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: 27 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 **27424** individuals from **278** sites across **30** 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. 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.

The analysis detailed in this report only includes individuals for whom data collection commenced on or before 13 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 **19463** individuals, including 11688 males and 7684 females – sex is unreported for 91 cases. SARS-COV-2 infection has been **confirmed by laboratory testing in 15844 of these individuals**. 3619 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 were 0 and 104 years respectively.

Outcomes have been recorded for 11873 patients, consisting of 7595 recoveries and 4278 deaths. Follow-up is ongoing for 6464 patients. Outcome records are unavailable for 1126 patients.

The observed mean number of days from (first) symptom onset to hospital admission was 11.7, with a SD of 7.4 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 8.7, with a standard deviation (SD) of 8.1 days and a median of 7 days. These estimates are based on all cases which have complete records on length of hospital stay (N = 12829).

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.

2670 patients received non-invasive mechanical ventilation (NIV). The mean and median durations from admission to receiving NIV were 4.6 days and 2 days respectively (SD: 12 days) – estimated from records on cases with complete records on dates of hospital admission and NIV onset (N = 2307).

The mean and median durations for NIV were 2 days and 0.5 days respectively (SD: 3.5 days) – estimated based on only those cases which have complete NIV duration records (N = 1151).

3752 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 were 3.3 and 1 respectively (SD: 7) – estimated from records on cases with complete date records on hospital admission and ICU/HDU entry (N = 3709).

The duration of stay in ICU/HDU had a mean of 7.4 days and a median of 5.5 (SD: 7.5 days) – estimated on only those cases with complete records for ICU/HDU duration or ICU/HDU start/end dates (N = 1968). Of these 3752 patients who were admitted into ICU/HDU, 989 died, 1514 are still in hospital and 831 have recovered and been discharged. Outcome records are unavailable for 418 cases.

2249 patients received invasive mechanical ventilation (IMV). The mean and median durations from admission to receiving IMV were 3.5 days and 2 days respectively (SD: 7.2 days) – estimated from records on cases with complete records on dates of hospital admission and IMV onset (N = 2101).

The mean, median and SD for the duration of IMV – estimated based on all 1028 cases with complete records on IMV stays – were 9.6 days, 9 days and 6.5 days respectively.

Of 11407 patients with a recorded outcome and details of treatments received, 72.4% received an antibiotic and 8.8% received antivirals. These treatment categories are not mutually exclusive since some patients received multiple treatments. 68.6% of patients received some degree of oxygen supplementation: of these, 22.2% received NIV and 12.2% IMV.

Of 1804 patients admitted into ICU/HDU with a recorded outcome and details of treatments, 79.9% received antibiotics and 20.5% antivirals; and 93.0% received some degree of oxygen supplementation, of which 43.7% was NIV and 54.1% IMV.

Patient Characteristics

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

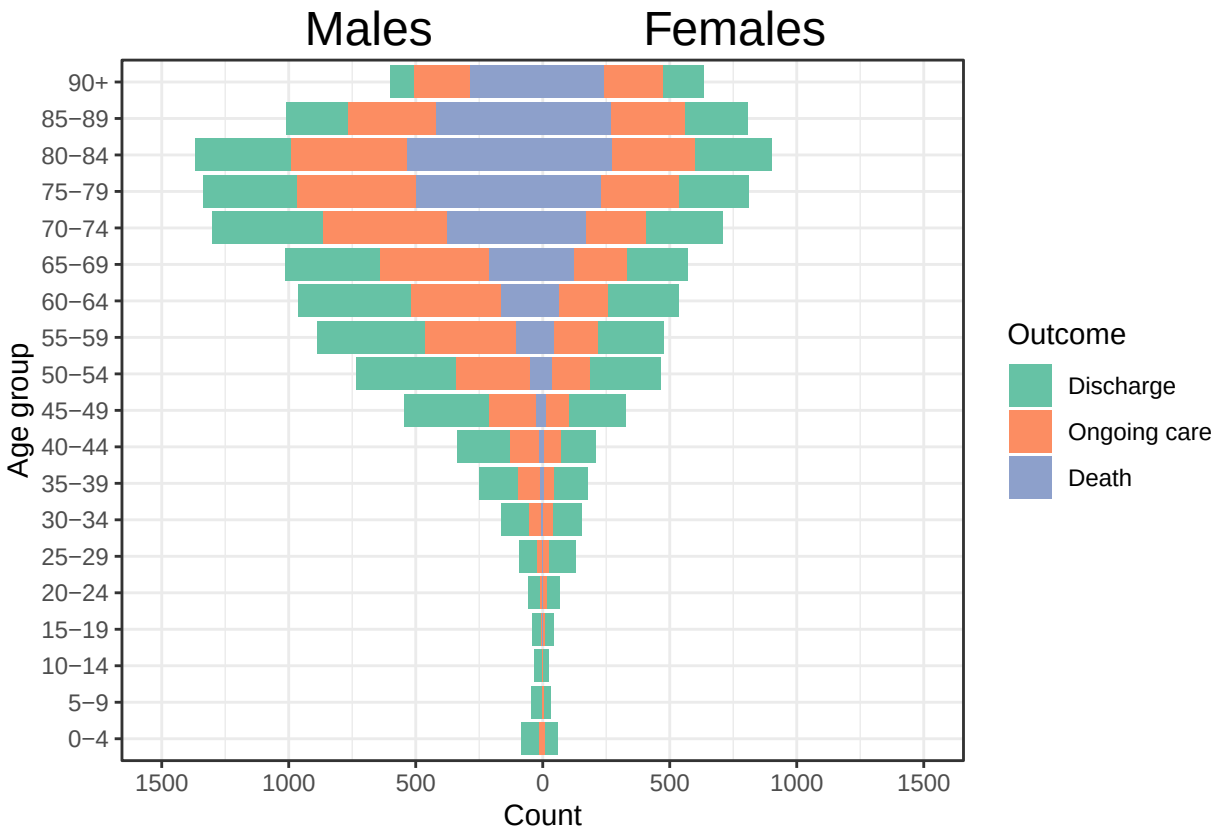
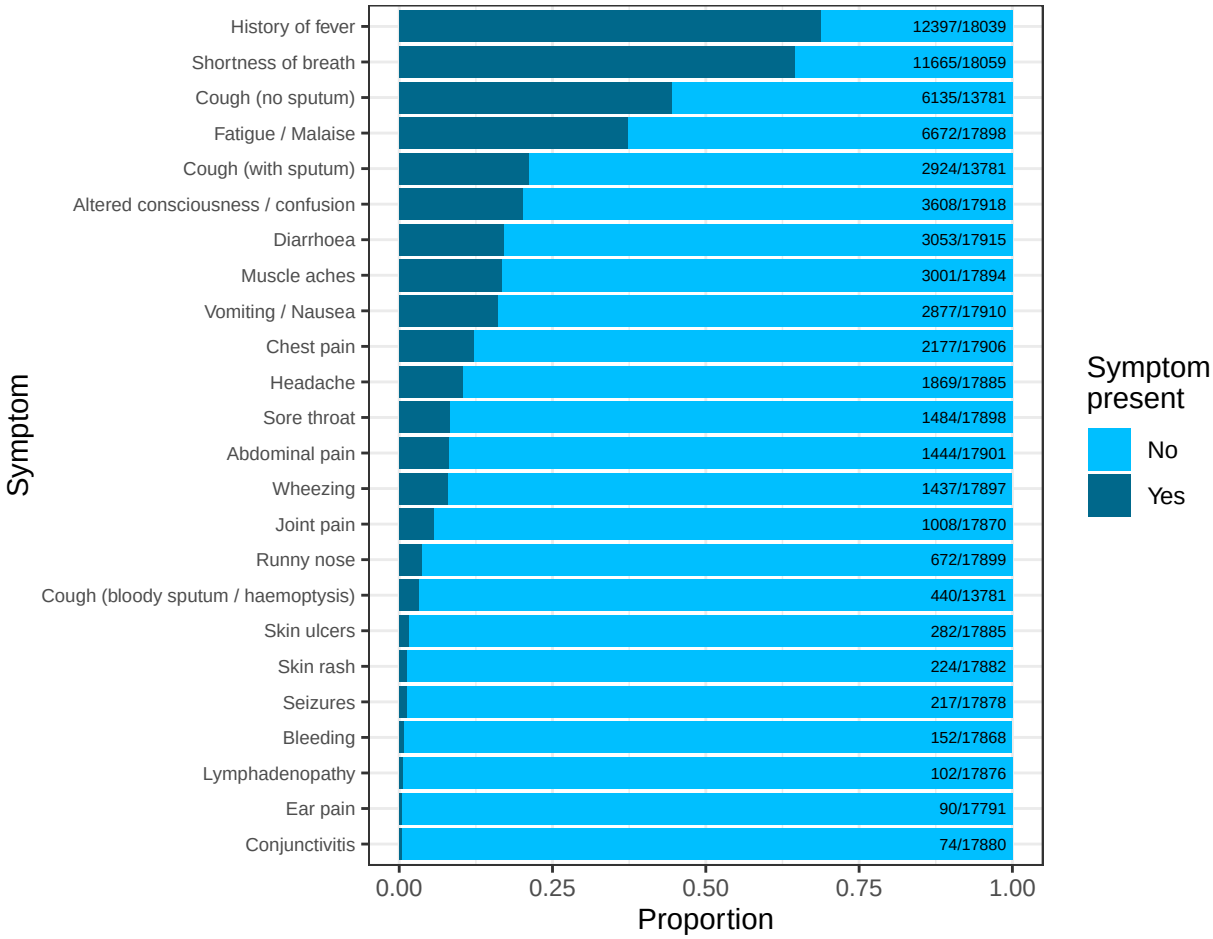
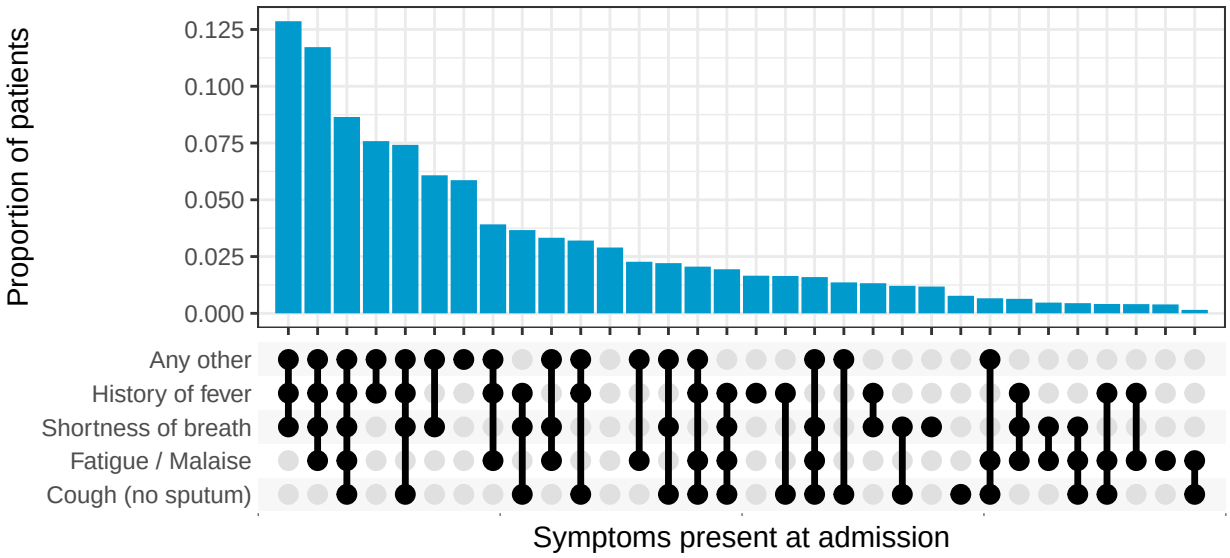
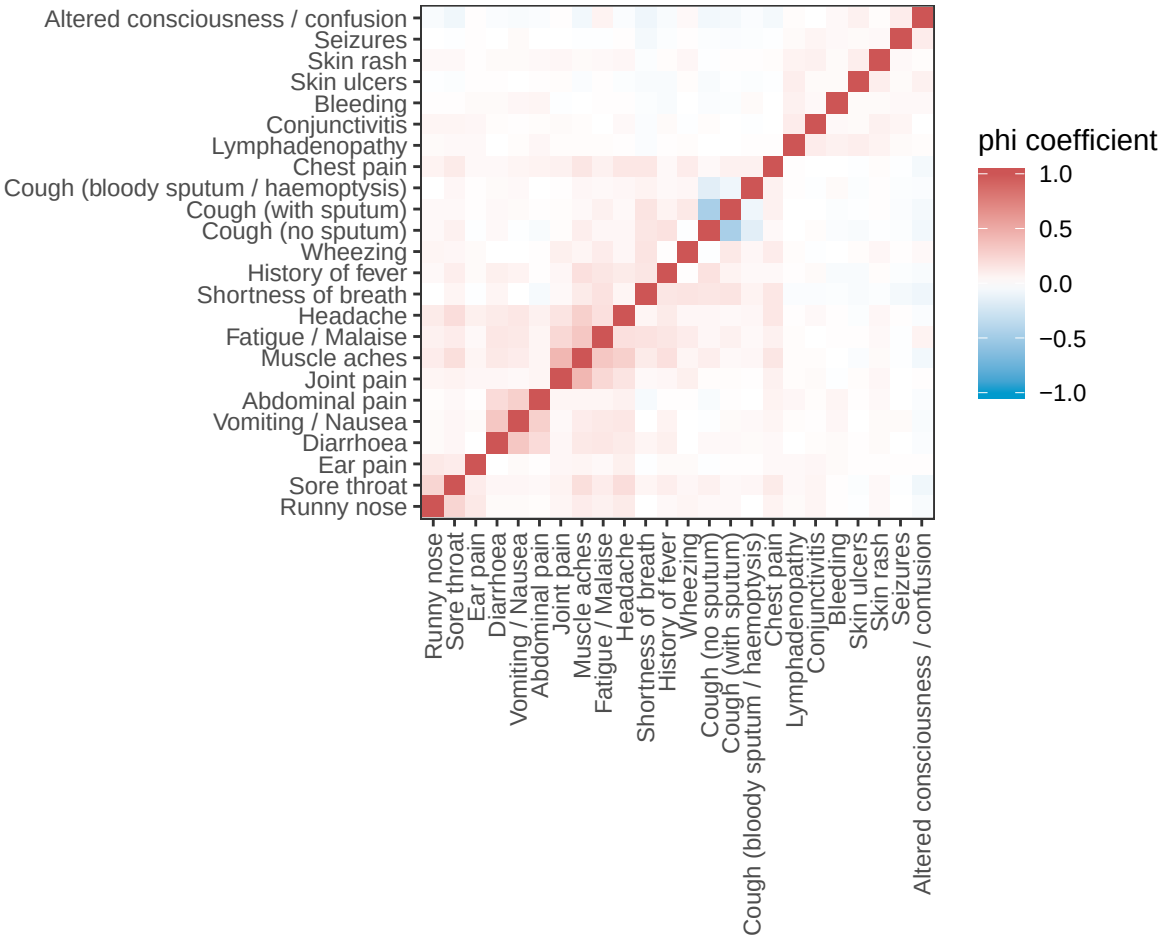


