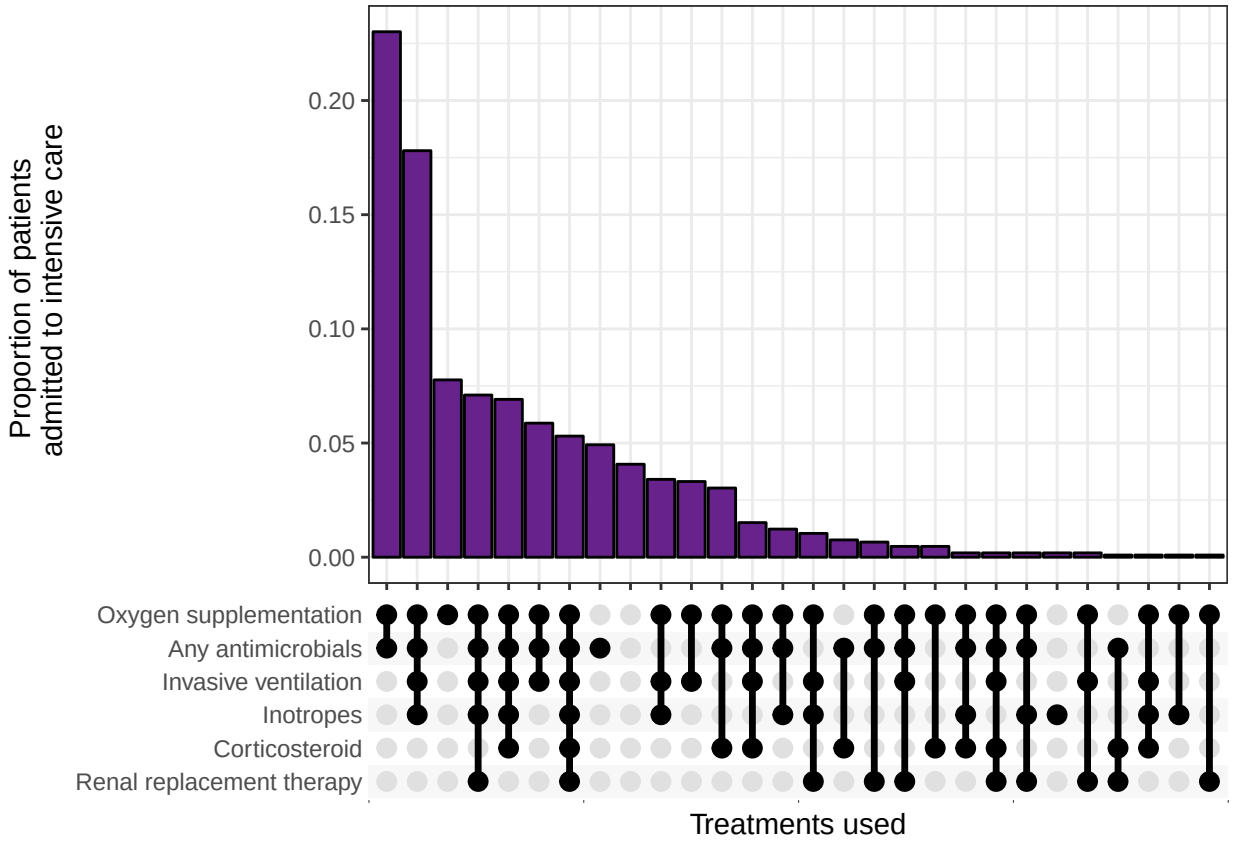