Figure 2: Top: Frequency of symptoms seen at admission amongst COVID-19 patients. Bars are annotated with a fraction representing the number of patients presenting with this symptom over the number of patients for whom presence or absence of this symptom was recorded. Middle: The distribution of combinations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

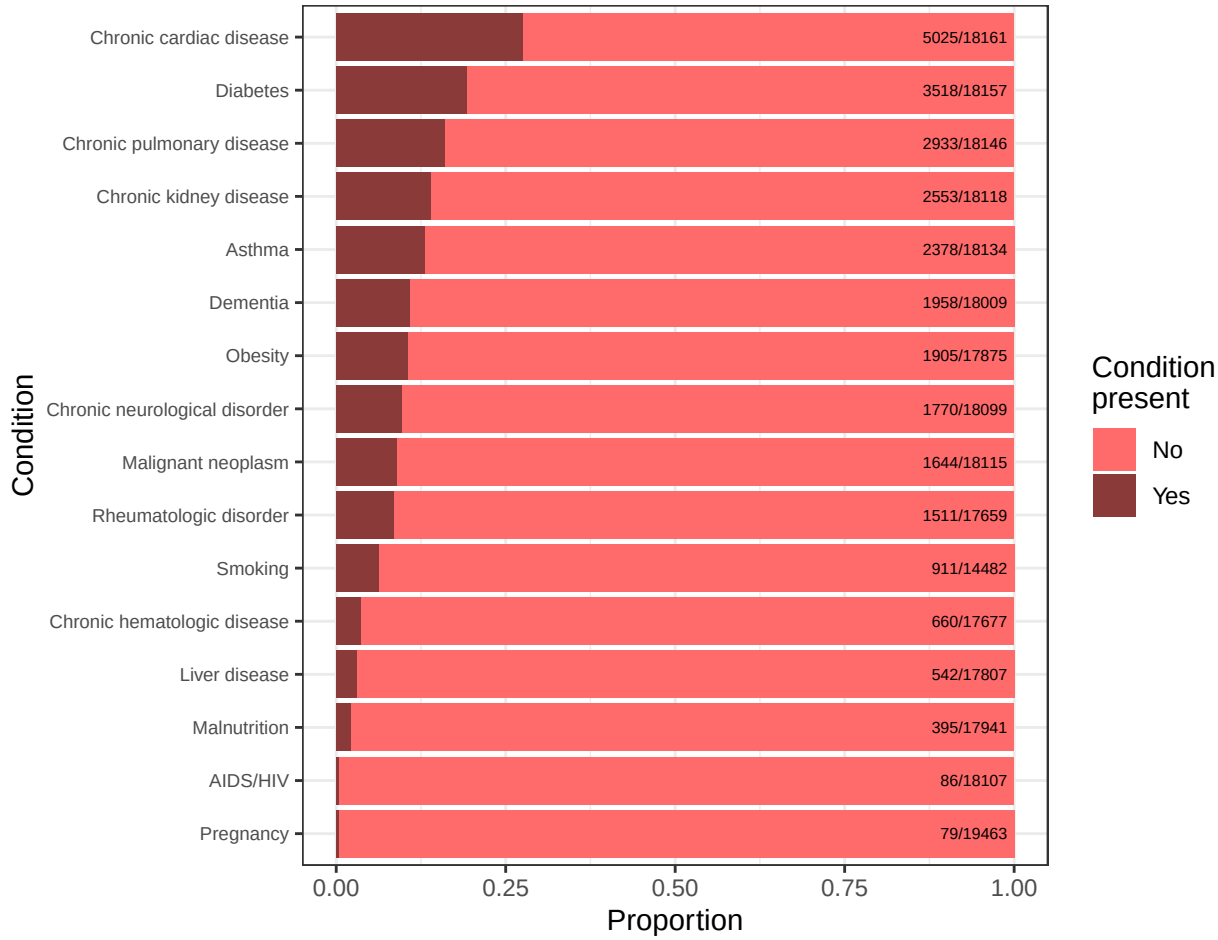


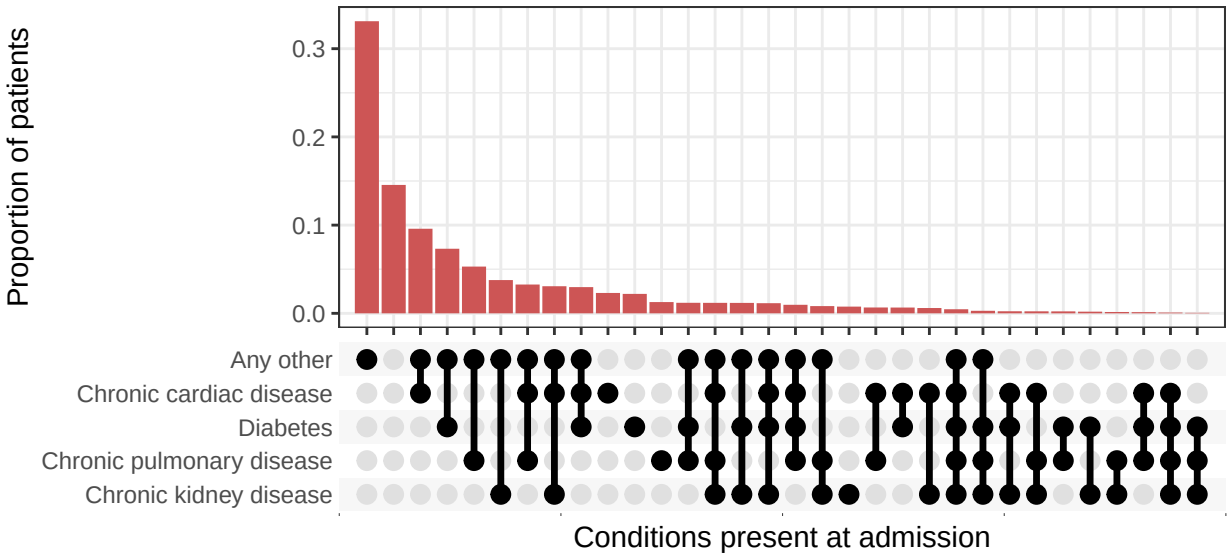




* We are working to gain a greater understanding of patients reported as having no presenting symptoms.

Figure 3: Top: Frequency of comorbidities 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.




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

Variables by age

Figure 4: 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).