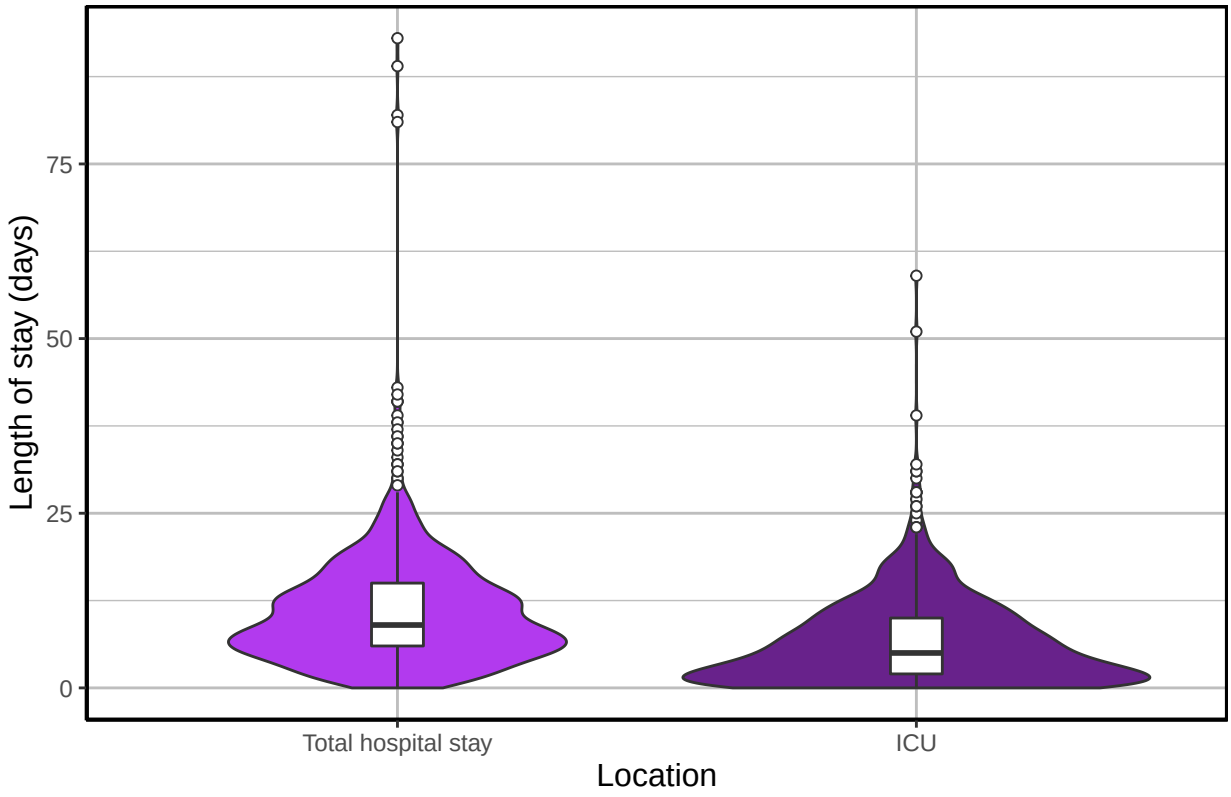


Figure 15: The distribution of combinations of treatments administered during ICU/HDU stay. Filled and empty circles below the x-axis indicate treatments that were and were not administered respectively.*



* We are working to gain a greater understanding of patients reported as having been admitted to ICU/HDU but having no intensive treatments recorded.

Figure 16: 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.



Statistical Analysis

Figure 17: 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. Expected estimates, accounting for unobserved outcomes, are provided in the summary tables at the end of this report.

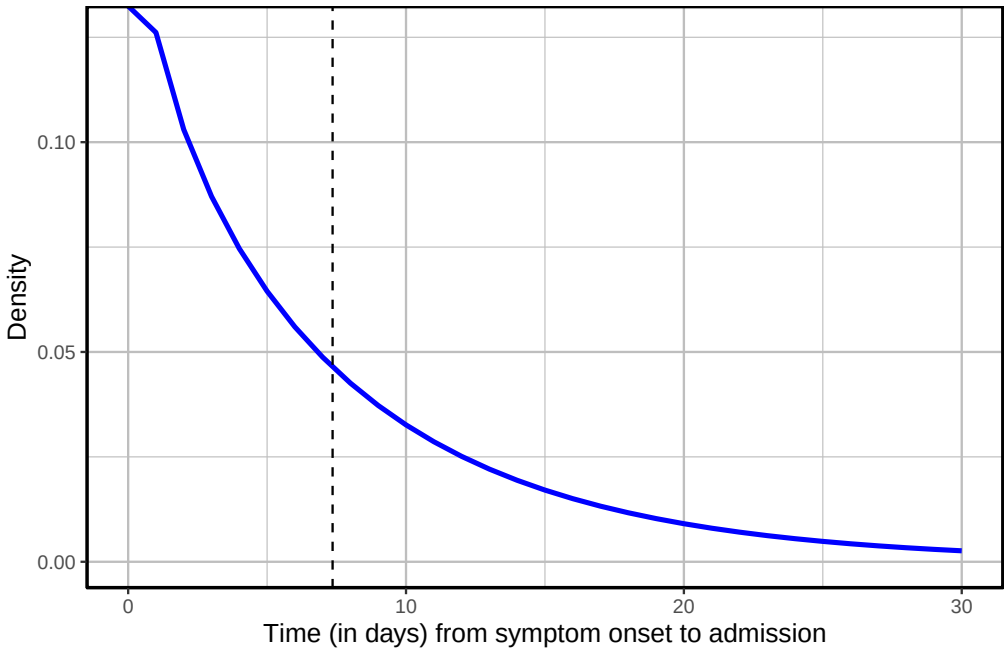


Figure 18: Distribution of time from admission to an outcome - either death or recovery (discharge). The blue curve is the Gamma distribution fit to the data. The black dashed line indicated the position of the expected mean.

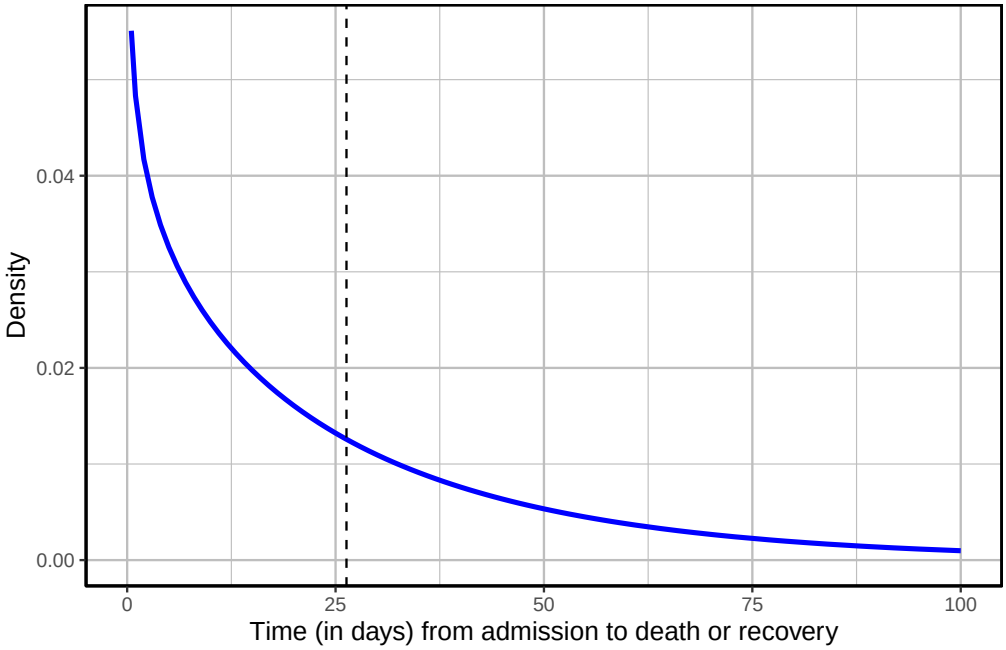
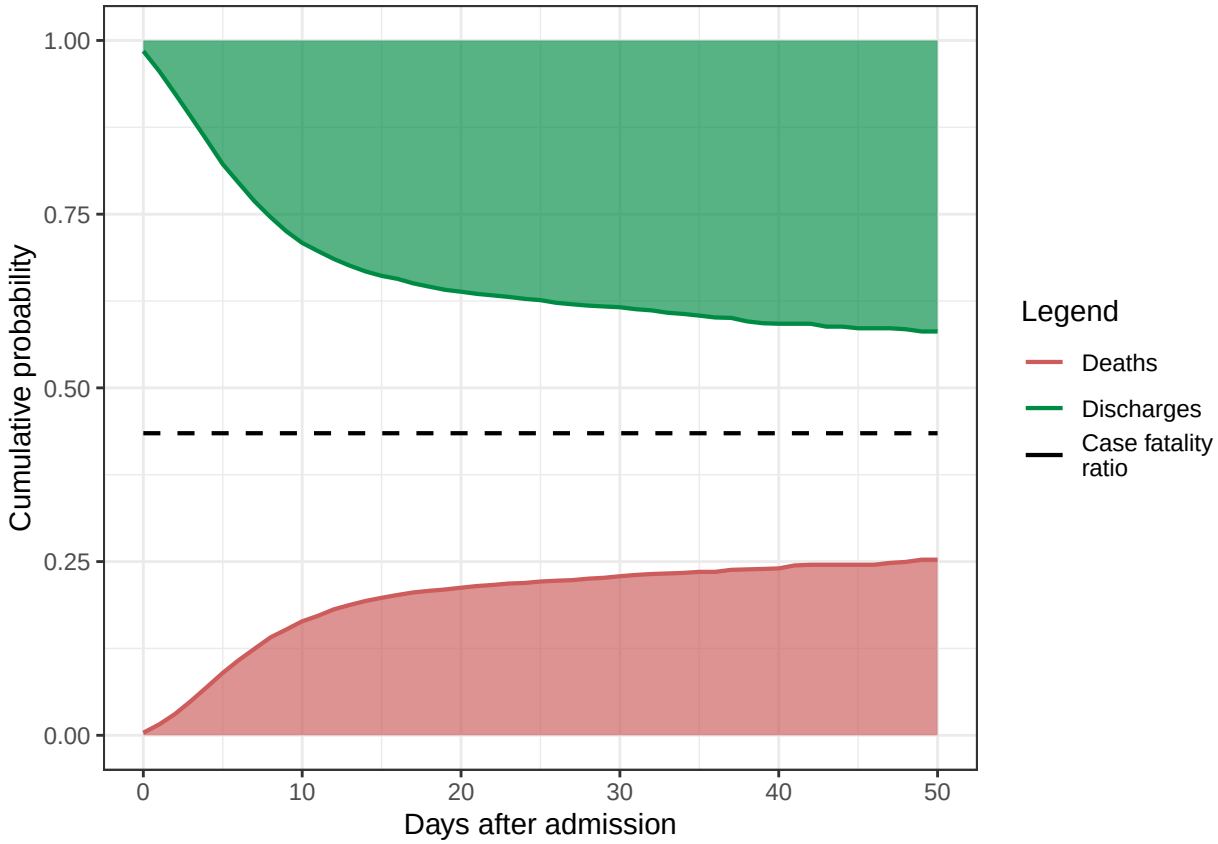