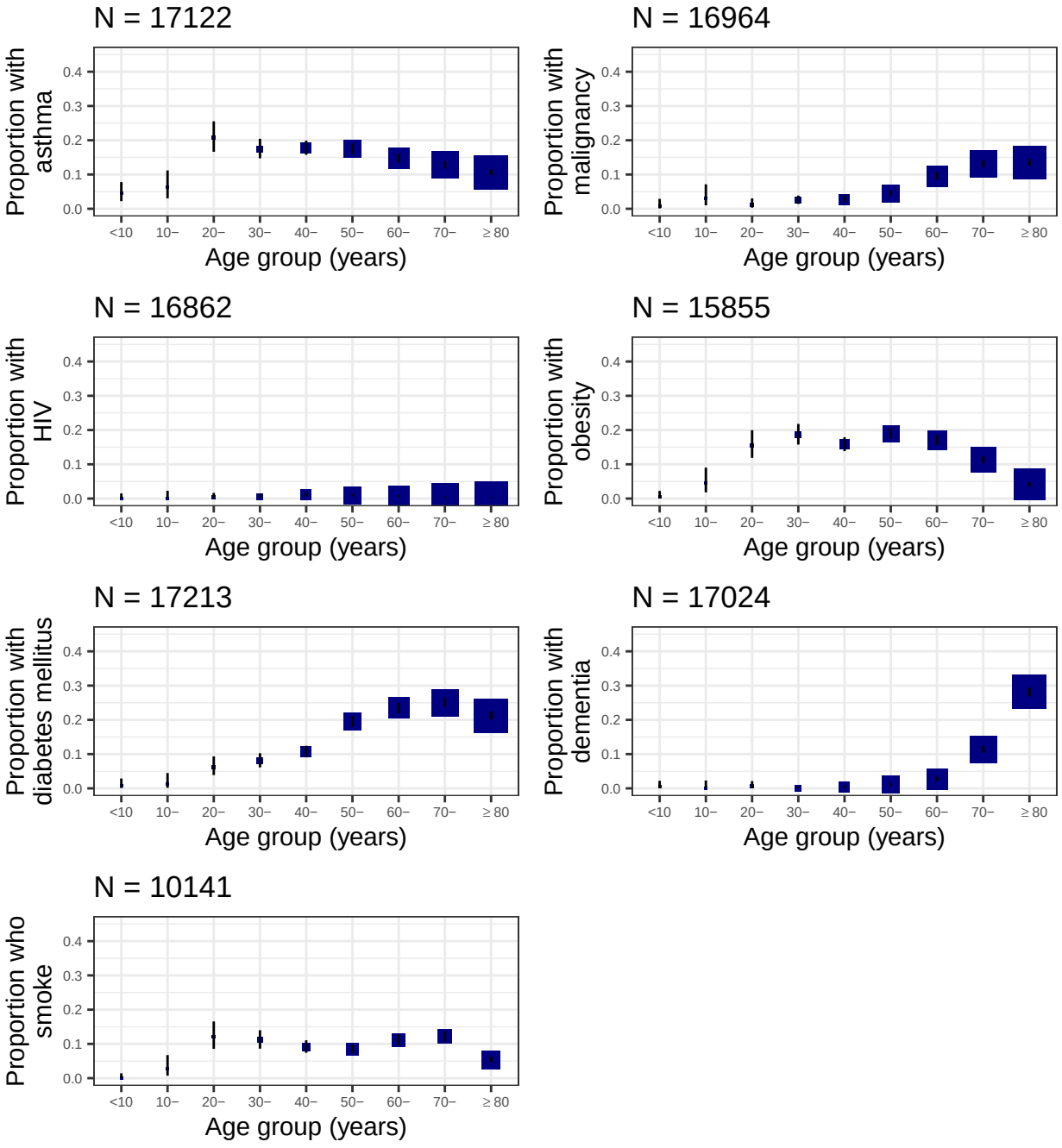


Figure 5: Symptoms recorded at hospital presentation stratified by age group. Boxes show the proportion of individuals with each comorbidity, with error bars showing 95% confidence intervals. The size of each box is proportional to the number of individuals represented. N is the number of individuals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

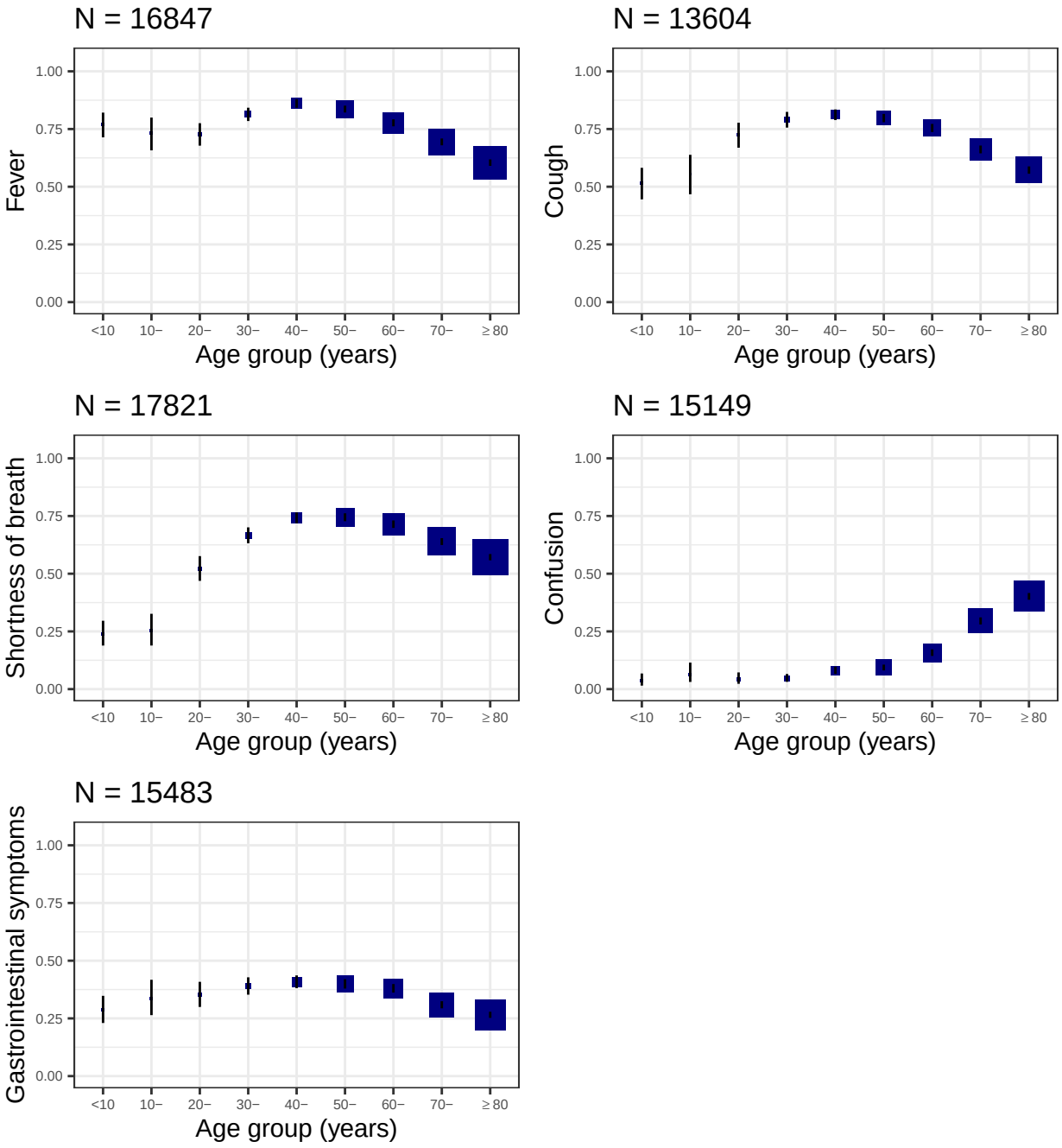


Figure 6: Box and whisker plots for observations at hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness).