Figure 19: Probabilities of death (red curve) and recovery (green curve) over time. The black line indicates the case fatality ratio (black). The method used here considers all cases, irrespective of whether an outcome has been observed. For a completed epidemic, the curves for death and recovery meet. Estimates were derived using a nonparametric Kaplan-Meier–based method proposed by Ghani *et al.* (2005).



Country Comparisons

Figure 20: Number of sites per country.

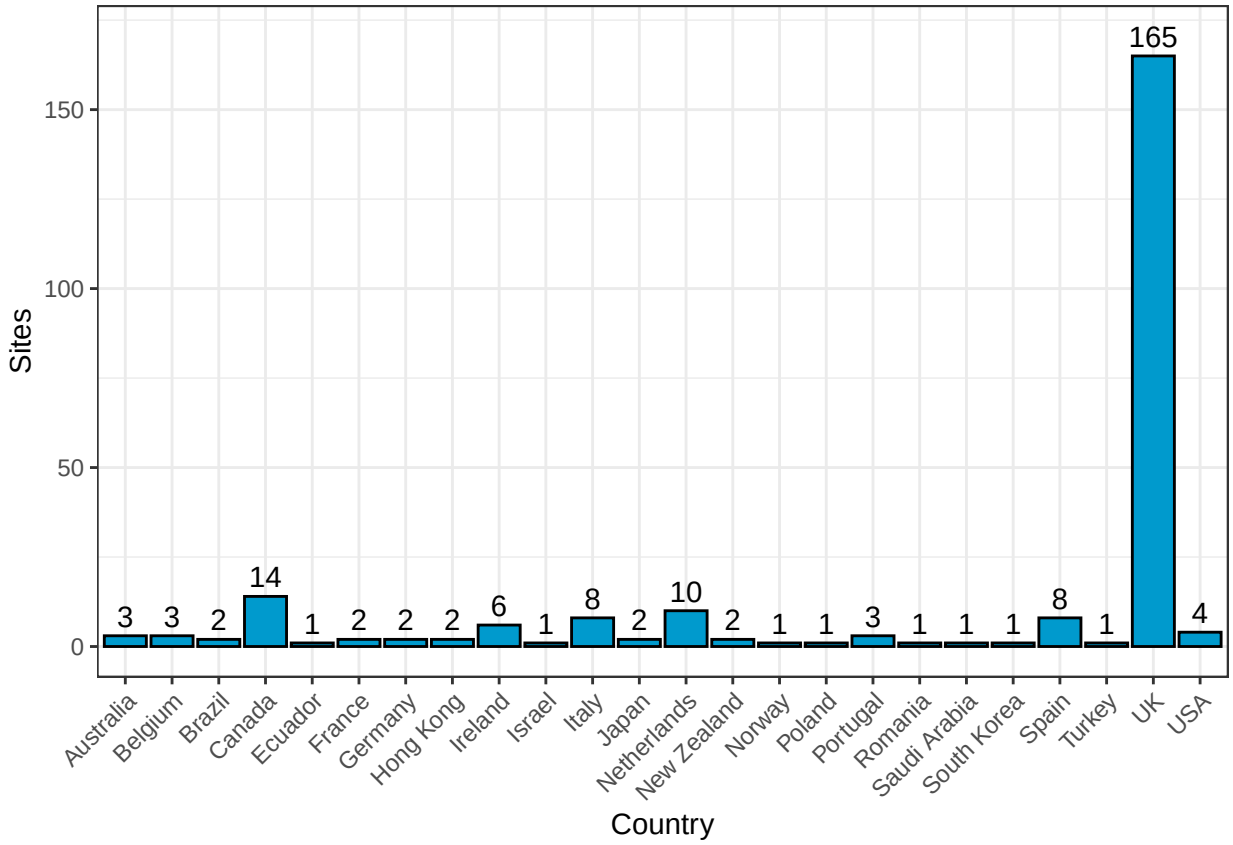
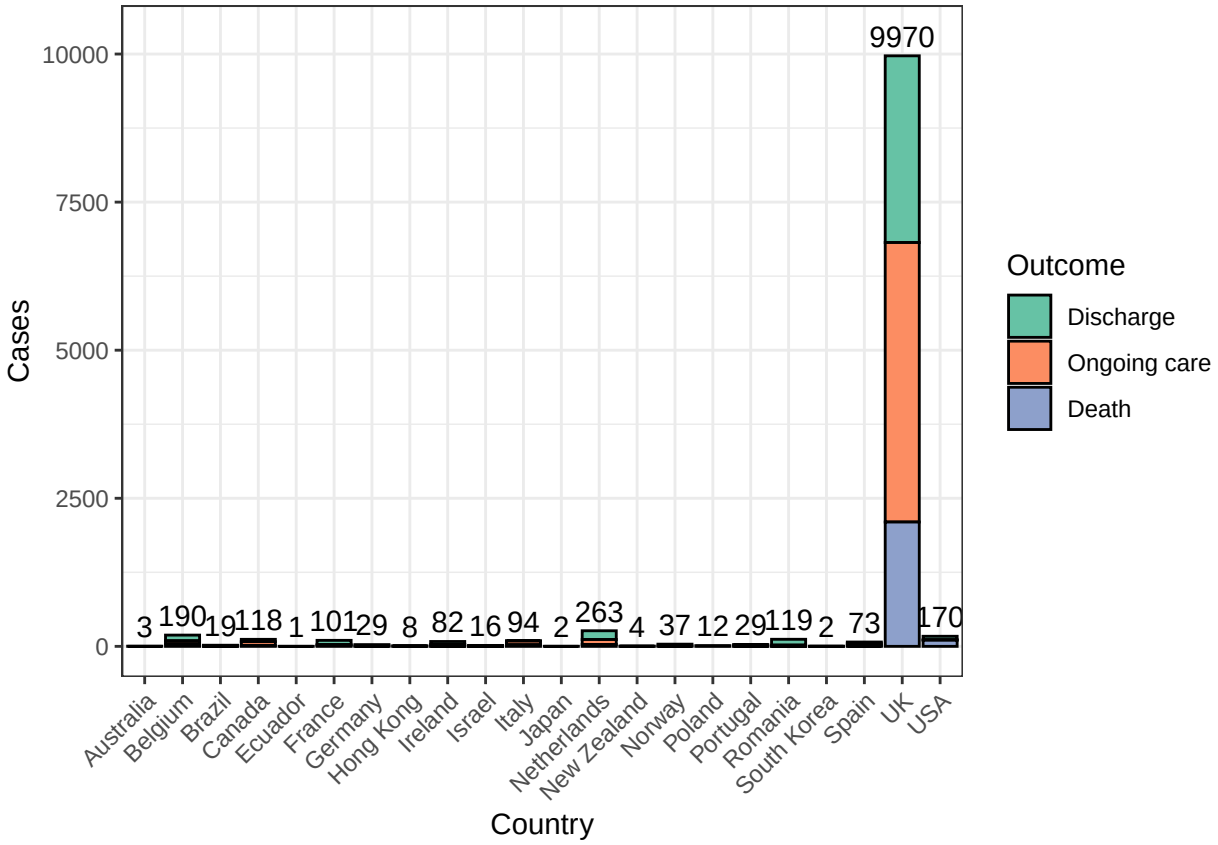
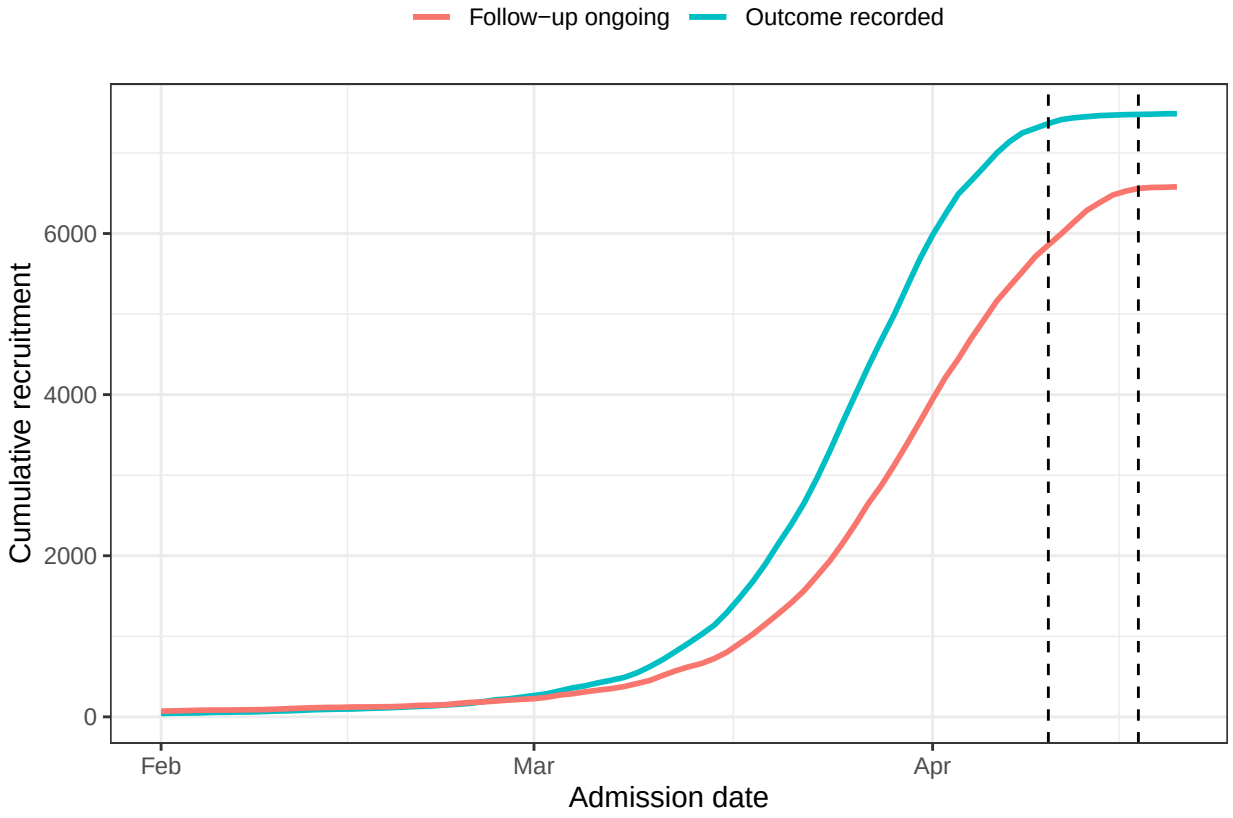