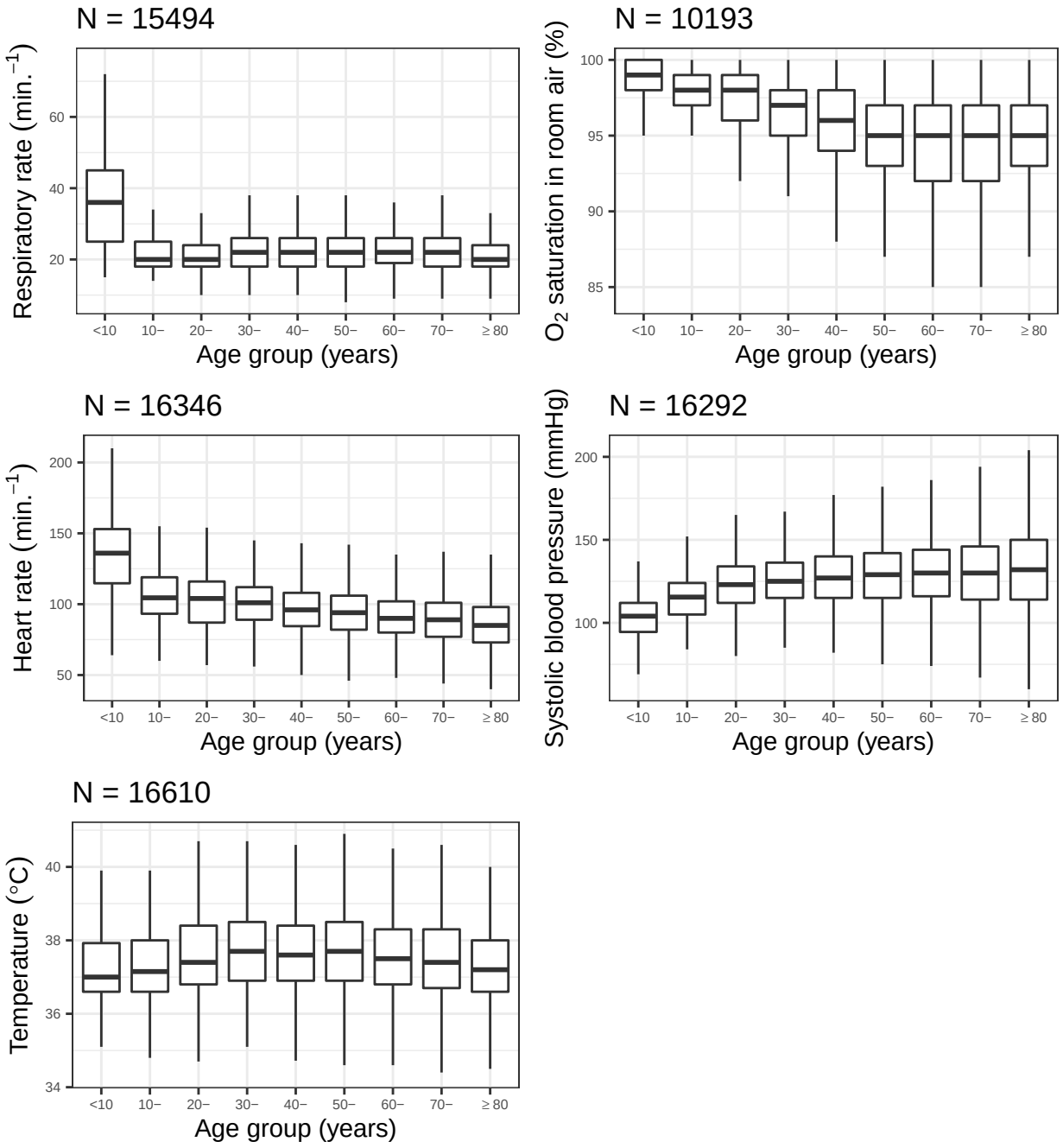
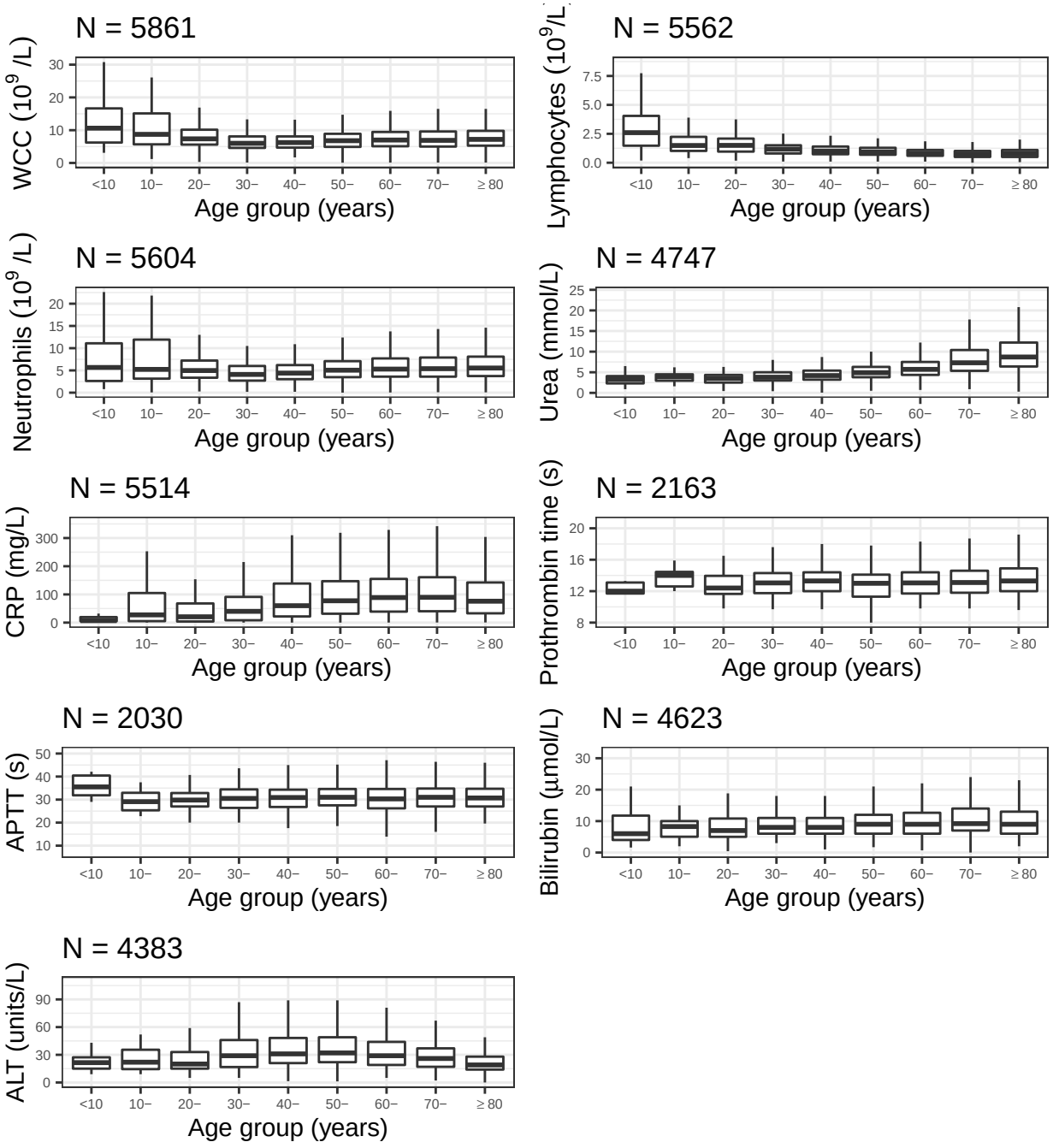


Figure 7: Box and whisker plots for laboratory results within 24 hours of hospital presentation stratified by age group. Outliers are omitted. N is the number of individuals included in the plot (this varies between plots due to data completeness). ALT, Alanine transaminase; APTT, Activated partial thromboplastin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

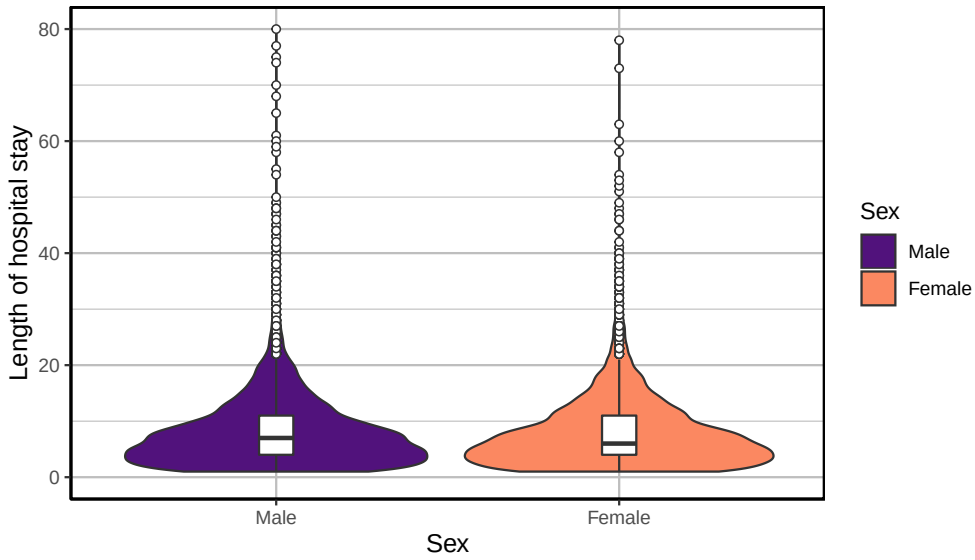
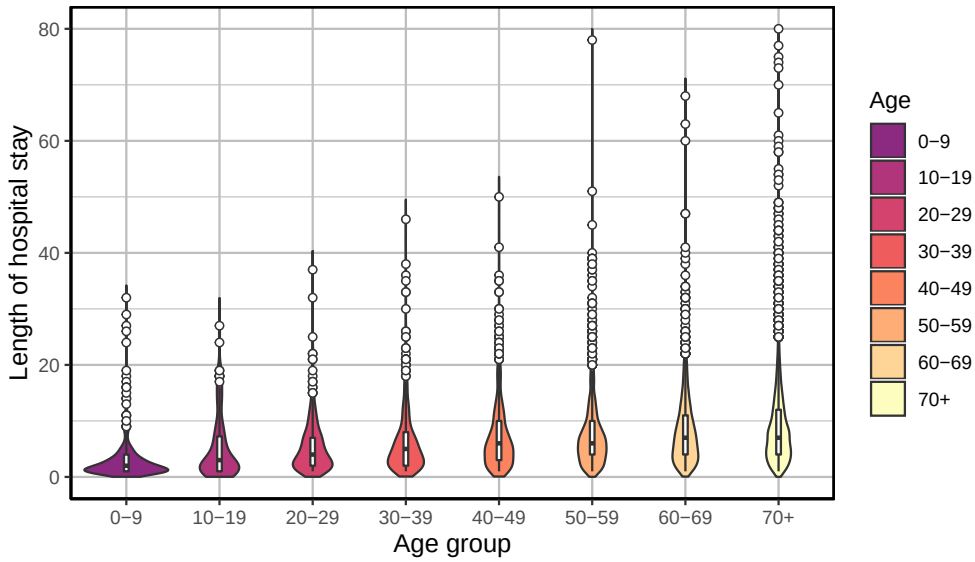


Figure 9: Distribution of length of hospital stay, according to patient age group. This only includes cases with reported outcomes. The coloured areas indicate the kernel probability density of the observed data and the box plots show the median and interquartile range of the variable of interest.*



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

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 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.

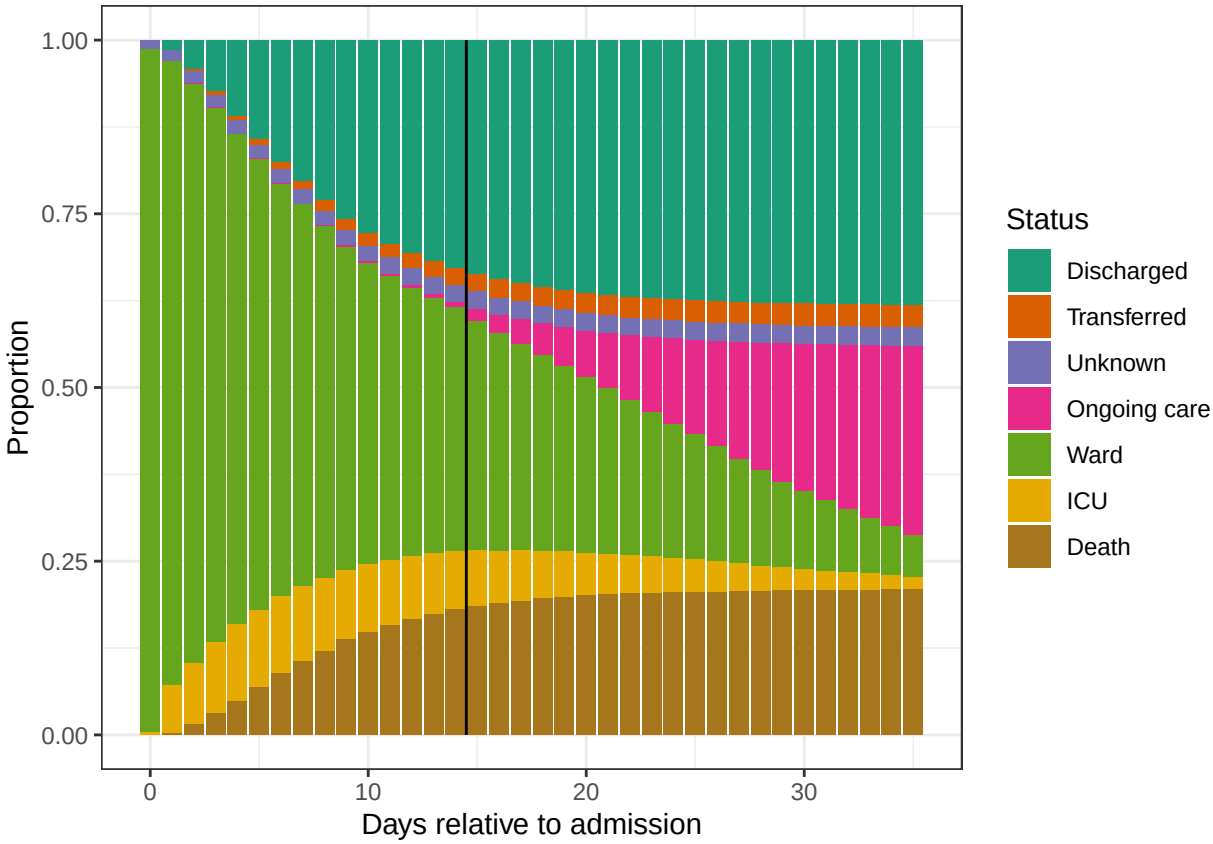
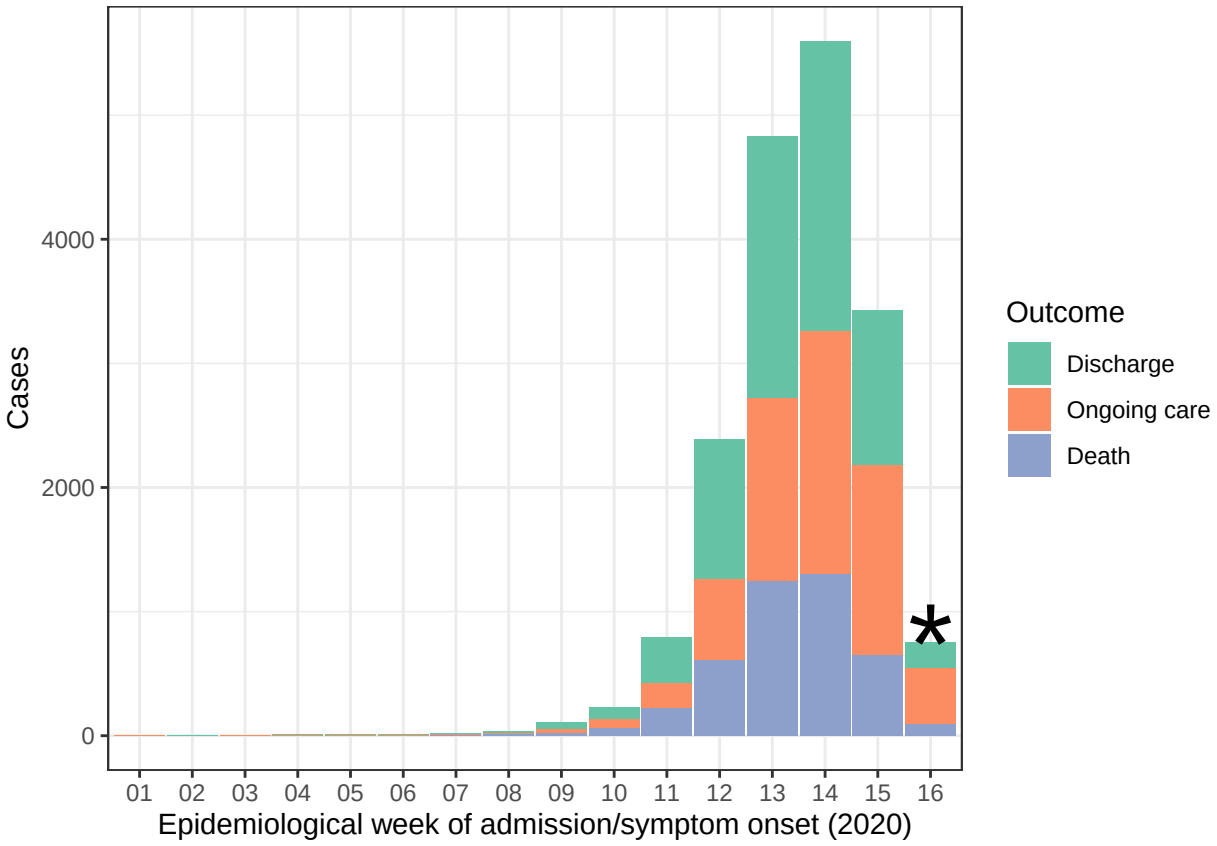
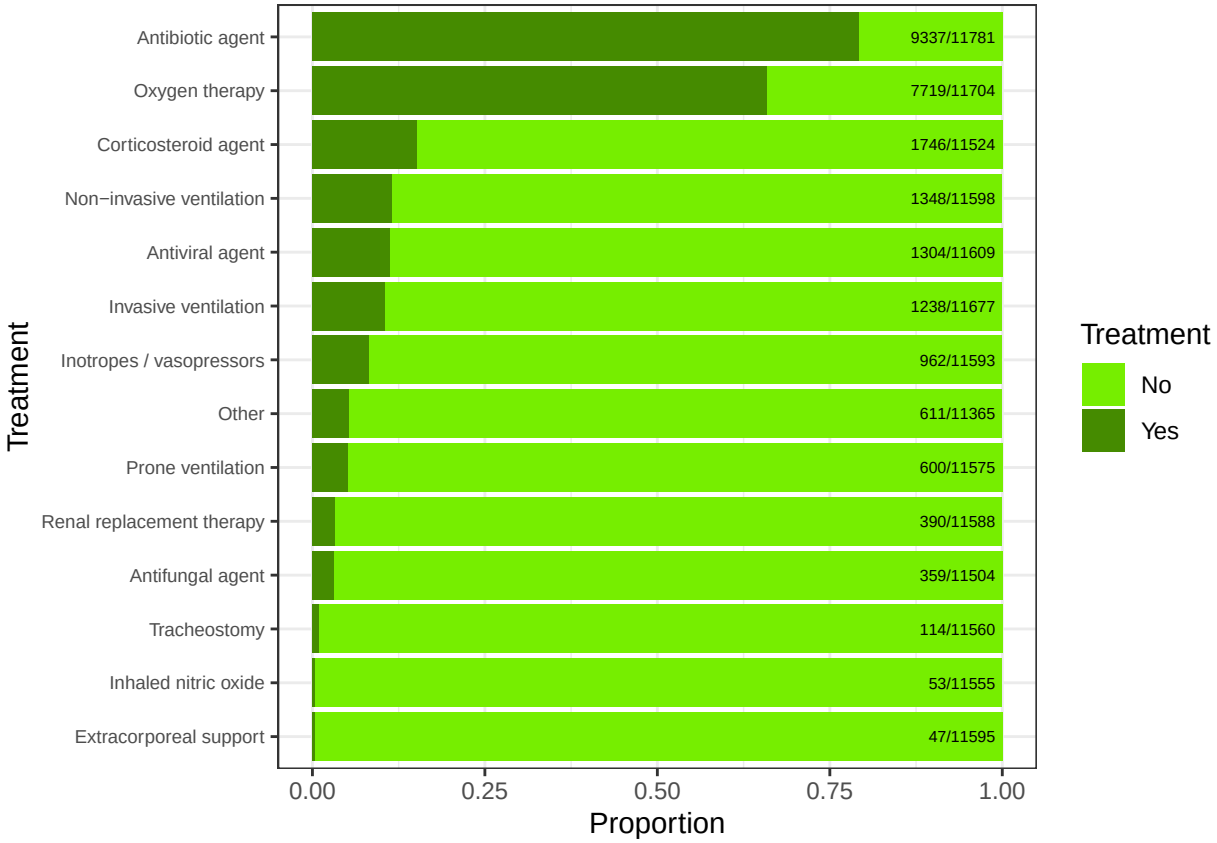


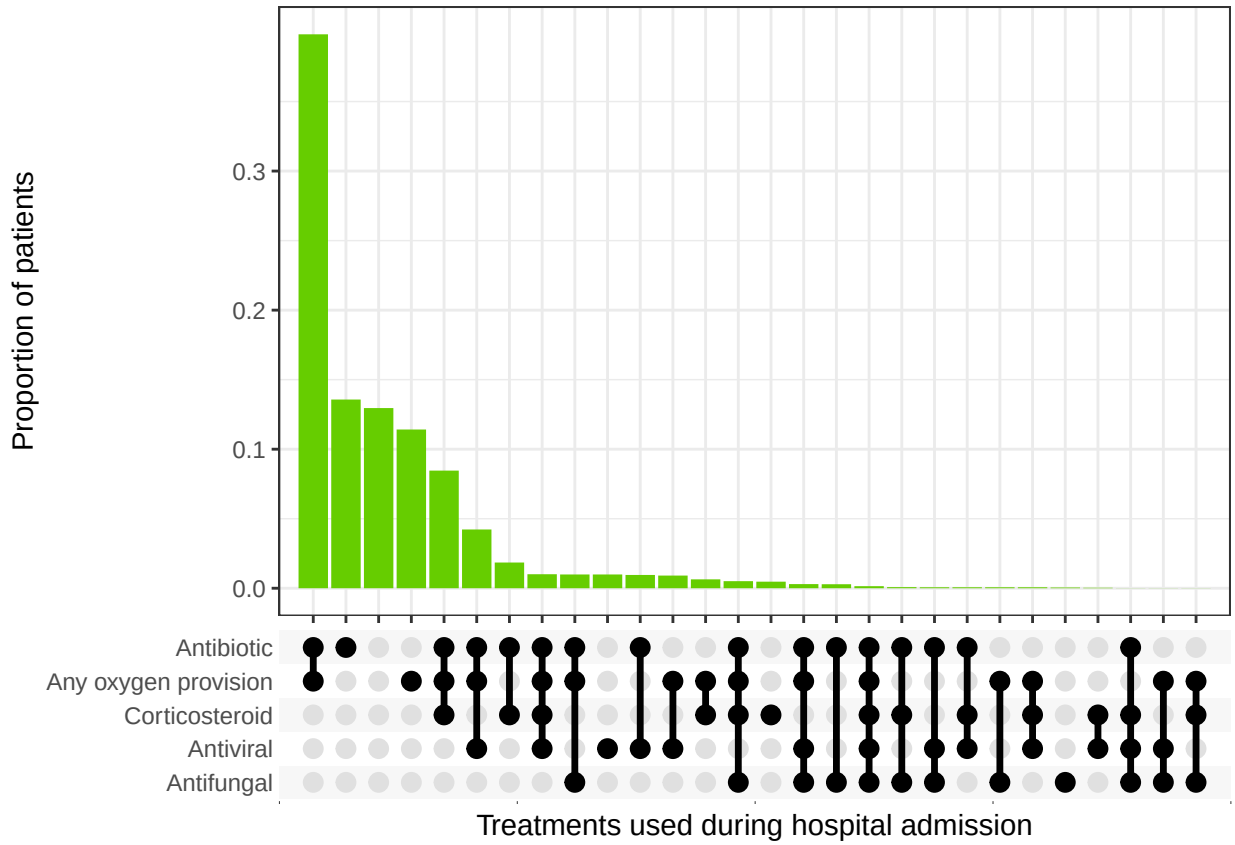
Figure 11: Patient numbers and outcomes by epidemiological week (of 2020) of admission (or, for patients infected in hospital, of symptom onset). The rightmost bar, marked with an asterisk, represents an incomplete week (due to the 14-day cutoff).