Figure 21: Distribution of patients by country and outcome



Recruitment

Figure 22: Cumulative recruitment of participants, separated by whether follow-up is ongoing or an outcome has been recorded. The first dashed black line indicates the exclusion date for this report: patients recruited after this date have not been included. The second black line is the exclusion date for next week's report.



Background

In response to the emergence of novel coronavirus (COVID-19), ISARIC launched a portfolio of resources to accelerate outbreak research and response. 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 the 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 the rapid implementation of standardised data collection and reporting, ISARIC hosts a data platform that includes an electronic data capture system, a secure repository and an analytic framework. Data are entered to a web-based REDCap data management system, securely stored, and used to inform regular reports as above. Data contributors are invited to input on the methods and contents of the reports, and are provided with the R code to execute analysis on their own data in the platform. For more information, visit the ISARIC website.

Following the launch of this these open resources, ISARIC received a massive response from the health and research communities. ISARIC supports researchers to retain control of the data and samples they collect. All decisions regarding data use are made by the institutions that enter the data. We keep our contributors informed of any plans and welcome their input to ensure that we are generating the best science and promoting the interests of your patients, your institutions and your public health authorities. Feedback and suggestions are welcome at 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 patience by sex and status (dead, recovered & still in hospital), the prevalence of individual symptoms - and combinations of them - on admission, the prevalence of individual comorbidities - and combinations of them - 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 parantheses. Proportions have been rounded to two decimal places.

Table 1: Patient Characteristics

Description	**Value**
Size of cohort	12188
By sex	
Male	6904 (0.57)
Female	4480 (0.37)
Unknown	804 (0.06)
By outcome status	
Dead	2382 (0.2)
Recovered (discharged alive)	3927 (0.32)
Still in hospital	5215 (0.43)
Tranferred to another facility	318 (0.03)
Unknown	346 (0.03)
By COVID-19 status	
Positive (laboratory-confirmed)	8967 (0.74)
Suspected	3221 (0.26)
By age group	
0-9	137 (0.01)
10-19	98 (0.01)
20-29	239 (0.02)
30-39	509 (0.04)
40-49	905 (0.07)
50-59	1612 (0.13)
60-69	1896 (0.16)
70+	5897 (0.48)
Unknown	895 (0.07)

Table 2: Outcome by age and sex

Variable	**Still in hospital**	**Death**	**Discharge**	**Transferred**	**Unknown**
Age					

Variable	**Still in hospital**	**Death**	**Discharge**	**Transferred**	**Unknown**
0-9	32 (0.01)	0 (0)	86 (0.02)	1 (0)	18 (0.05)
10-19	24 (0)	1 (0)	55 (0.01)	1 (0)	17 (0.05)
20-29	58 (0.01)	1 (0)	168 (0.04)	3 (0.01)	9 (0.03)
30-39	164 (0.03)	16 (0.01)	305 (0.08)	10 (0.03)	14 (0.04)
40-49	332 (0.06)	33 (0.01)	492 (0.13)	24 (0.08)	24 (0.07)
50-59	673 (0.13)	153 (0.06)	689 (0.18)	43 (0.14)	54 (0.16)
60-69	790 (0.15)	301 (0.13)	678 (0.17)	53 (0.17)	74 (0.21)
70+	2359 (0.45)	1822 (0.76)	1401 (0.36)	181 (0.57)	134 (0.39)
Sex					
Male	2787 (0.53)	1503 (0.63)	2215 (0.56)	192 (0.6)	207 (0.6)
Female	1681 (0.32)	840 (0.35)	1696 (0.43)	126 (0.4)	137 (0.4)
Unknown	10 (0)	4 (0)	7 (0)	0 (0)	0 (0)

Table 3: Prevalence of Symptoms

Symptoms	**Present**	**Absent**	**Unknown**
History of fever	7190 (0.59)	2581 (0.21)	2417 (0.2)
Shortness of breath	6573 (0.54)	3773 (0.31)	1842 (0.15)
Cough	5540 (0.45)	2319 (0.19)	4329 (0.36)
Fatigue / Malaise	3809 (0.31)	4115 (0.34)	4264 (0.35)
Altered consciousness / confusion	1927 (0.16)	6778 (0.56)	3483 (0.29)
Muscle aches	1795 (0.15)	5639 (0.46)	4754 (0.39)
Diarrhoea	1708 (0.14)	6841 (0.56)	3639 (0.3)
Vomiting / Nausea	1668 (0.14)	6894 (0.57)	3626 (0.3)
Chest pain	1273 (0.1)	6998 (0.57)	3917 (0.32)
Headache	1098 (0.09)	6322 (0.52)	4768 (0.39)
Sore throat	929 (0.08)	6277 (0.52)	4982 (0.41)
Wheezing	834 (0.07)	6812 (0.56)	4542 (0.37)
Abdominal pain	831 (0.07)	7384 (0.61)	3973 (0.33)
Joint pain	589 (0.05)	6499 (0.53)	5100 (0.42)
Runny nose	431 (0.04)	6619 (0.54)	5138 (0.42)
Skin ulcers	152 (0.01)	7683 (0.63)	4353 (0.36)
Skin rash	133 (0.01)	7686 (0.63)	4369 (0.36)
Seizures	124 (0.01)	8203 (0.67)	3861 (0.32)
Bleeding	88 (0.01)	8160 (0.67)	3940 (0.32)
Lymphadenopathy	70 (0.01)	7504 (0.62)	4614 (0.38)
Ear pain	64 (0.01)	6906 (0.57)	5218 (0.43)
Conjunctivitis	47 (0)	7578 (0.62)	4563 (0.37)