Treatment

Figure 12: 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.

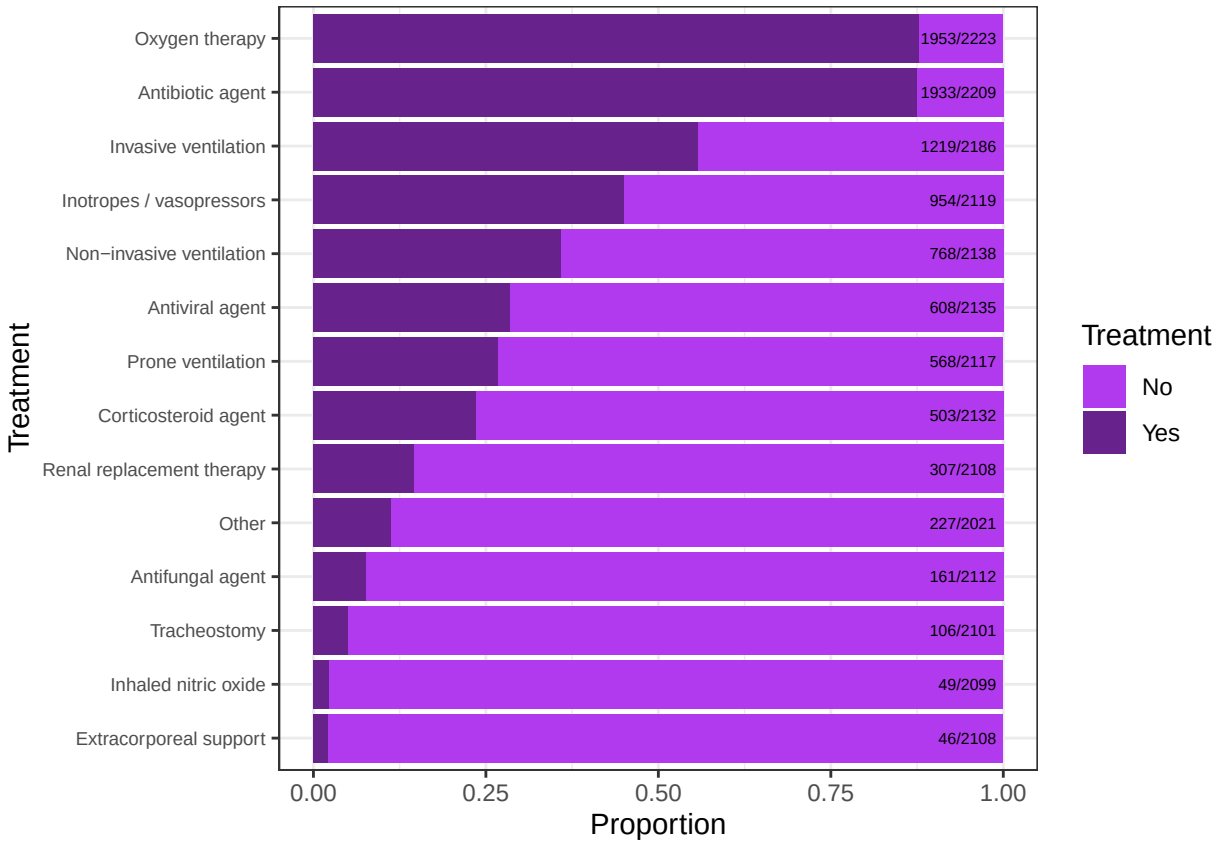


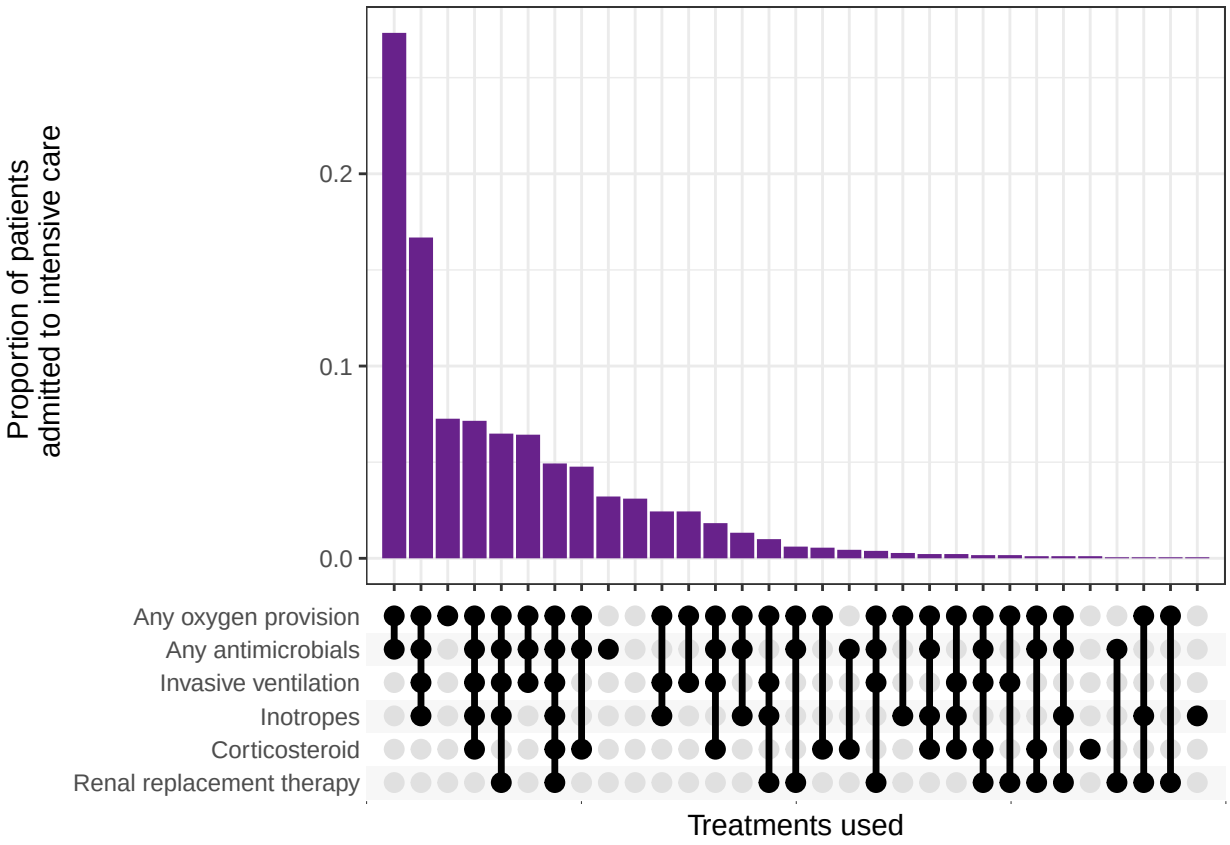

Proportion of patients
0.3
0.2
0.1
0.0
Antibiotic
Any oxygen provision
Corticosteroid
Antiviral
Antifungal
Treatments used during hospital admission

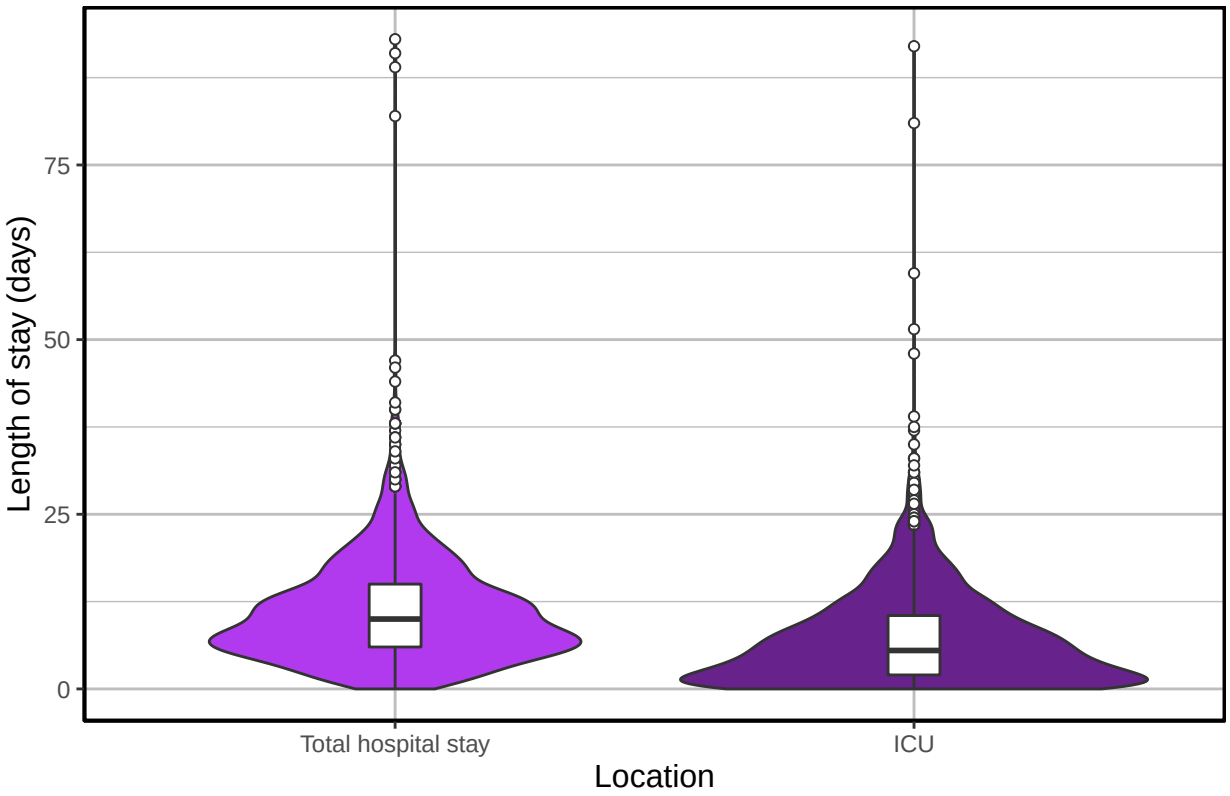
Intensive Care and High Dependency Unit Treatments

Figure 13: 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.

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




Proportion of patients admitted to intensive care
0.2
0.1
0.0
Any oxygen provision
Any antimicrobials
Invasive ventilation
Inotropes
Corticosteroid
Renal replacement therapy
Treatments used


Length of stay (days)
75
50
25
0
Total hospital stay
ICU
Location

Statistical Analysis

Figure 14: 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.

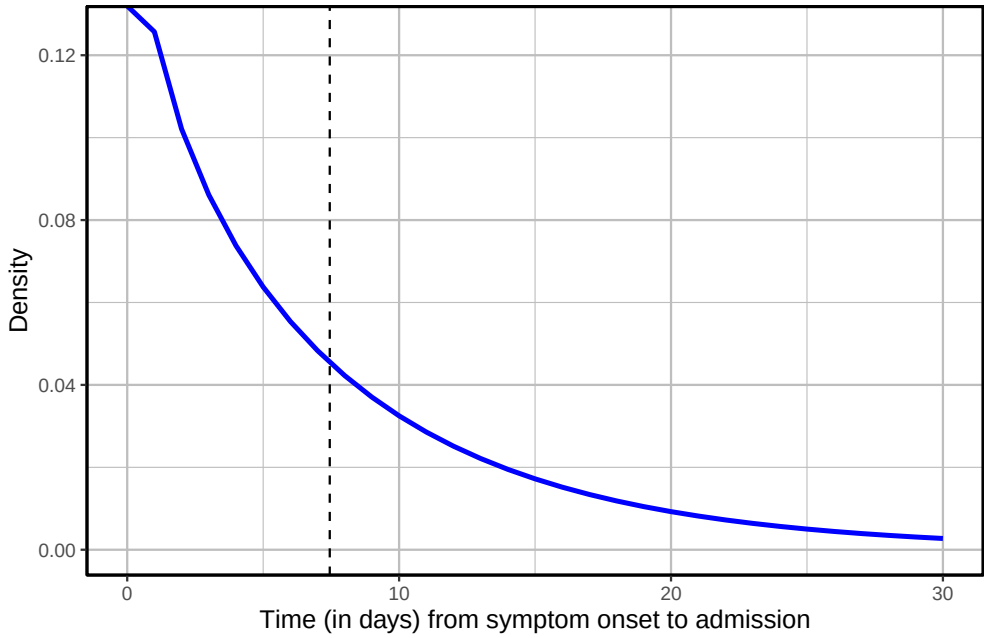


Figure 15: Distribution of time from admission to an outcome - either death or recovery (discharge). The blue curve is the Gamma distribution fit to the data. The black dashed line indicates the position of the expected mean. The expected mean differs from the observed mean in that it accounts for unobserved outcomes.

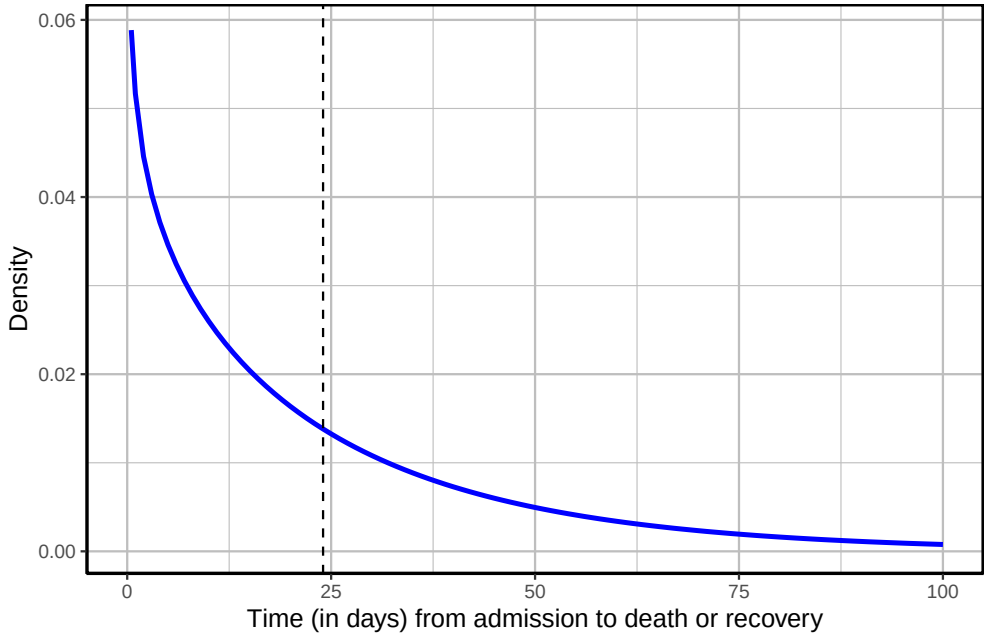
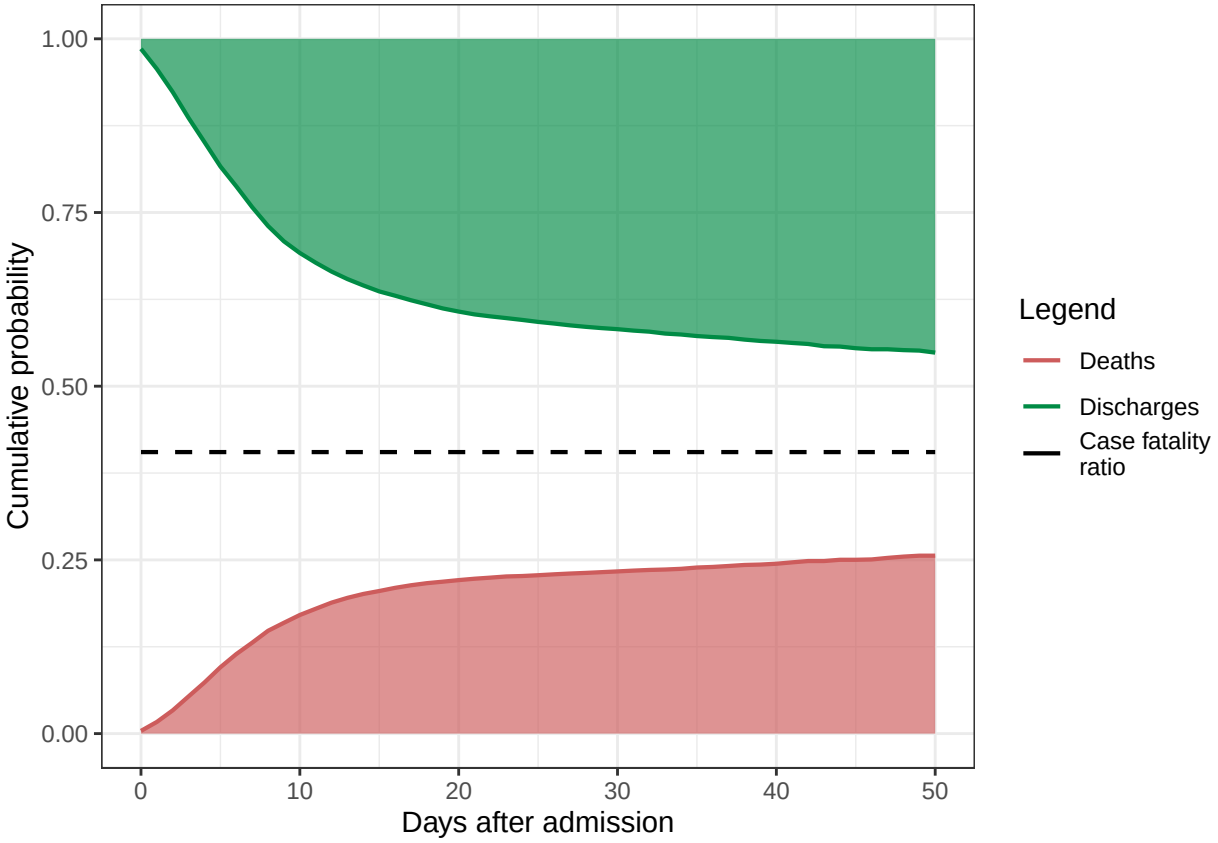


Figure 16: Probabilities of death (red curve) and recovery (green curve) over time. The black line indicates the case fatality ratio (black). The method used here considers all cases, irrespective of whether an outcome has been observed. For a completed epidemic, the curves for death and recovery meet. Estimates were derived using a nonparametric Kaplan-Meier–based method proposed by Ghani *et al.* (2005).



Country Comparisons

Figure 17: Number of sites per country.