Table 4: Prevalence of Comorbidities

Comorbidities	Present	Absent	Unknown
Other	4113 (0.34)	5399 (0.44)	2676 (0.22)
Chronic cardiac disease	2878 (0.24)	7180 (0.59)	2130 (0.17)
Diabetes	2022 (0.17)	8000 (0.66)	2166 (0.18)
Chronic pulmonary disease	1712 (0.14)	8304 (0.68)	2172 (0.18)
Asthma	1416 (0.12)	8555 (0.7)	2217 (0.18)
Chronic kidney disease	1408 (0.12)	8529 (0.7)	2251 (0.18)
Obesity	1077 (0.09)	8133 (0.67)	2978 (0.24)
Dementia	1036 (0.09)	8803 (0.72)	2349 (0.19)
Chronic neurological disorder	974 (0.08)	8908 (0.73)	2306 (0.19)
Malignant neoplasm	948 (0.08)	8914 (0.73)	2326 (0.19)
Rheumatologic disorder	858 (0.07)	8718 (0.72)	2612 (0.21)
Smoking	514 (0.04)	5410 (0.44)	6264 (0.51)
Chronic hematologic disease	358 (0.03)	9238 (0.76)	2592 (0.21)
Liver disease	311 (0.03)	9341 (0.77)	2536 (0.21)
Malnutrition	224 (0.02)	9196 (0.75)	2768 (0.23)
AIDS/HIV	58 (0)	9755 (0.8)	2375 (0.19)
Pregnancy	45 (0)	11017 (0.9)	1126 (0.09)

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
Oxygen therapy	5185 (0.43)	4584 (0.38)	2419 (0.2)
Invasive ventilation	1488 (0.12)	8397 (0.69)	2303 (0.19)
Non-invasive ventilation	1483 (0.12)	8345 (0.68)	2360 (0.19)
Antibiotic agent	967 (0.08)	439 (0.04)	10782 (0.88)
Antiviral agent	614 (0.05)	787 (0.06)	10787 (0.89)
Inotropes / vasopressors	375 (0.03)	1018 (0.08)	10795 (0.89)
Corticosteroid agent	258 (0.02)	1138 (0.09)	10792 (0.89)
Prone ventilation	163 (0.01)	1223 (0.1)	10802 (0.89)
Renal replacement therapy	140 (0.01)	1256 (0.1)	10792 (0.89)
Extracorporeal membrane oxygenation (ECMO)	126 (0.01)	9706 (0.8)	2356 (0.19)
Other	87 (0.01)	1245 (0.1)	10856 (0.89)
Antifungal agent	65 (0.01)	1319 (0.11)	10804 (0.89)
Inhaled nitric oxide	39 (0)	1353 (0.11)	10796 (0.89)
Tracheostomy	14 (0)	1374 (0.11)	10800 (0.89)

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 abbbreviated 'IQR'.

Time (in days)	Mean (observed)	SD (observed)	Median (observed)	IQR (observed)	Expected mean (95% CI)
Length of hospital stay	8.7	8.6	6	8	26.3 (25, 28.8)
Symptom onset to admission	10.9	7.4	5	7	7.4 (7, 8)
Admission to ICU entry	3.3	7.4	1	2.5	3.3 (3.1, 3.5)
Duration of ICU	6.6	6.2	5	8	NA
Admission to IMV	3.2	6.8	2	3.5	3.2 (3, 3.5)
Duration of IMV	9.7	6.4	9	9	NA
Admission to NIV	4.5	9.4	2	4.5	4.5 (4.2, 4.9)
Duration of NIV	1.8	3	0.5	4.5	NA

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