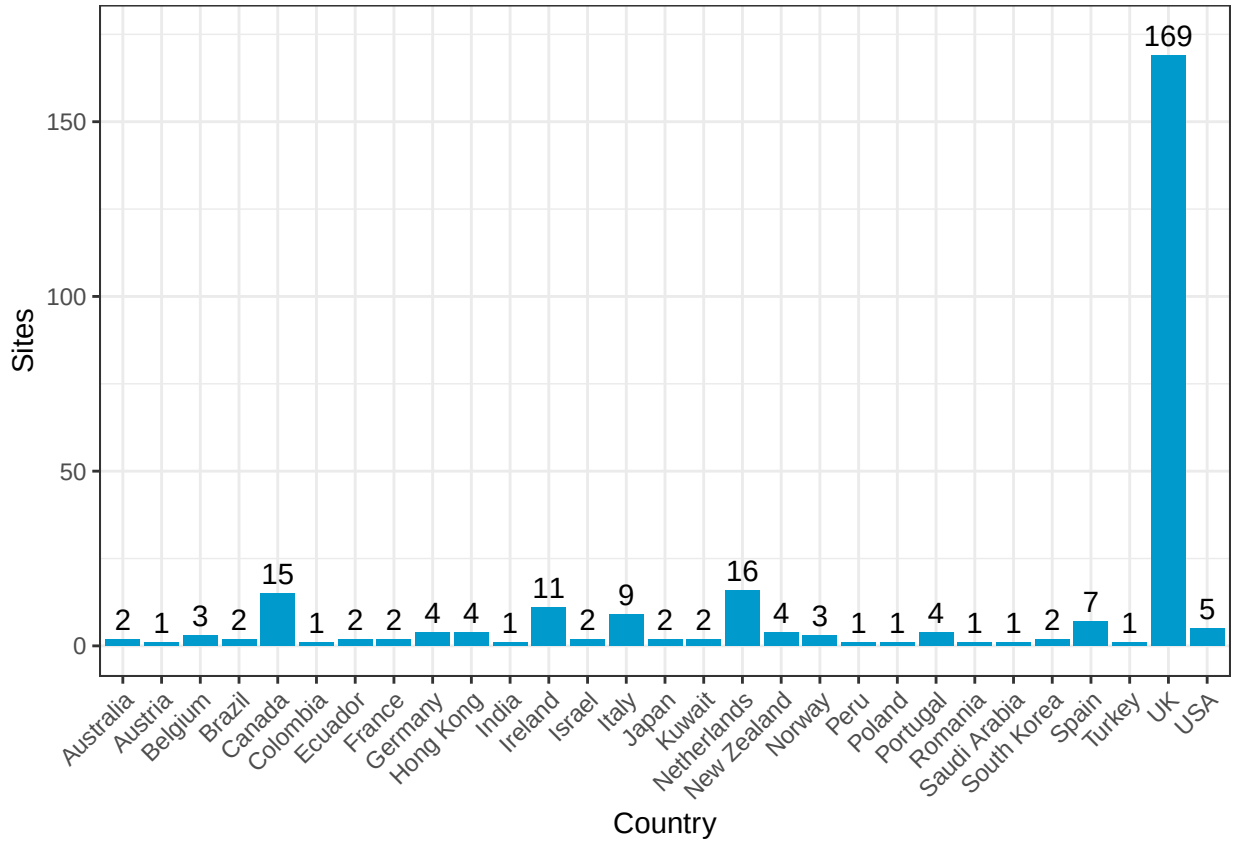
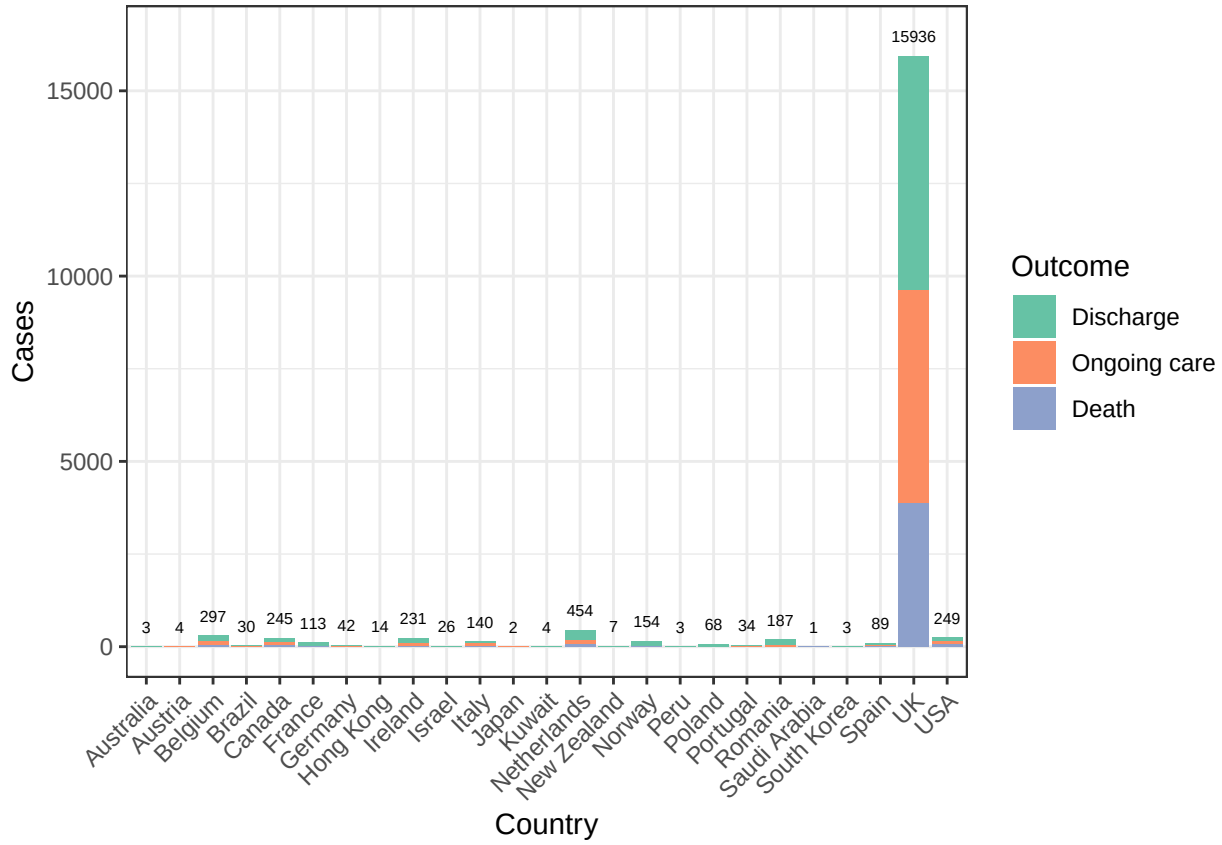


Figure 18: Distribution of patients by country and outcome.



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.

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 parantheses. Proportions have been rounded to two decimal places.

Table 1: Patient Characteristics

Description	Value
Size of cohort	19463
By sex	
Male	11688 (0.6)
Female	7684 (0.39)
Unknown	91 (0.01)
By outcome status	
Dead	4278 (0.22)
Recovered (discharged alive)	7595 (0.39)
Still in hospital	6464 (0.33)
Tranferred to another facility	694 (0.04)
Unknown	432 (0.02)
By COVID-19 status	
Positive (laboratory-confirmed)	15844 (0.81)
Suspected	3619 (0.19)
By age group	
0-9	275 (0.01)
10-19	173 (0.01)
20-29	364 (0.02)
30-39	789 (0.04)
40-49	1485 (0.08)
50-59	2742 (0.14)
60-69	3293 (0.17)
70+	10083 (0.52)
Unknown	259 (0.01)

Table 2: Outcome by age and sex

Variable	**Still in hospital**	**Death**	**Discharge**	**Transferred**	**Unknown**
Age					
0-9	37 (0.01)	0 (0)	189 (0.02)	17 (0.02)	32 (0.07)
10-19	23 (0)	2 (0)	118 (0.02)	7 (0.01)	23 (0.05)
20-29	69 (0.01)	10 (0)	271 (0.04)	7 (0.01)	7 (0.02)
30-39	218 (0.03)	27 (0.01)	507 (0.07)	19 (0.03)	18 (0.04)
40-49	454 (0.07)	66 (0.02)	901 (0.12)	35 (0.05)	29 (0.07)
50-59	985 (0.15)	239 (0.06)	1357 (0.18)	85 (0.12)	76 (0.18)
60-69	1187 (0.18)	572 (0.13)	1336 (0.18)	113 (0.16)	85 (0.2)
70+	3398 (0.53)	3316 (0.78)	2807 (0.37)	407 (0.59)	155 (0.36)
Sex					
Male	3954 (0.61)	2762 (0.65)	4310 (0.57)	401 (0.58)	261 (0.6)
Female	2467 (0.38)	1498 (0.35)	3256 (0.43)	293 (0.42)	170 (0.39)
Unknown	10 (0)	8 (0)	17 (0)	0 (0)	0 (0)

Table 3: Prevalence of Symptoms

Symptoms	**Present**	**Absent**	**Unknown**
History of fever	12397 (0.64)	4676 (0.24)	2390 (0.12)
Shortness of breath	11665 (0.6)	6386 (0.33)	1412 (0.07)
Cough	9499 (0.49)	4282 (0.22)	5682 (0.29)
Fatigue / Malaise	6672 (0.34)	7386 (0.38)	5405 (0.28)
Altered consciousness / confusion	3608 (0.19)	11746 (0.6)	4109 (0.21)
Diarrhoea	3053 (0.16)	11948 (0.61)	4462 (0.23)
Muscle aches	3001 (0.15)	10171 (0.52)	6291 (0.32)
Vomiting / Nausea	2877 (0.15)	12117 (0.62)	4469 (0.23)
Chest pain	2177 (0.11)	12298 (0.63)	4988 (0.26)
Headache	1869 (0.1)	11250 (0.58)	6344 (0.33)
Sore throat	1484 (0.08)	11350 (0.58)	6629 (0.34)
Abdominal pain	1444 (0.07)	12995 (0.67)	5024 (0.26)
Wheezing	1437 (0.07)	12137 (0.62)	5889 (0.3)
Joint pain	1008 (0.05)	11553 (0.59)	6902 (0.35)
Runny nose	672 (0.03)	11883 (0.61)	6908 (0.35)
Skin ulcers	282 (0.01)	13455 (0.69)	5726 (0.29)
Skin rash	224 (0.01)	13514 (0.69)	5725 (0.29)
Seizures	217 (0.01)	14374 (0.74)	4872 (0.25)
Bleeding	152 (0.01)	14274 (0.73)	5037 (0.26)
Lymphadenopathy	102 (0.01)	13264 (0.68)	6097 (0.31)
Ear pain	90 (0)	12298 (0.63)	7075 (0.36)
Conjunctivitis	74 (0)	13336 (0.69)	6053 (0.31)

Table 4: Prevalence of Comorbidities

Comorbidities	Present	Absent	Unknown
Other	7525 (0.39)	9203 (0.47)	2735 (0.14)
Chronic cardiac disease	5025 (0.26)	12449 (0.64)	1989 (0.1)
Diabetes	3518 (0.18)	13911 (0.71)	2034 (0.1)
Chronic pulmonary disease	2933 (0.15)	14480 (0.74)	2050 (0.11)
Chronic kidney disease	2553 (0.13)	14761 (0.76)	2149 (0.11)
Asthma	2378 (0.12)	14960 (0.77)	2125 (0.11)
Dementia	1958 (0.1)	15190 (0.78)	2315 (0.12)
Obesity	1905 (0.1)	14059 (0.72)	3499 (0.18)
Chronic neurological disorder	1770 (0.09)	15414 (0.79)	2279 (0.12)
Malignant neoplasm	1644 (0.08)	15535 (0.8)	2284 (0.12)
Rheumatologic disorder	1511 (0.08)	15189 (0.78)	2763 (0.14)
Smoking	911 (0.05)	9401 (0.48)	9151 (0.47)
Chronic hematologic disease	660 (0.03)	16083 (0.83)	2720 (0.14)
Liver disease	542 (0.03)	16326 (0.84)	2595 (0.13)
Malnutrition	395 (0.02)	16025 (0.82)	3043 (0.16)
AIDS/HIV	86 (0)	16982 (0.87)	2395 (0.12)
Pregnancy	79 (0)	18870 (0.97)	514 (0.03)

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	10747 (0.55)	6559 (0.34)	2157 (0.11)
Antibiotic agent	9337 (0.48)	2146 (0.11)	7980 (0.41)
Non-invasive ventilation	2670 (0.14)	14484 (0.74)	2309 (0.12)
Invasive ventilation	2249 (0.12)	14964 (0.77)	2250 (0.12)
Corticosteroid agent	1746 (0.09)	9236 (0.47)	8481 (0.44)
Antiviral agent	1304 (0.07)	9765 (0.5)	8394 (0.43)
Inotropes / vasopressors	962 (0.05)	9944 (0.51)	8557 (0.44)
Other	611 (0.03)	9779 (0.5)	9073 (0.47)
Prone ventilation	600 (0.03)	10215 (0.52)	8648 (0.44)
Renal replacement therapy	390 (0.02)	10529 (0.54)	8544 (0.44)
Antifungal agent	359 (0.02)	10602 (0.54)	8502 (0.44)
Extracorporeal membrane oxygenation (ECMO)	209 (0.01)	16945 (0.87)	2309 (0.12)
Tracheostomy	114 (0.01)	10724 (0.55)	8625 (0.44)
Inhaled nitric oxide	53 (0)	10723 (0.55)	8687 (0.45)

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	8.7	8.1	7	8	24 (22.8, 26.1)
Symptom onset to admission	11.7	7.4	5	7	7.4 (7.1, 8.1)
Admission to ICU entry	3.3	7	1	2.5	3.3 (3.1, 3.5)
Duration of ICU	7.4	7.5	5.5	8.5	NA
Admission to IMV	3.5	7.2	2	3.5	3.5 (3.3, 3.8)
Duration of IMV	9.6	6.5	9	8	NA
Admission to NIV	4.6	12	2	4.5	4.6 (4.3, 5)
Duration of NIV	2	3.5	0.5	4.5	NA

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